Vol. 45. No. 8
September 2013

Journal of REHABILITATION MEDICINE

The International Non-profit Journal

International official journal of the
– *International Society of Physical and Rehabilitation Medicine (ISPRM)*

Official journal of the
– *UEMS European Board and Section of Physical and Rehabilitation Medicine (EBPRM)*
– *European Academy of Rehabilitation Medicine (EARM)*

Published in association with the
– *European Society of Physical and Rehabilitation Medicine (ESPRM)*
– *Canadian Association of Physical Medicine and Rehabilitation (CAPM&R)*
– *Asia Oceania Society of Physical and Rehabilitation Medicine (AOSPRM)*
– *Baltic and North Sea Forum for Physical and Rehabilitation Medicine (BNFPRM)*

Special issue

TRAUMATIC BRAIN INJURY IN SCANDINAVIAN COUNTRIES: RECENT RESEARCH AND NEW FRONTIERS

Guest Editors

Nada Andelic, Juan Carlos Arango-Lasprilla, and Cecilie Roe

Published by the non-profit
Foundation for Rehabilitation Information
www.medicaljournals.se/jrm

ISSN 1650-1977

J Rehabil Med 2013; 45: 705–842

TRAUMATIC BRAIN INJURY IN SCANDINAVIAN COUNTRIES: RECENT RESEARCH AND NEW FRONTIERS

Guest Editors

Nada Andelic, MD, PhD, Juan Carlos Arango-Lasprilla, PhD and Cecilie Røe, MD, PhD

 doi: 10.2340/16501977-1224
 ISSN 1650-1977

CONTENTS

J Rehabil Med 2013; 45: 708–709

COMMENT FROM THE EDITOR-IN-CHIEF

It is a great pleasure for me to thank the guest editors of this special issue, Nada Andelic, Juan Carlos Arango Lasprilla and Cecilie Roe for their timely proposal as well as for contacting suitable research groups to report their work and for making this special issue on traumatic brain injury possible. They have also been instrumental as referees along with one senior member of our Editorial Board and many TBI experts world wide. As usual, I have personally taken all decisions on acceptance of the contributions to this issue.

Malmö, August 6 , 2013
Bengt H. Sjölund
Professor, Editor-in-Chief

FOREWORD

THE COMPLEXITY OF TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI), defined as brain injury caused by external trauma, affects as many as 12% of adults worldwide (1). Recent years have seen an increasing focus on the burden of TBI on global healthcare resources. In the Scandinavian countries, effort has been directed into the development of guidelines for initial management of TBI and trauma triage (2–5). However, TBI frequently causes long-term physical, cognitive, behavioural and emotional impairments, along with difficulties with activities of daily living, community integration, employment, social life and family functioning, and partner relationships. Although TBI prevention, emergency treatment and acute care are important, effective delivery of longer-term services, including rehabilitation, vocational, educational and community support, is equally necessary and far more complex. Some level of rehabilitation is required for the majority of patients with TBI, and studies from different countries are required to provide "an accurate reflection of population needs, allowing better understanding of regional, national and international differences and needs in the area of brain injury rehabilitation" (6).

The Scandinavian countries are welfare states with fairly homogenous socio-demography and healthcare systems, with a long tradition of organization and resource allocation for comprehensive rehabilitation after TBI. The systematic processes for data collection in these areas mean that Scandinavian TBI populations can be studied in representative cohorts, making studies of international interest (7). Furthermore, in order to understand the extent of disability following TBI and to identify high-risk groups in Scandinavian countries, it is necessary to identify an accurate documentation of TBI management, outcomes and needs for healthcare services. Such knowledge may be helpful when developing injury prevention strategies as well improving acute care, rehabilitation, and long-term service delivery.

This Special Issue of JRM presents current TBI rehabilitation research trends in Sweden, Norway, Denmark and Finland. Rehabilitation research should be built on and integrate trends in acute TBI care. The review of the development of neurocritical care in university hospitals during a period of 50 years (Nordström et al) and management of mild traumatic brain injury (MTBI) in emergency departments (Carlsson & af Geijerstam) illustrates today's basis for TBI rehabilitation. Furthermore, an important advance in TBI research is the understanding of the pathophysiology behind brain injury development and recovery. As such, aspects of our new understanding of brain pathology after MTBI, using magnetic resonance (MR) imaging, are addressed by Lannsjö et al., and the developmental aspect of recovery in children with MTBI by Dahl & Emanuelson. The focus of subsequent two articles is on the recovery trajectories of severe TBI, assessing the impact of age and incidence, outcomes and implications for optimizing care pathways of disorders of consciousness after severe TBI (Roe et al. and Godbolt et al.).

In line with the long-term disability often resulting from TBI, the majority of articles in this issue address the symptoms and outcomes after mild-to-severe TBI in the first several years post-injury, as well as in the long-term, identifying factors that predict functional status, disability, health, health-related

quality of life and life satisfaction (Styrke et al,. Åhman et al., Larsson et al., Esbjörnsson et al., Sommer et al., Soberg et al., Stenberg et al., Forslund et al., Sigurdardottir et al. and Åhlander et al.). Taken together, these articles suggest that individuals with TBI experience a large number of problems and a great deal of variance in outcomes that may, in part, depend upon interactions between socio-demographic and injury-related characteristics, cognitive abilities and psychological adjustment.

The perspective of relatives is also of major importance in rehabilitation after severe and/or impairing injuries. Family support and caregiving influence recovery of individuals with TBI and, in addition, relatives and caregivers of individuals with TBI may experience changes in their own health. Two articles by Norup et al. discuss rehabilitation efforts directed at the TBI relatives and evaluate an acute neuropsychological intervention for family members of patients with severe brain injury.

Last, but not least, the current issue contains an article assessing the psychometric properties of a new measure for quality of life after TBI, the QOLIBRI, in the Finnish TBI population (Siponkoski et al.). The QOLIBRI adds important information to the standard clinical procedure, as it brings out the patient's subjective experience and values in a structured, comprehensive and practical manner.

It is our goal that the articles in this issue will contribute to an increasing recognition of recovery, outcomes, and needs of individuals with TBI. Due to its complexity, the rehabilitation of patients with TBI should involve a continuum of care, from the acute, inpatient stage to reintegration in the community. Only through an integrated and systematic effort will we be able to achieve optimal results in reducing symptoms, improving functional capacity and enhancing quality of life for individuals affected by TBI.

REFERENCES

1. Frost RB, Farrer TJ, Primosch M, Hedges DW. Prevalence of traumatic brain injury in the general adult population: a meta-analysis. Neuroepidemiology 2013; 40: 154–159.
2. Kristiansen T, Lossius HM, Soreide K, Steen PA, Gaarder C, Naess PA. Patients Referred to a Norwegian Trauma Centre: effect of transfer distance on injury patterns, use of resources and outcomes. J Trauma Manag Outcomes 2011; 5: 9.
3. Sollid S, Sundstrom T, Kock-Jensen C, Juul N, Eskesen V, Bellander BM, et al. [Scandinavian guidelines for prehospital management of severe traumatic brain injury]. Tidsskr Nor Laegeforen 2008; 128: 1524–1527 (in Norwegian).
4. Ingebrigtsen T, Romner B, Kock-Jensen C. Scandinavian guidelines for initial management of minimal, mild, and moderate head injuries.The Scandinavian Neurotrauma Committee. J Trauma 2000; 48: 760–766.
5. Af Geijerstam JL, Oredsson S, Britton M. Medical outcome after immediate computed tomography or admission for observation in patients with mild head injury: randomised controlled trial. BMJ 2006; 333: 465.
6. Bilbao A, Kennedy C, Chatterji S, Ustun B, Barquero JL, Barth JT. The ICF: applications of the WHO model of functioning, disability and health to brain injury rehabilitation. NeuroRehabilitation 2003; 18: 239–250.
7. Borg J, Roe C, Nordenbo A, Andelic N, de BC, Af Geijerstam JL. Trends and challenges in the early rehabilitation of patients with traumatic brain injury: a Scandinavian perspective. Am J Phys Med Rehabil 2011; 90: 65–73.

Nada Andelic, MD, PhD[1,2], Juan Carlos Arango-Lasprilla, PhD[3] and Cecilie Røe, MD, PhD[1,4]

From the [1]Department of Physical Medicine and Rehabilitation, Oslo University Hospital, [2]Institute of Health and Society, CHARM (Research Centre for Habilitation and Rehabilitation Models and Services), Faculty of Medicine, University of Oslo, Oslo, Norway, [3]IKERBASQUE, Basque Foundation for Science, University of Deusto, Bilbao, Spain and [4]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway

J Rehabil Med 2013; 45: 710–717

REVIEW ARTICLE

TECHNIQUES AND STRATEGIES IN NEUROCRITICAL CARE ORIGINATING FROM SOUTHERN SCANDINAVIA

Carl-Henrik Nordström, MD, PhD, Troels Halfeld Nielsen, MD and Anne Jacobsen, MD

From the Department of Neurosurgery, Odense University Hospital, Odense, Denmark

Objective: **To describe innovations in neurocritical care originating from university hospitals in southern Scandinavia over a period of 50 years.**

Discussion: **Several techniques and strategies that are now included in clinical routine were initially developed in southern Scandinavia: continuous recording of intracranial pressure, monitoring of cerebral blood flow, analyses of cerebral energy metabolism under physiological and pathological conditions, and intracerebral microdialysis with bedside biochemical analysis and display of data. This background and, in particular, knowledge of the physiological prerequisites for water transport across the blood–brain barrier and the regulation of brain volume constituted the basis for the "Lund Concept" for treatment of increased intracranial pressure. The development of neurocritical care has resulted in a dramatic decrease in mortality for patients with severe traumatic brain injury.**

Conclusion: **The focus in the future may be on improved biochemical supervision at the bedside to avoid secondary episodes of ischaemia and to identify and treat secondary non-ischaemic mitochondrial dysfunction. As mortality has decreased, demand for qualified post-traumatic rehabilitation has increased. Further improvements will necessitate close cooperation between critical care physicians, neurosurgeons and specialists in rehabilitation medicine.**

Key words: critical care; intracranial pressure; craniocerebral trauma; cerebrovascular circulation; microdialysis.

J Rehabil Med 2013; 45: 710–717

Correspondence address: Carl-Henrik Nordström, Department of Neurosurgery, Odense University Hospital, Odense, Denmark. E-mail: carl-henrik.nordstrom@med.lu.se

Accepted February 19, 2013

INTRODUCTION

Critical, or intensive, care medicine is defined as a branch of medicine concerned with the diagnosis and treatment of life-threatening conditions requiring invasive monitoring and sophisticated pharmacological or instrumental organ support. To accomplish this task it is necessary to have specially educated personnel as well as specially designed intensive care units. The first critical care unit in the world opened in Copenhagen in December 1953 (1).

The pivotal point for the development of intensive care occurred during the 1952 polio epidemic in Copenhagen. When 27 out of 31 poliomyelitis patients with respiratory involvement had died during the first weeks of the epidemic the anaesthetist Bjørn Ibsen (1915–2007) was asked for advice. He quickly realized that the patients died from respiratory insufficiency with carbon dioxide retention. On the 27 August 1952 he initiated protracted positive pressure ventilation with tracheal intubation via a tracheostomy in the first patient. For several weeks he had 40–70 patients requiring continuous or intermittent bag ventilation. To accomplish this, approximately 200 medical students were enlisted to ventilate the patients manually. It was reported that this management decreased mortality from close to 90% to approximately 25% (1–3). As a result of this remarkable achievement the first intensive care unit was opened by Dr Ibsen in the Observation Room at Kommunehospitalet (the Municipal Hospital) in Copenhagen in 1953. However, it was almost 4 decades before the first intensive care unit dedicated to neurocritical care was opened. This paper reviews the many techniques and strategies now used worldwide within neurocritical care that originate from southern Scandinavia.

INTRACRANIAL PRESSURE MONITORING

Neurocritical care is characterized by monitoring techniques necessary for identifying secondary cerebral adverse events and for the evaluation of specific therapies. Among these techniques intracranial pressure (ICP) monitoring is by far the most important. The technique for continuous monitoring of ICP was developed during the 1950s at the Department of Neurosurgery, Lund University Hospital by Nils Lundberg (1908–2002) (Fig. 1). His experiences were collected in a doctoral thesis (4) that was defended on 11 February 1961. Both faculty opponents considered the thesis a very valuable scientific contribution, but opposition *ex auditorio* claimed that the work was unethical and that it had led to mortality in some patients. Due to this criticism the evaluation board had extensive discussions for 3 days [*sic*] before the thesis was accepted with very high marks (5).

In 1959, Lundberg had presented data showing that controlled hyperventilation led to a reduction in increased ICP (6) and in his doctoral thesis he documented that intravenous (i.v.) infusion of hypertonic solutions (e.g. urea, mannitol) could also be used for this purpose (4). Lundberg also described the variations in ICP that occurred under physiological and

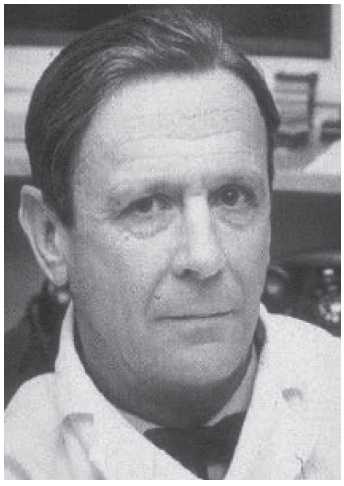


Fig. 1. Nils Lundberg (1908–2002), Professor of Neurosurgery at Lund University Hospital 1962–1974, introduced the technique for continuous monitoring of intracranial pressure.

pathophysiological conditions. Most importantly, he described the A-waves ("plateau waves") that are observed primarily in patients with intracranial mass lesions and may precede the final brainstem incarceration (4). The first study of ICP in patients with severe brain trauma was published in 1965 by Lundberg and collaborators (7). The fact that the thesis and subsequent studies had proven that protracted continuous monitoring of ICP was possible without serious complications (8) meant that his technique became the cornerstone for the development of neurocritical care.

REGIONAL CEREBRAL BLOOD FLOW

In the 1940s Kety & Schmidt (9), in a series of publications, had demonstrated that it was possible to measure human global cerebral blood flow (CBF) by the use of the inert gas nitrous oxide. The Danish physiologist Niels Lassen (1926–1997) extended the measurement of global CBF by including radioactive isotopes (10). In collaboration with the Swedish neurophysiologist David Ingvar (1924–2000) he presented a novel method for the measurement of regional cerebral blood flow (rCBF) based on intracarotid injection of the radioactive substances ^{85}Krypton or ^{133}Xenon dissolved in saline. Clearance of the isotopes was recorded by extracranial detectors (11, 12). The combined studies, performed in Copenhagen and Lund, introduced a new era in experimental and clinical brain research. The Lassen group in Copenhagen focused their interest on the physiology and pathophysiology of the cerebral circulation, while Ingvar and his collaborators in Lund studied predominantly neuropsychological and neuropsychiatric problems.

In the original technique for measuring rCBF the radioactive isotope was infused via the carotid artery. During the early 1970s this technique was also introduced in studies of patients with severe brain trauma (13, 14). Among these pioneers were Jørn Overgaard (1927–1984) and collaborators at the University Hospital in Odense (15) and Georg Cold and collaborators at the University Hospital in Aarhus (16–18). Many important observations were published in their studies, but 3 of these primarily influenced neurocritical care. First, global CBF was found to be unrelated to neurological state and clinical outcome (14, 15). Secondly, impaired cerebral pressure autoregulation was frequently observed and was not related to clinical outcome (15, 18). Thirdly, cerebrovascular CO_2 reactivity was often impaired during the acute phase after trauma, in particular in patients with very severe lesions and a poor outcome (15, 17). However, the technique of infusing the radioactive tracer into the carotid artery was a severe limitation for repeated measurements and prevented the technique from being introduced in clinical practice within critical care. For further development it was also necessary to combine measurements of CBF and aspects of cerebral energy metabolism.

LABORATORY FOR EXPERIMENTAL BRAIN RESEARCH IN LUND

In the early 1960s Nils Lundberg was contacted by the young, promising neuroscientist Bo Siesjö. The contact led to the creation of the Laboratory for Experimental Brain Research, which came to be of fundamental importance for the development of neurocritical care. The laboratory originally focused on the regulation of extra- and intra-cellular acid–base relations in the brain (19). Techniques for quantitative measurements of global and regional CBF in small animals were gradually developed and, simultaneously, advanced micro-techniques for determination of a large number of biochemical variables were introduced. It was then possible for a whole generation of young clinicians to study complicated problems related to neurocritical care in experimental models: cerebral ischaemia, hypoxia and hypoglycaemia; induced epileptic seizures; hyper- and hypo-thermia; mechanisms of irreversible cell damage leading to cell death. Neurosurgeons, neurologists, surgeons, paediatricians and anaesthetists received their scientific education in the laboratory and presented their doctoral theses here. At that time the Laboratory for Experimental Brain Research was generally considered one of the leading laboratories in the world, and international neuroscientists regularly visited the laboratory. Many aspects of the work and the results obtained were summarized by Dr Siesjö in a series of review articles in clinical scientific papers and in a comprehensive textbook (20–22).

For many years the results of these experimental studies were of importance mainly for the understanding of the pathophysiological processes in neurocritical care. It was not until the technique of microdialysis was introduced in the 1990s as a bedside method of surveillance that cerebral biochemistry was integrated into the treatment of individual patients.

BEDSIDE MEASUREMENT OF CEREBRAL BLOOD FLOW, VASOREACTIVITY AND OXYGEN CONSUMPTION

The anaesthetist Kenneth Messeter (1932–2003) was of crucial importance for the development of new therapeutic strategies in severe head injuries. Dr Messeter had received his scientific education at the Laboratory for Experimental Brain Research, and he introduced a technique for measurement of CBF that could be used at the bedside. The tracer substance ^{133}Xenon dissolved in saline was injected intravenously, followed by a rapid injection of 20 ml isotonic saline. Clearance of the tracer was monitored from both parietotemporal regions by two scintillation detectors and from the expired air. The CBF data were automatically calculated from the clearance curves by conventional bicompartmental analysis and a delayed-start fit time (23).

Based on previous clinical experiences from Odense and Aarhus, and experimental studies at the Laboratory for Experimental Brain Research it was decided to focus on 3 areas of interest: (*i*) cerebral vasoreactivity, as determined from changes in CBF due to a change in $PaCO_2$ induced by hyperventilation; (*ii*) CBF after i.v. injection of phenobarbital to achieve a burst-suppression pattern on EEG; (*iii*) measurement of cerebral oxygen consumption ($CMRO_2$) after induced barbiturate coma. The studies showed that, in patients with preserved cerebral vasoreactivity to hyperventilation (CO_2-reactivity), barbiturate coma therapy was accompanied by a decrease in ICP due to a reduction in CBF with a parallel decrease in $CMRO_2$ (24). In patients with impaired CO_2-reactivity, these changes in CBF and $CMRO_2$ were not obtained (24). As a lasting decrease in ICP was not obtained the prognosis was extremely bad in the latter group.

Introduction of the barbiturate coma therapy was paralleled by efforts to evaluate the efficacy of improvements in critical care. Inspired by Dr Messeter a careful follow-up study of all patients treated for severe traumatic brain lesions had previously been performed at the Department of Neurosurgery in Lund. The patients were selected according to the Glasgow definition of severe brain trauma (25) and clinical outcome was judged according to the Glasgow Outcome Scale (GOS) (26). The results are shown in Table I. The results in Lund were, at that time, equal to the experiences in other large international studies (27, 28). After the introduction of a standardized protocol for critical care in these patients (including induction of barbiturate coma in selected patients), the outcome results improved significantly (Table I) (29). In particular, it was noted that the reduction in mortality did not lead to an increase in the proportion of patients remaining in severe disability or a vegetative state.

The department now focused on two problems. First, the fact that a large proportion of our patients were classified as good recovery/moderate disability did not imply that they could return to a normal life (30, 31). This experience indicated that, in the future, more interest should be directed to the rehabilitation period. Secondly, as a subgroup of patients with extremely high mortality could be defined from objective, physiological data (CO_2-reactivity) it was considered ethically motivated to introduce a completely new therapy in these patients. This subgroup consisted of patients with high ICP (> 20 mmHg) with impaired cerebrovascular reactivity to changes in $PaCO_2$ (32).

LUND CONCEPT

As a subgroup of patients with extremely high mortality had been identified (32) the interest was directed towards the basic principles for reduction in increased ICP. Here the physiologist and anaesthetist Per-Olof Grände contributed with knowledge regarding physiological principles for tissue volume regulation under experimental conditions (33). These principles, which constituted the scientific basis for the "Lund Concept" (34), were to a large extent based on extensive basic studies previously presented by the US physiologist JD Fenstermacher (35).

Volume regulation of the brain is, as in other organs, determined mainly by mechanisms controlling the water exchange across the capillaries. However, the brain differs from all other organs in its highly sophisticated capillary membrane function, the blood–brain barrier (BBB). In addition to its other physiological functions the BBB is the most important regulator of cerebral volume (35). The principles are illustrated schematically in Fig. 2 for 3 hypothetical situations: (*i*) the normal brain with intact BBB; (*ii*) the injured brain with BBB permeable for crystalloids but not colloids; (*iii*) the injured brain with a ruptured BBB permeable for crystalloids as well as colloids.

Due to the BBB the prerequisite for water transport across cerebral capillaries is different from all other tissues. The intact BBB is impermeable for the two major solutes of biological fluids (Na^+ and Cl^-) (Fig. 2A). Water passing the BBB in any direction will thus be virtually devoid of crystalloids and an opposing osmotic gradient, which counteracts further fluid movement, will immediately be created. In all other tissues transcapillary water transport is governed by the balance between intracapillary hydrostatic pressure and blood colloidal pressure, both amounting to approximately 20 mmHg. As the total crystalloid osmotic pressure is approximately 5700 mmHg intracapillary pressure as well as variations in blood colloidal osmotic pressure is of very limited importance provided the BBB is intact. Under physiological conditions the brain is also protected from increases in intracapillary hydrostatic pressure during an increase in mean arterial blood pressure (MAP) and

Table I. *Data from the Department of Neurosurgery, University Hospital in Lund during 3 time periods (27, 29, 37)*

Outcome	1977–1982 *n* = 425 Original conventional therapy	1983–1984 *n* = 162 Barbiturate coma therapy	1989–1994 *n* = 53 Lund Concept
Good recovery/ moderate disability, %	39	54	79
Severe disability/ vegetative state, %	13	11	13
Dead, %	48	35	8

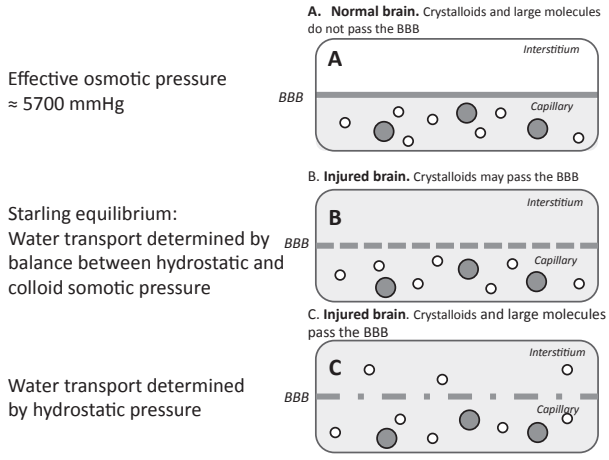


Fig. 2. Water exchange across cerebral capillaries in 3 hypothetical situations: (A) the normal brain with intact blood–brain barrier (BBB); (B) the injured brain with a BBB permeable for crystalloids but not colloids; (C) the injured brain with a ruptured BBB permeable for crystalloids as well as colloids. Grey area: crystalloids in the capillary; open circles: large (colloidal) molecules; filled circles: blood cells.

cerebral perfusion pressure (CPP) by autoregulation of CBF. Accordingly, the brain is under normal conditions effectively protected from variations in volume, which is extremely important as it is surrounded by the rigid skull.

In the injured brain the BBB may be partly ruptured and permeable to crystalloids. In these patients cerebral autoregulation is also often impaired (15, 18) and cerebral transcapillary water flux will then, as in all other tissues, behave according to the Starling equilibrium: water transport is determined by the balance between the differences in hydrostatic and colloidal osmotic pressure (Fig. 2B). If these patients develop increased ICP, the adequate treatment is to reabsorb water over the capillary endothelium by decreasing intracapillary hydrostatic pressure, e.g. by a pharmacological reduction in MAP, while colloidal osmotic pressure should be kept within physiological limits.

If the BBB of the injured brain is more or less completely ruptured, then large colloidal molecules will also pass into the interstitium. In this situation transcapillary water transport is determined by the difference in hydrostatic pressure across the capillary wall (Fig. 2C). This situation is not infrequently experienced by neurosurgeons: when the skull bone and the dura are opened in a patient with a serious cerebral insult the momentary increase in the transcapillary pressure gradient may cause a rapid increase in transcapillary water transport, pronounced brain swelling and a bulging of the brain outside the craniotomy.

The physiological and pathophysiological considerations schematically depicted in Fig. 2 constituted the background for the "Lund Concept" for treatment of elevated ICP (36). Introduction of the "Lund Concept" resulted in a dramatic decrease in mortality at the Department of Neurosurgery in Lund (Table I). The marked decrease in mortality was associated with significant increases in the groups of "good recovery" and "moderate disability", but did not increase the number of patients in the groups of "severe disability" or "vegetative state". In the original study, which included a selected group of patients with very severe traumatic brain lesion and ICP above 25 mmHg in spite of conventional treatment, the mortality decreased from 47% to 8% (37). Similar good results were published from other Swedish neurosurgical centres adopting the "Lund Concept" (38, 39). These studies were all based on comparisons with outcome in historical control patients. Recently, however, a prospective, randomized study showed a similar improvement in patients treated according to the "Lund Concept" (40).

The fact that a pronounced reduction in mortality had been achieved without increasing the number of patients in a vegetative state or with remaining severe disability did not, however, decrease the demands for qualified rehabilitation after the acute phase. The results of a careful follow-up study documented that the improvements in neurocritical care increased the demands for rehabilitation in patients classified as good recovery/moderate disability (41). In an attempt to quantify the specific effects of rehabilitation data obtained from neuropsychological tests and occupational performance (assessment of motor and process skills, AMPS) was evaluated on admission to the rehabilitation centre and compared 3, 6 and 12 months later (42). The study showed that AMPS gave a different view of the patient's restitution than neuropsychological tests and might be a better indicator of the patient's ability to resume independent living. Furthermore, the study indicated a direct positive effect of rehabilitation on AMPS and the deterioration of process skills post-rehabilitation suggested that lasting contact in an outpatient setting might facilitate return to social life (42).

In spite of the favourable clinical results obtained, an important problem related to the "Lund Concept" remained. As a pharmacologically induced reduction in MAP is a fundamental component of the concept, it was compulsory to define the lower acceptable limit for CPP in the individual patient. If this limit is unknown there is a risk that the therapy might lead to ischaemia, in particular in the sensitive penumbra zone surrounding focal brain lesions. To accomplish this task it was necessary to monitor cerebral energy metabolism at the beside during neurocritical care.

BEDSIDE BIOCHEMICAL MONITORING BY MICRODIALYSIS

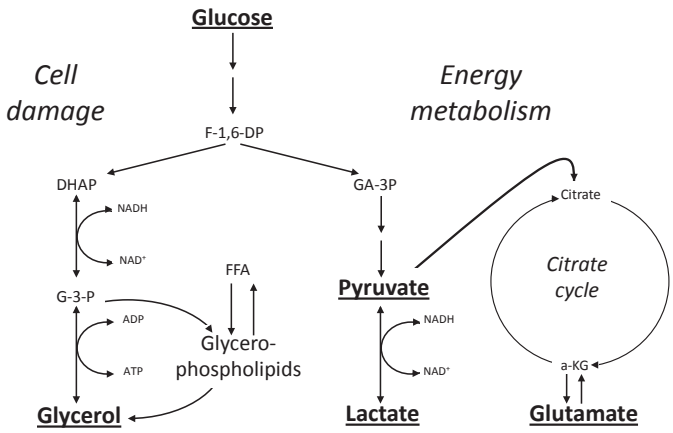
Microdialysis was introduced almost 40 years ago by Urban Ungerstedt (43) at the Karolinska Institute in Stockholm primarily for experimental monitoring of the animal brain. Due to our collaboration with Dr Ungerstedt, in 1996 we had the opportunity to pioneer microdialysis with bedside biochemical analysis and display of the data.

The basic idea of microdialysis is to mimic the function of a blood capillary by inserting a thin dialysis tube (< 0.6 mm) into the tissue. The membranous wall of the tube allows free diffusion of water and solutes between the surrounding

interstitial fluid and the perfused solution (perfusate). The concentration gradients between the interstitial fluid and the perfusate constitute the driving force for diffusion. The molecular weight of the molecules being sampled is limited by the pore size of the dialysis membrane (cut-off). The perfusate flows along the dialysis membrane slowly and at a constant speed, and the sample (dialysate) is collected and analysed biochemically. Accordingly, the technique allows analysis of virtually all chemical compounds that pass through the dialysis membrane. During clinical conditions these analyses are performed by utilizing conventional enzymatic techniques (44). The bedside analyses focus on two aspects of cerebral metabolism: variables involved in cerebral energy metabolism and variables indicating threatening energy crises and degradation of cellular membranes. Fig. 3 provides a schematic picture of the chemistry relevant for routine neurocritical care. As discussed before, much of the biochemical changes during various patho-physiological conditions had been clarified in animal experiments at the Laboratory for Experimental Brain Research decades before (20–22). However, it should be recognized that the biochemical information during neurocritical care is obtained exclusively from the extracellular space, while the animal studies were performed on homogenized whole brain.

Under normal circumstances glucose is the sole substrate for cerebral energy metabolism. The interstitial level obtained by microdialysis reflects the relationship between the delivery of glucose from the capillaries and its uptake into the cells. In the cellular cytoplasm it is stepwise degraded to pyruvate (anaerobic glycolysis). Under physiological conditions (i.e. sufficient oxygenation, functioning mitochondria) most of the pyruvate is in the mitochondria degraded completely to CO_2 and H_2O, where most of the energy released is transferred into ATP. Under normal conditions approximately 5% of the pyruvate is converted to lactate by lactate dehydrogenase in the cytoplasm (Fig. 3). The reaction is a reversible equilibrium reaction reflecting cytoplasmatic redox state, i.e. tissue oxygenation and mitochondrial function. When tissue oxygenation is insufficient, or when the mitochondrial function is impaired the lactate/pyruvate (La/Py) ratio will increase. As lactate and pyruvate are equally permeable across the cell membranes the La/Py ratio measured in the intercellular space will give true information regarding the cytoplasmatic redox state.

Secondary cerebral ischaemia was originally considered the main target for clinical microdialysis, and most clinical studies initially focused on this problem in conditions such as severe brain trauma (45), subarachnoid (46) and intracerebral haemorrhage (47). Tissue microdialysis, by necessity, provides biochemical information from a very small zone surrounding the catheter. As cerebral energy metabolism varies in different brain regions the positioning of the catheter is of paramount importance (48). Furthermore, as microdialysis is a very local technique it is usually futile to correlate changes observed in biochemistry with the eventual clinical outcome. Data obtained from microdialysis provide information about *local* tissue damage and *local* tissue outcome. Accordingly, to be of clinical relevance it is necessary to localize the position of the microdialysis catheter in relation to the pathological process and, if necessary, insert multiple intracerebral catheters (48). When cerebral microdialysis is used in an optimal way it offers a possibility to detect secondary cerebral ischaemia before it is



	Glucose	Lactate	Pyruvate	La/Py ratio	Glutamate	Glycerol
Normal human brain	1.7±0.9 mmol/L	2.9±0.9 mmol/L	166±47 µmol/L	23±4	16±16 µmol/L	80±40 µmol/L

Fig. 3. Simplified diagram of cerebral intermediary metabolism, with a focus on the glycolytic chain and its relation to glycerol and glycerophospholipids and to the citric acid cycle (Krebs cycle). F-1,6-DP: fructose-1,6-diposphate; DHAP: dihydroxyacetone-phosphate; GA-3P: glyceraldehyde-3-phosphate; G-3-P: glycerol-3-phosphate; FFA: free fatty acids; α-KG: α-ketoglutarate. Underlined metabolites are measured at the bedside with enzymatic techniques. References levels of the various metabolites for normal human brain obtained from (44).

revealed by global techniques, to start adequate therapy early, and thus prevent further tissue damage (49).

As mentioned above, clinical microdialysis was introduced at the Department of Neurosurgery in Lund in order to monitor patients with severe brain trauma treated according to the "Lund Concept" and to ensure that the decrease in CPP did not cause secondary brain damage. In a comprehensive study it was documented that cerebral energy metabolism usually tolerated a decrease in CPP to our previously defined lower level of 50 mmHg (50). However, this level should not be regarded as fixed: it varies between different patients and the lower acceptable level for the individual patient can only be assessed by monitoring cerebral energy metabolism in the sensitive penumbra zone.

BEDSIDE DIAGNOSIS OF CEREBRAL ISCHAEMIA AND MITOCHONDRIAL DYSFUNCTION

Clinical microdialysis initially focused on identifying, and avoiding, episodes of secondary clinical ischaemia. However, clinical studies from several neurocritical care units indicated that prolonged disturbance of cerebral energy metabolism, including increase in the La/Py ratio, was often not due to ischaemia (51). The condition observed was generally named "hyperglycolysis" or "metabolic crisis".

By the 1970s animal experiments had shown that transient cerebral ischaemia often lead to a prolonged period of mitochondrial dysfunction (52, 53). Although the pattern of variables related to cerebral energy metabolism was documented in many studies the importance of these observations were not noticed. We have recently completed a series of animal experiments at the Department of Neurosurgery, Odense University Hospital. The experiments were performed to define the biochemical pattern obtained during mitochondrial dysfunction in order to distinguish and separate it from cerebral ischaemia (54, 55). The results are shown schematically in Fig. 4.

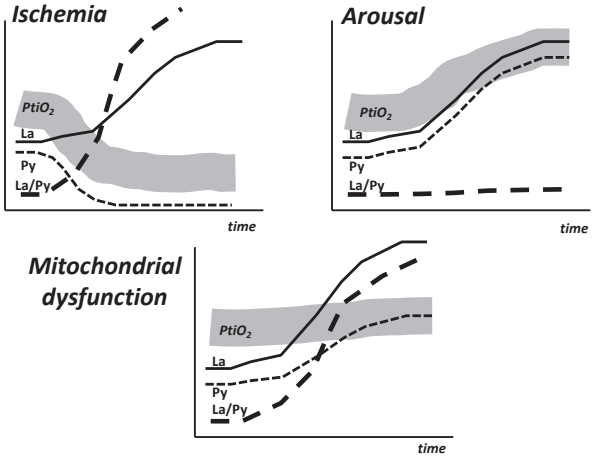


Fig. 4. Cerebral tissue oxygenation ($PtiO_2$) and changes in the levels of lactate (La), pyruvate (Py), and the lactate/pyruvate ratio (La/Py) in 3 conditions: ischaemia, arousal, and mitochondrial dysfunction.

Fig. 4 illustrates the biochemical changes and the change in tissue oxygenation ($PtiO_2$) in 3 situations. In cerebral ischaemia the cessation of blood flow and decrease in $PtiO_2$ causes a very rapid increase in La/Py ratio (Fig. 4). As the cerebral delivery of substrate for energy metabolism (glucose) is also interrupted, pyruvate decreases to a very low level. As a result the La/Py ratio increases to extremely high levels. In mitochondrial dysfunction $PtiO_2$ is unchanged but, due to impaired mitochondrial function, oxidative metabolism is insufficient to meet the energy demands. The increase in glycolytic rate causes a massive production of lactate and increase in the La/Py ratio although tissue pyruvate remains at a normal level or increases slightly (Fig. 4). For comparison, Fig. 4 also illustrates the situation during arousal/awakening. In this situation the increase in energy consumption is met by an increase in oxidative metabolism, lactate and pyruvate increase in parallel, and the La/Py ratio remains constant.

Under clinical conditions an increase in La/Py ratio may be caused by a variety of mechanisms (56). Irrespective of the mechanisms underlying mitochondrial dysfunction, a beneficial therapeutic intervention would probably be reflected in normalization of the biochemical variables analysed and displayed at the beside. There is reason to believe that drugs that are effective in mitochondrial dysfunction will soon be clinically available. One example is cyclosporine A, which is thought to decrease mitochondrial damage by blocking opening of the mitochondrial permeability transition pore (57). The protective effect of cyclosporine in cerebral ischaemia was first described at the Laboratory for Experimental Brain Research (58), and the drug is presently being prepared for the first clinical trial in patients with traumatic brain injury.

The development of new pharmacological therapies may improve outcome after severe brain trauma. Since mortality has already been reduced to a very low level with conventional management (Table I), it is unlikely that new drugs will reduce it further. The hope is rather that new therapies may prevent secondary damage in the sensitive penumbra zone, thereby improving quality of life for survivors. The possible positive effect will be difficult to evaluate objectively and will necessitate close cooperation between critical care physicians, neurosurgeons and specialists in rehabilitation medicine. For evaluation of the efficacy of new therapies it will also be necessary to improve techniques for physiological and biochemical evaluation of tissue outcome.

CONCLUSION

This review has focused on important innovations within neurocritical care that originate from a few university hospitals in southern Scandinavia: the first unit for intensive care, the development of techniques for measuring ICP, CBF and analyses of cerebral energy metabolism and the introduction of microdialysis as a routine clinical technique leading to the possibility to diagnose and separate ischaemia and mitochondrial dysfunction at the bedside.

In this review we have demonstrated that the introduction of new physiological and biochemical monitoring techniques

have increased our knowledge of the complex pathophysiological situation in severe brain trauma. The knowledge has resulted in a new therapeutic principle, the "Lund Concept" for treatment of brain oedema, and a significant improvement in clinical outcome. Furthermore, we have noted that a decrease in mortality may result in an increasing number of patients in need of qualified rehabilitation. In our experience, the examination and evaluation of the patients by the rehabilitation team already during the latter phase of neurocritical care facilitates cooperation between the departments and a smooth transfer. Our data also indicate that following the initial treatment within the rehabilitation centre a continuous, protracted and structured contact with the outpatient's department will improve the long-term clinical result.

Improvements within critical care were linked to the introduction of new techniques to evaluate the physiological and biochemical state of the patients. New monitoring techniques are, however, necessary not only for the development and evaluation of new treatments in groups of patients. As measures and therapies used during life-threatening conditions are often by themselves associated with serious adverse effects and complications, advanced monitoring is also necessary for the benefit of the individual patient. This experience was formulated long before the development of modern medicine: "Diseases desperate grown by desperate appliance are relieved, or not at all." (Shakespeare, 1603; *Hamlet*).

REFERENCES

1. Berthelsen PG, Cronquist M. The first intensive care unit in the world: Copenhagen 1953. Acta Anaesthesiol Scand 2003; 47: 1190–1195.
2. Lassen HCA. Preliminary report on the 1952 epidemic of poliomyelitis in Copenhagen with special reference to the treatment of acute respiratory insufficiency. Lancet 1953; 1: 37–41.
3. Trubuhovich RV. Further commentary on Denmark's 1952–1953 poliomyelitis epidemic, especially regarding mortality; with a correction. Acta Anaesthesiol Scand 2004; 48: 1310–1315.
4. Lundberg N. Continuous recording and control of ventricular pressure in neurosurgical practice. Acta Psychiatr Scand Suppl 1960; 36: 1–93.
5. Nordström CH, Sundbärg G, Kullberg G, Pontén U, Kjällquist Å. [The man behind the method: Nils Lundberg. He measured the classical "plateau waves".] Läkartidningen 1993; 90: 931–932 (in Swedish).
6. Lundberg N, Kjällquist Å, Bien C. Reduction of increased intracranial pressure by hyperventilation. A therapeutic aid in neurological surgery. Acta Psychiatr Scand Suppl 1959; 34: 1–64.
7. Lundberg N, Troupp H, Lorin H. Continuous recording of the ventricular-fluid pressure in patients with severe traumatic brain injury. A preliminary report. J Neurosurg 1965; 22: 581–590.
8. Lundberg N. Monitoring of intracranial pressure. Proc R Soc Med 1972; 65: 19–22.
9. Kety SS, Schmidt CF. The nitrous oxide method for the quantitative determination of cerebral blood flow in man: theory, procedure and normal values. J Clin Invest 1948; 27: 476–483.
10. Lassen Na, Munck O. The cerebral blood flow in man determined by the use of radioactive krypton. Acta Physiol Scand 1955; 33: 30–49.
11. Lassen NA, Ingvar DH. The blood flow of the cerebral cortex determined by radioactive krypton. Experientia 1961; 17: 42–43.
12. Ingvar DH, Lassen NA. Methods for cerebral blood flow measurements in man. Br J Anaesth 1965; 37: 216–224.
13. Gordon E, Bergvall U. The effect of controlled hyperventilation on cerebral blood flow and oxygen uptake in patients with brain lesions. Acta Anaesthesiol Scand 1973; 17: 63–69.
14. Bruce DA, Langfitt TW, Miller JD, Schutz H, Vapalahti MP, Stanek A, et al. Regional cerebral blood flow, intracranial pressure, and brain metabolism in comatose patients. J Neurosurg 1973; 38: 131–144.
15. Overgaard J, Tweed WA. Cerebral circulation after head injury. Part 1: Cerebral blood flow and its regulation after closed head injury with emphasis on clinical correlations. J Neurosurg 1974; 41: 531–541.
16. Enevoldsen E, Cold J, Jensen FT, Malmros R. Dynamic changes in regional CBF, intraventricular pressure, CSF pH and lactate levels during the acute phase of head injury. Neurosurg 1976; 44: 191–214.
17. Cold J, Jensen FT, Malmros R. The cerebrovascular CO_2 reactivity during the acute phase of brain injury. Acta Anaesth Scand 1977; 21: 222–231.
18. Cold J, Jensen FT. Cerebral autoregulation in unconscious patients with brain injury. Acta Anaesth Scand 1978; 22: 270–280.
19. Siesjö BK, Pontén U. Intracellular pH – true parameter or misnomer? Ann N Y Acad Sci 1966; 133: 78–86.
20. Siesjö BK. Pathophysiology and treatment of focal cerebral ischemia. Part I: Pathophysiology. J Neurosurg 1992; 77: 169–184.
21. Siesjö BK. Pathophysiology and treatment of focal cerebral ischemia. Part II: Mechanisms of damage and treatment. J Neurosurg 1992; 77: 337–354.
22. Siesjö BK. Brain energy metabolism. Chichester: John Wiley & Sons, 1978.
23. Messeter K, Nordström CH, Sundbärg G, Algotsson L, Ryding E. Cerebral hemodynamics in patients with acute severe head trauma. J Neurosurg 1986; 64: 231–237.
24. Nordström CH, Messeter K, Sundbärg G, Schalén W, Werner M, Ryding E. Cerebral blood flow, vasoreactivity and oxygen consumption during barbiturate therapy in severe traumatic brain lesions. J Neurosurg 1988; 68: 424–431.
25. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
26. Jennet B, Bond M: Assessment of outcome after severe brain damage. A practical scale. Lancet 1975; 1: 480–484.
27. Nordström CH, Messeter K, Sundbärg G, Wåhlander S: Severe traumatic brain lesions in Sweden. Part 1: Aspects on management in non-neurosurgical clinics. Brain Inj 1989; 3: 247–265.
28. Jennett B, Teasdale G, Galbraith S, Pickard J, Grant H, Braakman R, et al. Severe head injuries in three countries. J Neurol Neurosurg Psychiatry 1977; 40: 291–298.
29. Nordström C-H, Sundbärg G, Messeter K, Schalén W. Severe traumatic brain lesions in Sweden. Part 2: Impact of aggressive neurosurgical intensive care. Brain Inj 1989; 3: 267–281.
30. Schalén W, Sonesson, Messeter K, Nordström G, Nordström C-H. Clinical outcome and cognitive impairment in patients with severe head injuries treated with barbiturate coma. Acta Neurochir 1992; 117: 153–159.
31. Schalén W, Nordström G, Nordström C-H. Psycho-social outcome in patients with severe traumatic brain lesions and the impact of rehabilitation. A follow-up study 5-8 years after injury. Brain Inj 1994; 8: 49–64.
32. Schalén W, Messeter K, Nordström C-H. Cerebral vasoreactivity and the prediction of outcome in severe traumatic brain lesions. Acta Anaesth Scand 1991; 35: 113–122.
33. Grände PO, Asgeirsson B, Nordström CH. Physiologic principles for volume regulation of a tissue enclosed in a rigid shell with application to the injured brain. J Trauma 1997; 42: S23–S31.
34. Asgeirsson B, Grände PO, Nordström CH. A new therapy of post-trauma brain oedema based on haemodynamic principles for brain volume regulation. Intensive Care Med 1994; 20: 260–267.
35. Fenstermacher JD. Volume regulation of the central nervous sys-

tem. In: Staub NC, Taylor AE, editors. Edema. New York: Raven Press; 1984, p. 383–404.
36. Grände PO, Asgeirsson B, Nordström CH. Volume targeted therapy of increased intracranial pressure: the Lund concept unifies surgical and non-surgical treatments. Acta Anaesthesiol Scand 2002: 46: 929–941.
37. Eker C, Asgeirsson B, Grande PO, Schalen W, Nordstrom CH. Improved outcome after severe head injury with a new therapy based on principles for brain volume regulation and preserved microcirculation. Critical Care Med 1998; 26: 1881–1886.
38. Naredi S, Edén E, Zäll S, Stephensen H, Rydenhag B. A standardized neurosurgical/neurointensive therapy directed toward vasogenic edema after severe traumatic brain injury: clinical results. Intensive Care Med 1998: 24: 446–451.
39. Naredi S, Olivecrona M, Lindgren A, Ostlund AL, Grände PO, Koskinen LO. An outcome study of severe traumatic head injury using the 'Lund therapy' with low-dose prostacyclin. Acta Anaesthesiol Scand 2001: 45: 401–405.
40. Dizdarevic K, Hamdan A, Omerhodzic I, Kominlija-Smajic E. Modified Lund concept versus cerebral perfusion pressure-targeted therapy: a randomised controlled study in patients with severe brain ischemia. Clin Neurol Neurosurg 2012; 114: 142–148.
41. Eker C, Schalén W, Asgeirsson B, Grände P-O, Ranstam J, Nordström C-H. Reduced mortality after severe head injury will increase the demands for rehabilitation services. Brain Inj 2000; 14: 605–619.
42. Lindén A, Boschian K, Eker C, Schalén W, Nordström CH. Assessment of motor and process skills reflects brain-injured patients ability to resume independent living better than neuropsychological tests. Acta Neurol Scand 2005; 111: 48–53.
43. Ungerstedt U. Microdialysis – principles and application for studies in animal and man. J Internal Med 1991: 230: 365–373.
44. Reinstrup P, Ståhl N, Hallström Å, Mellergård P, Uski T, Ungerstedt U, Nordström CH. Intracerebral microdialysis in clinical practice. Normal values and variations during anaesthesia and neurosurgical operations. Neurosurgery 2000; 47: 701–710.
45. Ståhl N, Ungerstedt U, Nordström CH. Brain energy metabolism during controlled reduction of cerebral perfusion pressure in severe head injuries. Intensive Care Med 2001; 27: 1215–1223.
46. Skjøth-Rasmussen J, Schulz M, Kristensen SR, Bjerre P. Delayed neurological deficits detected by an ischemic pattern in the extracellular cerebral metabolites in patients with aneurysmal subarachnoid hemorrhage. J Neurosurg 2004; 100: 8–15.
47. Nilsson OG, Polito A, Säveland H, Ungerstedt U, Nordström CH. Are primary supratentorial intracerebral hemorrhages surrounded by a biochemical penumbra? A microdialysis study. Neurosurgery 2006; 59: 521–528.
48. Engström M, Polito A, Reinstrup P, Romner B, Ryding E, Ungerstedt U, Nordström CH. Intracerebral microdialysis in clinical routine – the importance of catheter location. J Neurosurg 2005; 102: 460–469.
49. Reinstrup P, Nordström CH. Prostacyclin infusion may prevent secondary damage in pericontusional brain tissue. Neurocrit Care 2011; 14: 441–446.
50. Nordström CH, Reinstrup P, Xu W, Gärdenfors A, Ungerstedt U. Assessment of the lower limit for cerebral perfusion pressure in severe head injuries by bedside monitoring of regional energy metabolism. Anesthesiology 2003; 98: 809–814.
51. Vespa P, Bergsneider M, Hattori N, Wu HM, Huang SC, Nartin NA, et al. Metabolic crisis without brain ischemia is common after traumatic brain injury: a combined microdialysis and positron emission tomography study. J Cerebral Blood Flow Metab 2005; 25: 763–774.
52. Rehncrona S, Mela L, Siesjo BK. Recovery of brain mitochondrial function in the rat after complete and incomplete cerebral ischemia. Stroke 1979; 10: 437–446.
53. Nordstrom CH, Rehncrona S, Siesjo BK. Restitution of cerebral energy state, as well as of glycolytic metabolites, citric acid cycle intermediates and associated amino acids after 30 minutes of complete ischemia in rats anaesthetized with nitrous oxide or phenobarbital. J Neurochem 1978; 30: 479–486.
54. Nielsen TH, Bindslev TT, Pedersen SM, Toft P, Nordström CH. Cererbral energy metabolism during induced mitochondrial dysfunction. Acta Anaesthesiol Scand 2013; 57: 229–235.
55. Nielsen, TH, Olsen NV, Toft P, Nordström CH. Cerebral energy metabolism during mitochondrial dysfunction induced by cyanide in piglets. Acta Anaesthesiol Scand 2013, Mar 18 [Epub ahead of print].
56. Larach DB, Kofke A, Le Roux P. Potential non-hypoxic/ischemic causes of increase cerebral interstitial fluid lactate/pyruvate ratio: a review of available litterature. Neurocrit Care 2011; 15: 609–622.
57. Osman MM, Lulic D, Glover L, Stahl CE, Lau T, van Loveren H, Borlongan CV. Cyclosporine-A as a neuroprotective agent against stroke: its translation from laboratory research to clinical application. Neuropeptides 2011; 45: 359–368.
58. Uchino H, Elmér E, Uchino K, Lindvall O, Siesjö BK. Cyclosporin A dramatically ameliorates CA1 hippocampal damage following transient forebrain ischaemia in the rat. Acta Physiol Scand 1995; 155: 469–471.

J Rehabil Med 2013; 45: 718–720

ORIGINAL REPORT

MANAGEMENT OF MILD TRAUMATIC BRAIN INJURIES IN EMERGENCY DEPARTMENTS IN SWEDEN: EVIDENCE OF A CHANGE IN CLINICAL PRACTICE

Samuel Carlsson, MD[1] and Jean-Luc af Geijerstam, MD, PhD[2]

From the [1]Department of Medicine Västerås Hospital, Västerås and [2]Clinical Epidemiology Unit, Karolinska University Hospital, Stockholm, Sweden

Objective: **A study published in 2000 on the acute clinical management of mild traumatic brain injuries in Sweden showed that these patients were routinely admitted to hospital for observation. This study aims to compare current clinical management of mild traumatic brain injury with clinical practice a decade ago.**

Design: **Questionnaire to senior residents in all emergency departments in Sweden and data from registers covering all in-hospital care in Sweden.**

Results: **The response rate to the questionnaire was 100%. In Sweden, 71 emergency departments treat patients with mild traumatic brain injuries. An estimated mean of 58% of patients with mild traumatic brain injuries receive computerized tomography scanning, which represents a 3-fold increase compared with 2000. In 2010, Swedish hospitals admitted 8,821 patients for mild traumatic brain injuries (94 per 100,000 inhabitants). This figure is approximately half that of 1996, when 16,877 patients were treated as inpatients for mild traumatic brain injuries (191 per 100,000 inhabitants). However, admission rates continue to vary widely among departments. The mean hospital stay 2010 was 1.21 days, compared with 1.6 days in 1996.**

Conclusion: **This study provides evidence of a change in clinical practice in the acute management of mild traumatic brain injuries in Sweden. Acute management is increasingly based on computed tomography, and in-hospital observation is used less frequently as a strategy for these patients.**

Key words: mild traumatic brain injury; computed tomography; clinical management; in-hospital observation; incidence; admission rate.

J Rehabil Med 2013; 45: 718–720

Correspondence address: Jean-Luc af Geijerstam, Clinical Epidemiology Unit, Karolinska University Hospital, SE-171 76 Stockholm, Sweden. E-mail: jean-luc.af.geijerstam@ki.se

Accepted June 4, 2013

INTRODUCTION

Worldwide, between 100 and 300/100,000 adult patients per year are treated in hospital for mild traumatic brain injury (MTBI) (1). There are numerous definitions of MTBI, a commonly used one was proposed by the American Congress of Rehabilitation Medicine (2). Most patients with MTBI will recover completely, but some will develop long-term, non-neurosurgical sequelae (3). A few patients will develop serious intracranial complications requiring neurosurgical intervention in the acute phase (4). The aim of any acute management strategy must be to identify accurately, and at reasonable cost, those at risk for deterioration requiring neurosurgical intervention.

In 2000, we published a study on the clinical management of MTBI in Sweden, which drew a clear conclusion; patients with MTBI were routinely admitted to hospital for observation (5). MTBI was commonly defined as patients sustaining a head trauma with "a history of amnesia or loss of consciousness". Annually, approximately 200/100,000 patients were treated as inpatients for MTBI. All emergency departments (EDs) had access to a 24-h computed tomography (CT) scanner service. No clinics reported using CT to triage patients for admission. Subsequent systematic reviews of the literature showed that using CT to decide who required admission was both a safe and a cost-effective acute management strategy for MTBI compared with a strategy based on in-hospital observation (6). Between 2000 and 2004, a nationwide pragmatic randomized controlled trial (RCT) was also conducted in Sweden to compare the two management strategies. More than half of all Swedish emergency departments participated in the trial. The results provided solid evidence supporting the CT triage strategy (7, 8).

The aims of the present study were to describe current clinical management of MTBI and compare these results with those from our previous study, in order to determine whether management has changed in light of new evidence.

METHODS

In June/July 2009 we surveyed all emergency departments in Sweden's 80 hospitals, asking questions about clinical routines for MTBI (e.g. indications for in-hospital observation, and estimated use of CT). A self-completion postal questionnaire was posted to the senior resident in all the hospitals' emergency departments. The questionnaire used in this study was identical to the one used in our previous study, in order to facilitate comparing the results from the two surveys (5).

Epidemiological data on in-hospital care (number of admissions and length-of-stay) were obtained from the Swedish National Board of Health and Welfare (NBHW) (website: http://www.socialstyrelsen.se/english). All healthcare in Sweden is publicly funded, and the NBHW collects data on all in-hospital care in the country. Data in the NBHW register have high validity (9). The present study includes data from 1990 through 2010 on

all patients with a discharge diagnosis of *commotio cerebri* (International Classification of Diseases (ICD)-9 code 850/ICD-10 S06.0). We chose to include data up until 2010, since this was the latest available year for data-capture at the time of analysis and preparation of the manuscript.

RESULTS

Characteristics of hospitals treating patients with mild traumatic brain injuries

A total of 80 emergency departments were sent the questionnaire. Non-responders were contacted by post with an additional questionnaire. The few remaining non-responders were contacted by phone or fax. The final response rate was 94%. The 5 clinics that did not submit questionnaires were contacted by phone. All confirmed that they did not accept patients with MTBI, thus the response rate from clinics relevant to this study was 100%.

Seventy-one emergency departments in Sweden accept patients with MTBI. Four of these are specialized paediatric emergency departments, all at university hospitals.

All 71 emergency departments reported having access to a 24-h computerized tomography scanner service. Only 6 clinics reported any restrictions regarding availability; either that the radiologist on call was at home during the night or that qualified neuroradiological interpretation could not be assured during the night.

Evaluation in the emergency department

The basic structure for evaluating MTBI patients in the emergency department is largely unchanged; general surgeons most commonly evaluate patients with MTBI (86%), and most hospitals report treating children with MTBI (86%).

Changes are obvious in two areas: (*i*) 60% of the hospitals report having written guidelines for MTBI management compared with 32% in our previous study; and (*ii*) 40% now give written instructions to patients at discharge, whereas only 4% reported doing so in 1998.

Admission for in-hospital observation

Most routines (i.e. where patients are observed, frequency of assessment during the observation period, what is being observed) regarding the in-hospital observation period are reportedly unchanged since 1998. One obvious change is that, in 1998, most clinics reporting a fixed minimum time for in-hospital observation stated that it was 24 h, whereas today the most common minimum time is 12 h. Although the Reaction Level Scale (RLS) remains the dominant scale to evaluate consciousness, utilization of the Glasgow Coma Scale (GCS) has more than doubled.

Radiological imaging

The predominant indications for ordering a CT scan in patients with MTBI were basically unchanged. CT is used for between 5% and 100% of patients with MTBI, with a mean value of 58%. This represents nearly a 3-fold increase in the use of CT compared with 1998, when CT was used for between 2% and 80% of patients, with a mean value of 22%. Fig. 1 shows the estimates for 2009 compared with 1998.

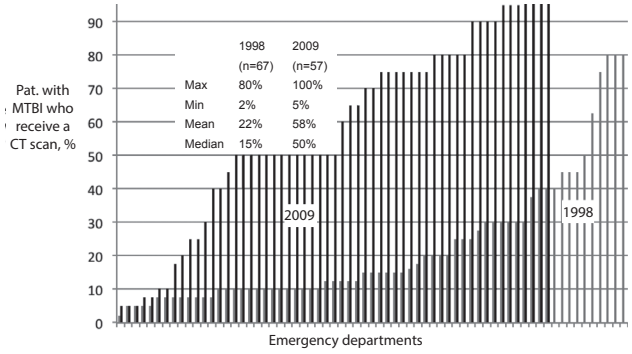


Fig. 1. Estimated use (by the senior resident) of computerized tomography (CT) scanning for patients with mild traumatic brain injury (MTBI) in emergency departments in Sweden, in 1998 (*grey*) and 2009 (*black*) (responses were missing from 8 departments in 1998 and 14 in 2009).

As in 1998, no hospitals perform routine skull radiography in the work-up of MTBI patients.

Epidemiological data and resource consumption

In our previous study we could observe a relatively stable yearly incidence of MTBI patients admitted to hospital for the decade leading up to our study (1987–1996). This stability in incidence suggested a consistency in clinical policy in MTBI management in Sweden throughout the period. This has clearly changed. Fig. 2 shows the yearly incidence of MTBI patients admitted to hospital from 1990 to 2010. In 2010, 8,821 patients were admitted to hospital for MTBI (94 per 100,000 inhabitants). This represents approximately a 50% reduction in admissions for MTBI compared with 1996, when 16,877 patients were treated as inpatients (191 per 100,000 inhabitants). No apparent change in the age and sex distribution was noted in this cohort compared with previous years. In 1998 the mean hospital stay for patients with MTBI was 1.6 days, while in 2010 it was 1.2 days. As in 1998, the admission rates continue to vary widely among departments.

DISCUSSION

Our results show several changes in the acute management of MTBI patients in Sweden, compared with our earlier

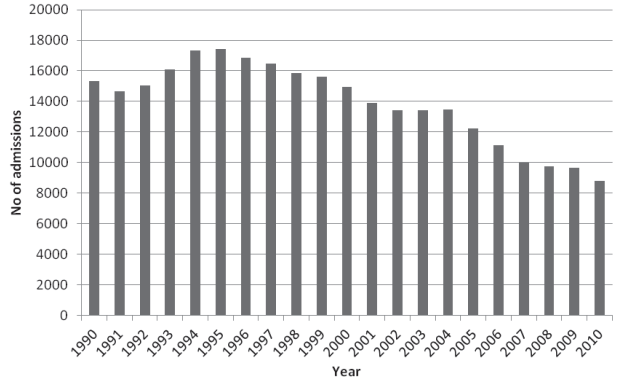


Fig. 2. Number of patients admitted to hospital for mild traumatic brain injury in Sweden, 1990–2010.

study. Fewer patients are admitted for in-hospital observation, and the mean hospital stay is shorter than previously. The reported fixed minimum time for observation is shorter, a larger proportion of clinics have written guidelines for MTBI care, and patients are more frequently given written instructions at discharge. The estimated use of CT in MTBI shows nearly a 3-fold increase.

All of these changes indicate that CT is being used as a screening tool for admission. Annually, however, many patients are still being admitted after MTBI. It is possible that a number of those patients are both being admitted and receive a CT. Such clinical practice represents unnecessary resource utilization (8). If CT findings are normal, and there are no other reasons for admission, most patients with MTBI can be discharged early without an in-hospital observation period. A large, pragmatic RCT in Sweden, where almost 90% of MTBI patients were discharged early, showed the feasibility of such a practice (7). Similar trends regarding MTBI incidence and CT use have been observed recently in other Nordic countries (10, 11). In general, most current guidelines on MTBI management include CT scanning in the acute phase (12, 13).

Why have we not observed an even more drastic change in the clinical management of MTBI? One simple reason is that clinical practice is often difficult to change, and when such changes occur they tend to take a long time (14). The routine of observation after MTBI has been used in Sweden for many decades, and staff in the emergency departments have all been trained and accustomed to such a practice. Another possible reason could be the lack of incentive to change. If beds for in-hospital observation are not in short supply, then new routines for MTBI might not seem particularly appealing. Another reason might be purely administrative; many emergency departments in Sweden have adopted patient flow processes to reduce patients' waiting time to see a physician and the overall length of stay in the ED (15). Hence, MTBI patients in some hospitals are "admitted" to a short-stay ward adjacent to the ED while awaiting CT. Such a practice will result in an entry in the in-hospital register for MTBI and, falsely, in our study be interpreted as management by observation strategy when in fact CT triage is being used (16). The number of cases reported in this manner is unclear.

An obvious weakness of our study concerns the questionnaire design, which is an indirect measure of clinical management. However, coupled with the analysis of epidemiological data, we believe that our main conclusions in this paper are valid. Further analyses of MTBI management should focus on aspects such as exploring barriers to change and the reasons for wide variations in admission rates between clinics. Furthermore, acute strategies for selecting patients for CT need to be further developed and validated as regards long-term functional outcomes and costs (13).

This study provides evidence of a change in clinical practice in the acute management of MTBI in Sweden over a 10-year period. Acute management is increasingly becoming CT based, and in-hospital observation is being used less frequently as a strategy for these patients.

ACKNOWLEDGEMENTS

The study received support from the Swedish Council on Health Technology Assessment. The authors declare that they have no conflicts of interest.

REFERENCES

1. Cassidy JD, Carroll LJ, Peloso PM, Borg J, von Holst H, Holm L, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; Suppl 43: 28–60.
2. The American Congress of Rehabilitation Medicine. Definition of mild traumatic brain injury. J Head Trauma Rehabil 1993; 8: 86–87.
3. Lannsjö M, af Geijerstam JL, Johansson U, Bring J, Borg J. Prevalence and structure of symptoms at three months after mild traumatic brain injury in a national cohort. Brain Inj 2009; 23: 213–219.
4. af Geijerstam JL, Britton M. Mild head injury – mortality and complication rate: meta-analysis of findings in a systematic literature review. Acta Neurochir (Wien) 2003; 145: 843–850; discussion 850.
5. af Geijerstam JL, Britton M, Mebius C. Management of minor head injuries in emergency departments in Sweden. Time for a new strategy? Eur J Surg 2000; 166: 526–529.
6. Swedish Council on Health Technology Assessment. Mild head injury – in-hospital observation or computed tomography? Stockholm: Swedish Council on Health Technology Assessment; 2005, report no. 153 [In Swedish, summary in English at http://www.sbu.se].
7. af Geijerstam JL, Oredsson S, Britton M. Medical outcome after immediate computed tomography or admission for observation in patients with mild head injury: randomised controlled trial. BMJ 2006; 333: 465.
8. Norlund A, Marke LA, af Geijerstam JL, Oredsson S, Britton M. Immediate computed tomography or admission for observation after mild head injury: cost comparison in randomised controlled trial. BMJ 2006; 333: 469.
9. Ludvigsson JF, Andersson E, Ekbom A, Feychting M, Kim JL, Reuterwall C, et al. External review and validation of the Swedish national inpatient register. BMC Public Health 2011; 11: 450.
10. Heskestad B, Baardsen R, Helseth E, Ingebrigtsen T. Guideline compliance in management of minimal, mild, and moderate head injury: high frequency of noncompliance among individual physicians despite strong guideline support from clinical leaders. J Trauma 2008; 65: 1309–1313.
11. Heskestad B, Baardsen R, Helseth E, Romner B, Waterloo K, Ingebrigtsen T. Incidence of hospital referred head injuries in Norway: a population based survey from the Stavanger region. Scand J Trauma Resusc Emerg Med 2009; 17: 6.
12. Unden J, Ingebrigtsen T, Romner B, Snc SN. Scandinavian guidelines for initial management of minimal, mild and moderate head injuries in adults: an evidence and consensus-based update. BMC Med 2013; 11: 50.
13. Smits M, Dippel DW, Nederkoorn PJ, Dekker HM, Vos PE, Kool DR, et al. Minor head injury: CT-based strategies for management – a cost-effectiveness analysis. Radiology 2010; 254: 532–540.
14. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. Lancet 2003; 362: 1225–1230.
15. Asplund K, Castren M, Ehrenberg A, Farrokhnia N, Goransson K, Jonsson H, et al. [SBU about "lean": process-oriented work in emergency departments yields shorter through-put.] Lakartidningen 2010; 107: 1164 (in Swedish).
16. Sjukhusläkaren. [Decrease of ED lead times is a fraud.] 2010 [cited 2013 June 20]. Available from: http://www.sjukhuslakaren.se/2010/10/28/%e2%80%9dminskning-av-akutens-ledtider-en-bluff%e2%80%9d/ (in Swedish).

J Rehabil Med 2013; 45: 721–728

ORIGINAL REPORT

BRAIN PATHOLOGY AFTER MILD TRAUMATIC BRAIN INJURY: AN EXPLORATORY STUDY BY REPEATED MAGNETIC RESONANCE EXAMINATION

Marianne Lannsjö, MD, PhD[1,2], Raili Raininko, MD, PhD[3], Mariana Bustamante, MSc[4], Charlotta von Seth, MD[1] and Jörgen Borg, MD, PhD[5]

From the [1]Department of Neuroscience, Rehabilitation Medicine, University of Uppsala, Uppsala, [2]Center for Research and Development, Uppsala University/County Council of Gavleborg, [3]Department of Radiology and [4]Center for Image Analysis, University of Uppsala, Uppsala and [5]Department of Clinical Sciences, Rehabilitation Medicine, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden

Objective: **To explore brain pathology after mild traumatic brain injury by repeated magnetic resonance examination.**
Design: **A prospective follow-up study.**
Subjects: **Nineteen patients with mild traumatic brain injury presenting with Glasgow Coma Scale (GCS) 14–15.**
Methods: **The patients were examined on day 2 or 3 and 3–7 months after the injury. The magnetic resonance protocol comprised conventional T1- and T2-weighted sequences including fluid attenuated inversion recovery (FLAIR), two susceptibility-weighted sequences to reveal haemorrhages, and diffusion-weighted sequences. Computer-aided volume comparison was performed. Clinical outcome was assessed by the Rivermead Post-Concussion Symptoms Questionnaire (RPQ), Hospital Anxiety and Depression Scale (HADS) and Glasgow Outcome Scale Extended (GOSE).**
Results: **At follow-up, 7 patients (37%) reported ≥ 3 symptoms in RPQ, 5 reported some anxiety and 1 reported mild depression. Fifteen patients reported upper level of good recovery and 4 patients lower level of good recovery (GOSE 8 and 7, respectively). Magnetic resonance pathology was found in 1 patient at the first examination, but 4 patients (21%) showed volume loss at the second examination, at which 3 of them reported < 3 symptoms and 1 ≥3 symptoms, all exhibiting GOSE scores of 8.**
Conclusion: **Loss of brain volume, demonstrated by computer-aided magnetic resonance imaging volumetry, may be a feasible marker of brain pathology after mild traumatic brain injury.**

Key words: mild traumatic brain injury; brain concussion; magnetic resonance imaging; Rivermead Post-Concussion Symptoms Questionnaire; Glasgow Outcome Scale Extended.

J Rehabil Med 2013; 45: 721–728

Correspondence address: Marianne Lannsjö, Rehabilitation Medicine, Sandviken Hospital, SE-811 89 Sandviken, Sweden. E-mail: marianne.lannsjo@lg.se

Accepted April 11, 2013

INTRODUCTION

Traumatic brain injury (TBI) is a global health problem and one of the most common causes of impaired function and disability, accountable for huge human and economic costs (1). The majority, 70% or more of patients with TBI, have a mild traumatic brain injury (MTBI) with a reported annual incidence of 100–300 per 100,000 inhabitants in Western countries (2). In Sweden, approximately 15,000 patents are admitted to hospital with a diagnosis of MTBI every year, most with a history of an uncomplicated brain concussion with brief loss of consciousness (LOC) and/or amnesia, presenting with a Glasgow Coma Scale (GCS) score of 15 and no clinical or radiological signs of brain injury (3). An increasing proportion of these patients have undergone an acute computed tomography (CT) and been discharged if this and their neurological condition have proven normal. Thus, head CT is now part of standard acute management of adults with MTBI.

Most patients with a MTBI have a favourable outcome (4), something that may be true even when the MTBI is complicated by intracranial haematoma and the need for neurosurgical management (5). There is, however, a subgroup of patients reporting problems that may impact on their social activities and work abilities for 3 months or longer post-injury (6). The labelling, definition, frequency and main determinants of such problems have been studied and debated for a long time and are still subject to debate (7, 8). There is evidence that factors associated with an increased risk for a poor outcome include advanced age (7, 9), female gender (9), psychiatric illness (10, 11), pre-morbid or co-morbid physical problems (11), associated injuries (7, 11) and litigation (4). In contrast, the impact of the brain injury itself after MTBI remains unclear over the longer term. Previous studies have demonstrated that head CT pathology is not a strong predictor of outcome with regard to symptoms or global function according to the Glasgow Outcome Scale Extended (GOSE) (7, 9). Consequently, there is a need for studies utilizing other methods to detect disordered brain structure and function in this area. Magnetic resonance imaging (MRI) is a more sensitive radiological method than CT.

TBI may cause not only focal damage with oedema and haemorrhage, but may also cause widespread damage to microcirculation and nerve cells, known as diffuse axonal injury (DAI) (12). MRI is more accurate in identifying DAI (13, 14). Animal studies have shown that even minimal haemor-

rhages can be detected by MRI immediately after haematoma inception (15). It has also been proven that minimal blood products remain in the brain for at least 7 months and can be visualized by MRI (16). Intracellular oedema in ischaemic injuries can be visualized by MRI as early as 1.5–2.5 min after blood circulation has stopped (17).

Human MRI studies have demonstrated clinically significant DAI after moderate or severe TBI, and its relation to clinical outcome according to the Glasgow Outcome Scale (GOS) (18). Some studies have also demonstrated that DAI may be visualized in patients with MTBI (13, 14), but the prevalence and clinical significance of MRI pathology remain to be clarified. Thus, although these studies demonstrate that DAI may be observed in patients with MTBI, further studies are needed to explore the optimal MRI methods and timing to visualize DAI after MTBI, in order to evaluate its clinical impact.

Another approach in this area is taken in follow-up studies using volume change as an indicator. Repeated MRI has demonstrated a loss of brain volume after TBI, but most of these studies include patients with all degrees of severity (18–20). Some have demonstrated a correlation between volume loss and acute lesion (18) or length of coma (20) and the correlation between atrophy and unfavourable outcome according to GOSE (19). Corresponding studies of patients specifically with MTBI are scarce. In a study of 18 patients diagnosed with brain concussion, Schrader et al. (21) found no MRI pathology on either the acute or follow-up MRI. In contrast, Hofman et al. (22) reported MRI pathology in the acute phase in 12 out of 17 patients, exhibiting atrophy at follow-up after 6 months. However, no correlation between atrophy and the results of cognitive tests could be observed.

While previous studies with small materials provide evidence that MRI may reveal brain pathology in patients exposed to MTBI, there is an obvious need to conduct further studies to explore the prevalence and clinical impact of such pathology, as well as the optimal MRI technique and timing. The aim of this study was to explore intracranial pathology after MTBI, using repeated MRI and computer-aided analyses of brain volume changes, in a prospective study.

MATERIAL AND METHODS

During the period April 2008 to October 2011, 22 subjects were recruited from the Emergency Unit of a University Hospital. The recruitment rate was low because some eligible patients declined to participate, and because the recruitment process was restricted to certain time-periods and days of the week. Inclusion criteria were: age 16–65 years, head trauma within the preceding 24 h with a loss or alteration of consciousness for not more than 30 min, and a GCS score of 13–15 at examination in the Emergency Unit, but otherwise normal findings at a neurological examination. Exclusion criteria were: a previous brain injury, any other neurological or psychiatric disorder causing ongoing disability or treatment, as well as substance abuse and other accompanying injuries needing special treatment. Three of the participants did not undergo the second MRI and were, therefore, excluded, resulting in a final study sample of 19 subjects. MRI, neurological examination and assessment with the Rivermead Post-Concussion Symptoms Questionnaire (RPQ), and the Hospital Anxiety and Depression Scale (HADS) were performed at day 2 or 3 after the injury. Follow-up at 3 months or later included MRI, neurological examination and assessment with RPQ, the Rivermead Head Injury Follow-Up Questionnaire (RHIFUQ), HADS and GOSE.

The local medical ethics committee approved the study plan and all patients received oral and written information about the study and gave their informed consent. No financial incentives were offered.

Radiological methods

Computed tomography. Head CT was not included in the study protocol, but was performed on the day of injury in all except 3 patients, as a part of a post-MTBI standard management procedure.

Magnetic resonance imaging. All magnetic resonance (MR) examinations were performed with the same MR imager, operating at 1.5 T, and using the same imaging protocol. Transverse images were obtained with a T2-weighted spin echo (SE) sequence and a T2-weighted FLAIR sequence, using a slice thickness of 5 mm, an interslice gap of 0.5 mm, and a pixel size of 0.90×1.0 mm. A sagittal 3D series with a T1-weighted gradient echo sequence using a slice thickness of 1.0 mm and a pixel size of 0.90 × 0.90 mm was also obtained, as well as a coronal 3D series with a T2-weighted FLAIR sequence using a slice thickness of 3 mm and a pixel size of 1.3 × 1.3 mm. Two susceptibility-weighted sequences were used. The first sequence was a T2*-weighted gradient echo sequence (FLASH) using repetition time (TR) 500 ms, echo time (TE) 14 ms and a flip angle of 30º. Slice thickness was 3 mm, the interslice gap 0.3 mm and pixel size 0.9 × 0.9 mm in transverse series and 5 mm, 0.5 mm, and 0.9 × 0.7 mm, respectively, in coronal series. The second sequence was a 3D susceptibility-weighted imaging (SWI) sequence taken in a transverse plane using TR 49 ms, TE 40 ms, a flip angle of 15º, a slice thickness of 1.5 mm and a pixel size of 1.1 × 0.9 mm. SWI images were further reconstructed with a minimal intensity projection technique in the form of 12-mm thick transverse slices without gaps, and as transverse and coronal slices using the same slice thicknesses and interslice gaps as in the FLASH images. Diffusion-weighted imaging (DWI) was performed in 3 directions, using a SE echo planar technique with TR 4,600 ms, TE 89 ms, a slice thickness of 5 mm, a pixel size of 1.2 × 1.2 mm and b values of 0 s/mm^2 and 1000 s/mm^2. Trace images and apparent diffusion coefficient (ADC) maps were used for analyses.

All CTs were reviewed and all MR images visually analysed by a single experienced neuroradiologist who did not know the patient's outcome. The T1-weighted 3D series were also analysed with the help of a computer-aided volume comparison method developed from already existing ideas on voxel-based morphometry (23). It works by registering the first MRI of the patient to the second MRI using affine transformations, i.e. transformations that preserve straight lines and ratios of distances between points lying on a straight line. Once the two volumes are properly aligned, the program subtracts the first MRI (assumed to be the fixed-volume, or base) from the volume created by the registration. The result is another volume that indicates which voxels have changed the most according to the subtraction values.

Outcome measures

Rivermead Post-Concussion Symptoms Questionnaire. The RPQ (24) is a questionnaire designed to measure the severity of symptoms following mild or moderate traumatic brain injury. The RPQ comprises 16 items asking the patient about the degree of experienced headaches, dizziness, nausea/vomiting, noise sensitivity, sleep disturbance, fatigue, irritability, feeling depressed/tearful, feeling frustrated/impatient, forgetfulness, poor concentration, slowed-down thinking, blurred vision, light sensitivity, double vision, and restlessness over the previous 24 h compared with before the head injury. The items are rated on a 5-point scale, with the response alternatives: 0 = not experienced at all, 1 = no longer a problem, 2 = a mild problem, 3 = a moderate problem, and 4 = a severe problem. According to results from an earlier study on RPQ with Rasch analysis, in which we found multidimensionality and category dysfunction, we chose to not report

differentiated scores or sum scores (25).We used a report of 3 or more symptoms at 3 months to indicate persistent problems, in accordance with prior suggestions (26, 27).

Hospital Anxiety and Depression Scale. The HADS was developed to assess states of anxiety and depression (28) and consists of 14 items with ratings ranging between 0 and 3. The scale allows calculation of sub-scores to estimate the level of anxiety and of depression. A sub-score of 0–6 corresponds to an absence of anxiety/depression, 7–10 to mild-moderate anxiety/depression, and > 10 to a state of severe anxiety/depression.

Rivermead Head Injury Follow-Up Questionnaire. The RHIFUQ was developed to assess outcomes on activity and participation levels after mild to moderate brain injury. Changing ability to perform different activities for 10 items is rated 0–4 on the following scale: 0 = no change, 1 = no change but more difficult, 2 = a mild change, 3 = a moderate change, 4 = a very marked change. The scale has evidenced adequate reliability and validity to assess outcome after mild to moderate TBI (29).

Glasgow Outcome Scale Extended. The GOSE (30) is an ordinal 8-level scale assessing global outcome after TBI: 1 = dead, 2 = vegetative state, 3 = lower severe disability, 4 = upper severe disability, 5 = lower moderate disability, 6 = upper moderate disability, 7 = lower good recovery, and 8 = upper good recovery. The GOSE covers aspects of personal care and social functioning and has demonstrated good inter-rater reliability and content validity (31). The GOSE has been shown to be more sensitive to change after mild to moderate TBI in comparison with the GOS (32).

Statistics

This exploratory study reports frequencies, proportions, median and mean values. For RPQ and RHIFUQ, ratings were dichotomized into ratings in 2 ranges, 0–1 vs 2–4.

RESULTS

Demographic and injury data are summarized in Table I. Age ranged from 17 to 63 years (mean 34, median 28 years) and 12 out of 19 subjects were women. The mean and median educational years were 12 (range 9–18 years). Pre-injury morbidity was reported by 7 patients (4 with chronic pain, 2 with prior depression with no current need for treatment, and 1 with diabetes, renal failure and liver cirrhosis). Seventeen patients presented a GCS score of 15 and 2 exhibited a score of 14. The estimated duration of loss of unconsciousness ranged from 0 to 15 min (median approximately 1 min) and the estimated post-traumatic amnesia (including both retrograde and antegrade traumatic amnesia) ranged from 0 to 600 min (median 15 min). Routine neurological examinations revealed no impairments either at 2–3 days after MTBI or at follow-up.

Table I. *Demographic and injury data of the study sample*

	n
Gender	
Men	7
Women	12
Working status	
Working full-time	7
Working part-time	5
Studying	5
Retirement	1
Other	1
Cause of accident	
Fall	10
Traffic accident	6
Other	3
GCS at emergency unit	
GCS 14	2
GCS 15	17

GCS: Glasgow Coma Scale.

Computed tomography

No cranial or intracranial changes consistent with a recent trauma could be seen in 15/16 patients examined with CT. In one patient, there was a very slight suspicion of a minimal amount of subarachnoid blood or calcification in one parietal sulcus.

Magnetic resonance imaging

The first MRI was performed on day 2 in 3 cases and on day 3 in 16 cases. The second MRI was performed after 3–7 months (with a mean of 4.4 months). The first examination revealed pathology related to a recent trauma in one patient (patient 1), the same patient who had uncertain subarachnoid blood on CT. His left hippocampus was oedematous with an increased T2 signal intensity (Fig. 1a–b) and mixed, both increased and decreased, diffusion. At follow-up, that hippocampus had shrunk

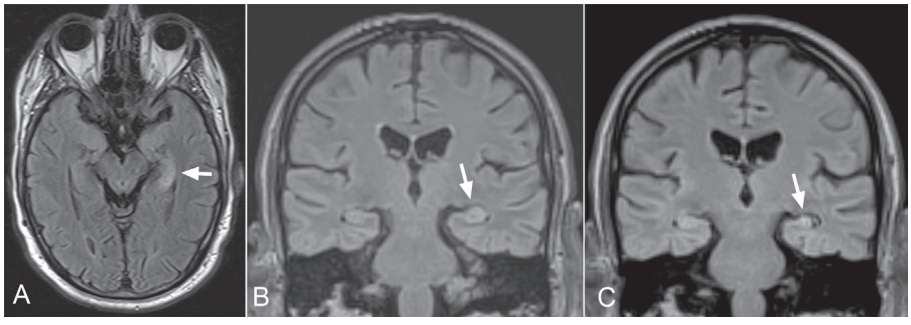


Fig. 1. Patient with hippocampal injury (patient 1). In the first examination, the left hippocampus (arrow) is oedemic: it is enlarged and shows high T2 signal intensity. (A) Axial and (B) coronal slices with a fluid attenuated inversion recovery (FLAIR) sequence. (C) In the second examination, the left hippocampus is shrunken and has a high T2 signal intensity.

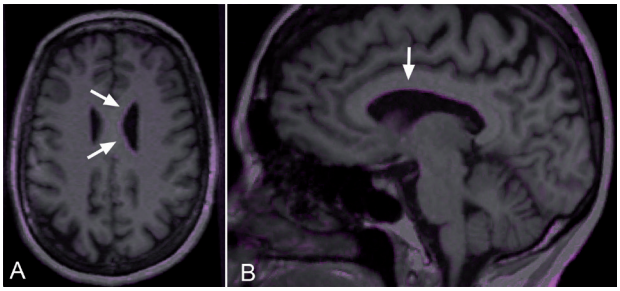


Fig. 2. Volume loss in the corpus callosum demonstrated by the computer-aided volume comparison method (patient 2). Volume loss is marked by red colour in the roof of the left lateral ventricle. (A) Axial image. (B) Sagittal image.

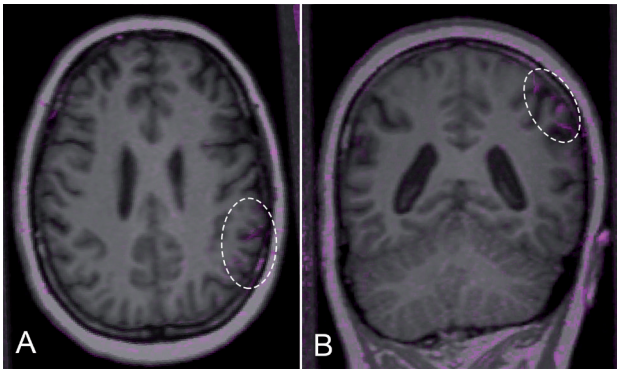


Fig. 3. Volume loss in left parietal gyri (patient 3). (A) Axial image. (B) Coronal image.

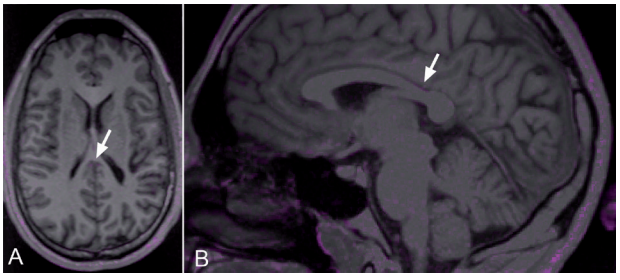


Fig. 4. Slight focal widening between the corpus callosum and the posterior cingulum (patient 4). (A) Axial image. (B) Sagittal image.

and showed a high T2 signal intensity (Fig. 1c) and high diffusion. No visually detectable changes had developed during the follow-up in the other 18 patients. The computer-aided volume comparison revealed mild focal substance loss in 3 additional patients. In the first of them (patient 2), the loss of parenchyma was localized in the corpus callosum (Fig. 2), while in the second patient (patient 3), it was localized in some gyri in the left lower parietal lobe (Fig. 3). In the third patient (patient 4) a slight focal, but bilateral, sulcal widening between the corpus callosum and the posterior cingulum was found (Fig. 4). In 14 patients, the computer-aided method did not detect any loss of substance. In two cases, the co-registration of the two examinations was suboptimal and the results could not be interpreted. One of these two patients was the patient with the hippocampal injury (patient 1) and visible substance loss described above.

Symptoms according to Rivermead Post-Concussion Symptoms Questionnaire

During the first assessment (2 or 3 days after the injury), 17 of the patients (89%) reported ≥3 symptoms. At follow-up, 7 patients (37%) reported ≥3 symptoms. The most common symptoms on both occasions were headache and fatigue.

Hospital Anxiety and Depression Scale

States of anxiety and depression are shown in Table II. The two patients with severe anxiety and/or mild to moderate depression at follow-up also reported a significantly greater number of lasting symptoms (8 and 16 remaining symptoms in RPQ, respectively) compared with a mean number of symptoms of 1.82 (median 1) in the other patients. The two patients with previous episodes of depression reported no anxiety or depression either at first investigation or at follow-up.

Rivermead Head Injury Follow-Up Questionnaire

At follow-up, 14 of the patients reported no change regarding activity and participation according to RHIFUQ, 4 reported changes in 1–3 items and 1 reported changes in 8 of the 11 items. There was a correlation between scoring a high number of changes in RHIFUQ and a high number of remaining symptoms, as well as having severe depression at follow-up.

Glasgow Outcome Scale Extended

At follow-up, 15 patients had a GOSE score of 8 and 4 had a GOSE score of 7.

Relationship of the magnetic resonance imaging findings and outcome

The patient with the hippocampal changes in the acute phase and at follow-up (patient 1) reported 4 symptoms (dizziness, nausea, fatigue and poor memory) in the first RPQ, but only 1 symptom (fatigue) at follow-up. The patient with a loss of parenchyma around the roof of the left lateral ventricle (patient 2) reported 8 symptoms (headaches, nausea, sleep disturbance, fatigue, irritability, frustration, poor memory and longer to think) in the first RPQ and 1 symptom (headaches)

Table II. *States of anxiety and depression according to the Hospital Anxiety and Depression Scale (HADS)*

	Ratings		
	None *n*	Mild to moderate *n*	Severe *n*
Anxiety			
Examination 1	17	0	2
Examination 2	13	3	2
Depression			
Examination 1	15	3	1
Examination 2	18	1	0

at follow-up. The patient with a volume loss in the left lower parietal lobe (patient 3) reported 13 symptoms (headaches, dizziness, nausea, noise sensitivity, sleep disturbance, fatigue, irritability, depression, frustration, poor memory, poor concentration, longer to think and restlessness) in the first RPQ and 6 symptoms (headaches, noise sensitivity, sleep disturbance, irritability, poor memory and double vision) at follow-up. The patient with a slight focal sulcal widening between the corpus callosum and the posterior cingulum (patient 4) reported 6 symptoms (headaches, dizziness, nausea, fatigue, irritability and depression) in the first RPQ, but no remaining symptoms at follow-up. None of them reported any anxiety or depression according to the HADS at follow-up.

Patient 1 with the hippocampal injury reported change in 2 out of 10 items regarding activity and participation according to RHIFUQ, while patients 2–4 reported no changes. All 4 patients reached upper level of good recovery according to the GOSE (i.e. score 8). Data regarding patient 1–4 are summarized in Table III.

DISCUSSION

This exploratory study included patients who fulfilled established criteria for MTBI and exhibited a typical response pattern with respect to long-term outcome. MRI, according to a study protocol that included DWI and two susceptibility-weighted sequences, revealed one trauma-related abnormality in the acute stage and at follow-up 3–7 months later. The computer-aided analyses of volume changes showed the loss of brain parenchyma in 3 additional patients. In total, the MR examinations detected atrophic changes in 4 patients. It should be pointed out that the study sample was small and the findings cannot be generalized. Data in the literature in this respect are scarce and inconsistent, but some previous reports indicate that an even more limited MRI protocol than that applied here (14, 33) may reveal traumatic pathology after MTBI. The interpretation of our observations will be discussed first with regard to the characteristics of the study sample and then with regard to the MRI methodology.

Study participants appear to be representative of the milder MTBI spectrum with regard to age and presentation of symptoms (2, 6, 27). We observed a certain occurrence of anxiety and depression, which are recognized, common co-morbidities or outcomes related to MTBI (10). Although the study design does not allow any conclusions to be drawn, interestingly, anxiety/depression according to HADS correlated with remaining symptoms according to RPQ and with activity and participation according to RHIFUQ. A somewhat larger proportion of women than expected (2, 27) participated, which may reflect a random effect, or that women perhaps are more prone to accept participation in studies that may be perceived as demanding. In fact, our study required not only an early visit after the injury, but also a later follow-up visit; both included not only clinical assessments but also MR examinations. The higher proportion of women may have increased the frequency of symptom-reporting at follow-up (10, 27). However, the small sample size does not allow any conclusions to be drawn on gender effects.

The majority of participants were examined by routine acute CT. Only one patient had uncertain trauma-related pathology, while the remaining 15 were uncomplicated in that respect. This finding is in accordance with a frequency of CT pathology to be approximately 5% in the mild part of the MTBI severity

Table III. *Characteristics of patients with signs of brain atrophy*

	Patient 1	Patient 2	Patient 3	Patient 4
Age, years	54	53	45	24
Gender	Male	Female	Female	Male
Cause of accident	Traffic	Fall	Fall	Traffic
GCS	15	15	15	15
LOC, min	2	<5	5–10	<1
RPQ 1, symptoms, first occasion, *n*	4 – dizziness, nausea, fatigue, poor memory	8 – headaches, nausea, sleep disturbance, fatigue, irritability, frustration, poor memory, longer to think	13 – headaches, dizziness, nausea, noise sensitivity, sleep disturbance, fatigue, irritability, depression, frustration, poor memory, poor concentration, longer to think, restlessness.	6 – headaches, dizziness, nausea, fatigue, irritability, depression
RPQ 2, symptoms, second occasion, *n*	1 – fatigue	1 – headaches	6 – headaches, noise sensitivity, sleep disturbance, irritability, poor memory, double vision	0
HADS 1 anxiety/depression at first occasion	No anxiety/no depression	No anxiety/no depression	No anxiety/mild depression	No anxiety/no depression
HADS 2 anxiety/depression at second occasion	No anxiety/no depression	No anxiety/no depression	No anxiety /no depression	No anxiety/no depression
RHIFUQ, variables with limited ability, *n*	2 – harder to keep standard of housing, work is tiring	0	0	0
GOSE	8	8	8	8

GCS: Glasgow Coma Scale; LOC: loss of consciousness; RPQ: Rivermead Post-Concussion Symptoms Questionnaire; HADS: Hospital Anxiety and Depression Scale; RHIFUQ: Rivermead Head Injury Follow-Up Questionnaire; GOSE: Glasgow Outcome Scale Extended.

spectrum (9, 34). However, congruent with earlier studies (7, 9), all had favourable outcomes according to GOSE.

The time increments chosen for the early and late MRI were carefully considered, taking into account the results of previous studies and clinical experience. The first time-point, i.e. on days 2 or 3 post-injury, was considered optimal in order to detect any oedema or haemorrhage, which may not be visible at the day of injury, but which may evolve during the initial days post-injury and also may wear off within 1 week. The late time-point, i.e. at 3 months or longer post-injury, would allow for atrophy to develop and be visualized. In addition to conventional sequences, MRI comprised DWI and two blood-sensitive sequences to capture early signs of DAI (35).

Earlier studies have reported the presence of MRI pathology after MTBI even in patients with normal head CT (13, 33). Compared with the present study, these studies probably included more severely injured patients at trauma centres or neurosurgical units presenting with GCS range of scores 13–15. In one study on patients with MTBI and GCS 13–15, microhaemorrhages were found in 1 of 20 patients (36). In the present study we also found pathology in 1 patient in the form of oedema at an acute stage. Some previous studies that applied both early (within 7 days after injury) and late (3–8 months) MRI demonstrated the development of atrophy after TBI (18, 19, 22) and that such atrophy may be correlated with early MRI pathology. Several of these earlier reports are based on studies of small samples and have also included participants with more severe TBI. Furthermore, the time between injury and MR examinations varies between studies and, thus, the interpretation of these data is difficult (37). The results of two specific MTBI studies are inconsistent. In a study of 17 subjects with GCS 13–15, Hofman et al. (22) reported atrophy in the form of increased ventricle-to-brain ratio, in patients (n 12) with acute MRI pathology. In contrast, Schrader et al. (21) found no atrophy or any other pathology in 18 patients diagnosed with concussion. It may be speculated that reasons for the discrepancy between these two studies include the use of a weaker MR-imager (1.0 T) and less severely injured patients in the study by Schrader (21). Interestingly, our study demonstrated volume loss in some patients within the mild MTBI spectrum. However, all these 3 studies comprised only small study samples and do not allow any firm conclusions to be drawn. Our study shows that post-traumatic volume loss can be minute, and that advanced methods are accordingly needed to detect them.

Regarding the inconsistency of data on brain pathology according to MRI after MTBI, it may not be surprising that the relationship between such pathology and clinical presentation is poorly understood. Previous studies demonstrating brain atrophy or other pathology according to MRI observed no significant correlation with cognitive functions (22, 33). Levin et al. (33) reported unintelligible differences between individuals with regard to the site of lesions and the patterns of neuropsychological findings. Another study observed a correlation between atrophy and unfavourable GOSE outcome; however in that study, only 3 out of 25 participants exhibited a mild TBI (19). In our study sample, we did not identify any obvious correlation between the location of brain pathology and number or types of symptoms, other disability or GOSE score at follow-up.

The main findings of our study must be interpreted with caution because of the small study sample and use of a new *computer-aided analysis of volume changes*. However, our study is one of the most comprehensive to date with regard to the number of participants and examining the same patients at a standardized early and late point in time after MTBI.

Further analysis of our data will include diffusion tensor imaging (DTI) results. DTI has been reported to be more sensitive than other MRI methods in detecting MTBI pathology (36, 37). Correlations have been reported between DTI pathology and cognitive function (38, 39) and clinical outcome (40). However, findings are not unequivocal regarding fractional anisotropy (FA) as an indicator in white matter injury (38, 40), and it remains unclear if DTI pathology is representative of DAI (41). The analysis of DTI data is difficult and the repeatability may be low.

Obviously, further studies are needed to clarify the role of brain pathology on MTBI outcome. There is increasing evidence that factors other than injury factors, such as pre-morbid or co-morbid illnesses or conditions, are at play (4, 6, 7, 9–11). Even though some factors offer targets for meaningful intervention to prevent and treat long-term problems after MTBI, the evidence in this respect is not very strong (34). Thus, there is a need for more effective intervention models, and a better understanding of the role of disordered brain structure and function seems crucial. Recent studies provide consistent evidence that CT pathology is not a strong predictor of outcome after MTBI (7, 9, 11), something which highlights the need for studying methods that are sensitive to pathology not detected by CT. The results of our study indicate a potential contribution of advanced MR examinations in patients within the milder spectrum of MTBI, and points to the need for further studies to uncover both structural and functional pathology.

Study limitations

This study was designed as an exploratory study to find out if MR methodology in repeated examinations may reveal pathology in patients with MTBI. The study sample was small, study participants were recruited from one emergency unit and only during restricted time-periods. Thus, the occurrence of the findings cannot be generalized to a larger MTBI population. Time to follow-up varied from 3 to 7 months after the injury, and this may have had an impact on both MR findings and clinical data at follow-up. However, participants exhibited symptoms and activity limitations similar to what is known from previous studies (4), and the findings may guide further studies in the area. Although we intended to include patients within the whole MTBI GCS spectrum, most participants had a GCS score of 15, and none had a score of 13, which reflects that the milder forms of MTBI are more frequent (42). Interestingly, all patients with signs of brain atrophy had a presenting GCS score of 15, indicating that the MR method used here may be

a relevant method in studies of these patients, which form the largest subgroup of patients with MTBI (42). The software used in volume comparisons is new and under further development. The software results might, in some cases, have been biased by the registration process, especially in cases where the patient's position changed significantly from one MRI to the other. Therefore, the volume comparison failed in two patients in our study. In summary, the results of this study are only suggestive and do not lend themselves to any generalization.

Conclusion

These findings indicate that patients with MTBI may have minor organic injuries that are not detectable by conventional radiological methods, which may be possible to visualize using more advanced methodology. The loss of brain volume after MTBI may be a sensitive MRI marker of traumatic brain pathology. Further studies are needed to clarify the prevalence of such pathology and of its clinical meaning.

ACKNOWLEDGEMENTS

The authors would like to thank research nurse Sandra Hallstrom for excellent administrative support and management of study participants.

This study was supported by grants from the Centre for Research & Development, Uppsala University/County Council of Gavleborg.

REFERENCES

1. Leibson CL, Brown AW, Long KH, Ransom JE, Mandrekar J, Osler TM, et al. Medical care costs associated with traumatic brain injury over the full spectrum of disease: a controlled population-based study. J Neurotrauma 2012; 29: 1–12.
2. Cassidy JD, Carroll LJ, Peloso PM, Borg J, Holst H, Holm J, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaboration Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; Suppl 43: 28–60.
3. Peloso P, von Holst H, Borg J. Mild traumatic brain injuries in patients admitted to hospital in Sweden during the years 1987 to 2000. J Rehabil Med 2004; Suppl 43: 22–27.
4. Carroll LJ, Cassidy JD, Peloso PM. Prognosis for mild traumatic brain injury: results of the WHO collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; Suppl 43: 84–105.
5. Jacobsson LJ, Westerberg M, Lexell J. Demographics, injury characteristics and outcome of traumatic brain injuries in northern Sweden. Acta Neurolog Scand 2007; 116: 300–306.
6. Lundin A, de Boussard C, Edman G, Borg J. Symptoms and disability until 3 months after mild TBI. Brain Injury 2006; 20: 799–806.
7. Jacobs B, Beems T, Stulemeijer M, van Vugt AB, van der Vliet TM, Borm GF, et al. Outcome prediction in mild traumatic brain injury: age and clinical variables are stronger predictors than CT abnormalities. J Neurotrauma 2010; 27: 655–668.
8. Ruff RM. Mild traumatic brain injury and neural recovery: rethinking the debate. NeuroRehabil 2011; 28: 167–180.
9. Lannsjö 2012, Eur J Neurol doi:10.1111/j.1468-1331.2012.03813.x
10. Ponsford J, Willmott C, Rothwell A, Cameron P, Kelly AM, Nelms R, et al. Factors influencing outcome following mild traumatic brain injury in adults. J Internat Neuropsychol Soc 2000; 6: 568–579.
11. Stulemeijer M, van der Werf, Borm GF, Vos PE. Early prediction of favourable recovery 6 months after mild traumatic brain injury. J Neurol Neurosurg Psychiatry 2008; 79: 936–942.
12. Povlishock JT, Katz DI. Update of neuropathology and neurological recovery after traumatic brain injury. J Neurotrauma 2005; 20: 76–94.
13. Topal NB, Hakyemez B, Erdogan C, Bulut M, Koksal O, Akkose S, et al. MR imaging in the detection of diffuse axonal injury with mild traumatic brain injury. Neurol Res 2008; 30: 974–978.
14. Lee H, Wintermark M, Gean AD, Ghajar J, Manley GT, Mukherjee P. Focal lesions in acute mild traumatic brain injury and neurocognitive outcome: CT versus 3T MRI. J Neurotrauma 2008; 25: 1049–1056.
15. Gustafsson O, Rossitti S. Ericsson A, Raininko R. MR imaging of experimentally induced intracranial hemorrhage in rabbits during the first 6 hours. Acta Radiol 1999; 40: 360–368.
16. Alemany Ripoll M, Siosteen B, Hartman M, Raininko R. MR detectability and appearance of small experimental hematomas at 1.5 T and 0.5 T. A 6–7-month follow-up study. Acta Radiol 2003; 44: 199–205.
17. Pierpaoli C, Alger JR, Righini A, Mattiello J, Dickerson R, Des Pres D, et al. High temporal resolution diffusion MRI of global cerebral ischemia and reperfusion. J Cereb Blood Flow Metab 1996; 16: 892–905.
18. Ding K, de la Plata CM, Wang JY, Mumphrey M, Moore C, Harper C, et al. Cerebral atrophy after traumatic white matter injury: correlation with acute neuroimaging and outcome. J Neurotrauma 2008; 25: 1433–1440.
19. Warner MA, Youn TS, Davis T, Chandra A, Marquez de la Plata C, Moore C, et al. Regionally selective atrophy after traumatic axonal injury. Arch Neurol 2010; 67: 1336–1344.
20. Trivedi MA, Ward MA, Hess TM, Gale SD, Dempsey RJ, Rowley HA, et al. Longitudinal changes in global brain volume between 79 and 409 days after traumatic brain injury: relationship with duration of coma. J Neurotrauma 2007; 24: 766–771.
21. Schrader H, Mickeviciene D, Gleizniene R, Jakstiene S, Surkiene D, Stovner LJ, et al. Magnetic resonance imaging after most common form of concussion. BMC Medical Imaging 2009; 9: 11.
22. Hofman PAM, Stapert SZ, van Kroonenburgh MJPG, JollesJ, de Kruijk J, Wilmink JT. MR imaging, single-photon emission CT, and neurocognitive performance after mild traumatic brain injury. Am J Neuroradiol 2001; 22: 441–449.
23. Ibanez L, Schroeder W, Ng L, Cates LNJ. The ITK software guide. NLM Insight Toolkit Publications; 2006.
24. King NS, Crawford S, Wenden FJ, Moss NE, Wade DT. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. J Neurology 1995; 242: 587–592.
25. Lannsjö M, Borg J, Björklund G, af Geijerstam JL, Lundgren-Nilsson Å. Internal construct validity of the Rivermead Post-concussion Symptoms Questionnaire. J Rehabil Med 2011; 43: 997–1002.
26. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization; 1993.
27. Lannsjö M, af Geijerstam JL, Johansson U, Bring J, Borg, J. Prevalence and structure of symptoms at three months after mild traumatic brain injury in a national cohort. Brain Injury 2009; 23: 213–219.
28. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983; 67: 361–370.
29. Crawford S, Wenden FJ, Wade DT. The Rivermead Head Injury Follow Up Questionnaire: a study of a new rating scale and other measures to evaluate outcome after head injury. J Neurol Neurosurg Psychiatry 1996; 60: 510–514.
30. Teasdale GM, Pettigrew LE, Wilson JT, Murray G, Jennett B. Analyzing outcome of treatment of severe head injury: a review and update on advancing the use of the Glasgow Outcome Scale. J Neurotrauma 1998; 15: 587–597.
31. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the Extended Glasgow Outcome

Scale: Guidelines for their use. J Neurotrauma 1998; 15: 573–585.
32. Levin HS, Boake C, Song J, McCauley S, Contant C, Diaz-Marchan P, et al. Validity and sensitivity to change of the extended Glasgow Outcome Scale in mild to moderate traumatic brain injury. J Neurotrauma 2001; 18: 575–584.
33. Levin HS, Williams DH, Eisenberg HM, High WM, Guinto FC. Serial MRI and neurobehavioural findings after mild to moderate closed head injury. J Neurol Neurosurg Psychiatry 1992; 55: 255–262.
34. Borg J, Borg J, Holm L, Cassidy JD, Peloso PM, Carroll LJ, von Holst H, et al. Diagnostic procedures in mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; Suppl 43: 61–75.
35. Kou Z, Wu Z, Tong KA, Holshouser B, Benson RR, Hu J, et al. The role of advanced MR imaging findings as biomarkers of traumatic brain injury. J Head Trauma Rehabil 2010; 25: 267–282.
36. Smits M, Houston GC, Dippel DW, Wielopolski PA, Vernooij MW, Koudstaal PJ, et al. Microstructural brain injury in post-concussion syndrome after minor head injury. Neuroradiology 2011; 53: 553–563.
37. Ross DE. Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury. Brain Injury 2011; 25: 1271–1278.
38. Lipton ML, Gulko E, Zimmerman ME, Friedman BW, Kim M, Gellella E, et al. Diffusion-tensor imaging implicates prefrontal axonal injury in executive function impairment following very mild traumatic brain injury. Radiology 2009; 252: 816–824.
39. Kraus MF, Susmaras T, Caughlin BP, Walker CJ, Sweeney JA, Little DM. White matter integrity and cognition in chronic traumatic brain injury: a diffusion tensor imaging study. Brain 2007; 130: 2508–2519.
40. Bazarian JJ, Zhong J, Blyth B, Zhu T, Kavcic V, Peterson D. Diffusion tensor imaging detects clinically important axonal damage after mild traumatic brain injury: a pilot study. J Neurotrauma 2007; 24: 1447–1459.
41. Johnson VE, Stewart W, Smith DH. Axonal pathology in traumatic brain injury. Exp Neurol 2012 jan 20 [Epub ahead of print].
42. Teasdale GM. Head injury. J Neurol Neurosurg Psychiatry 1995: 526–539.

J Rehabil Med 2013; 45: 729–733

ORIGINAL REPORT

MOTOR PROFICIENCY IN CHILDREN WITH MILD TRAUMATIC BRAIN INJURY COMPARED WITH A CONTROL GROUP

Ewa Dahl, MSc[1] and Ingrid Emanuelson, MD, PhD[2]

From the [1]Medical Rehabilitation Clinic, Borås Hospital, Borås and [2]Institution for Clinical Sciences, Department of Paediatrics, University of Gothenburg, Gothenburg, Sweden

Objective: **To assess motor proficiency and movement disorders in children with mild traumatic brain injury compared with an uninjured control group. Inclusion criteria were based on the definitions issued by the American Congress of Rehabilitation Medicine.**

Subjects: **A group of 27 children with mild traumatic brain injury (age range 4–17 years) and a control group of 79 healthy children.**

Methods: **Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) was administered. This is a standardized comprehensive test of gross- and fine-motor function that produces standard scores for children in this age group. It is divided into 4 gross-motor tasks, 3 fine-motor tasks, 1 combined task, and a test of hand and foot dominance. Tremor was also evaluated.**

Results: **The mean standard scores for both groups were within the normal range. For balance, the mild traumatic brain injury group had a significantly poorer performance than controls ($p = 0.03$). Tremor was significantly more frequent in the mild traumatic brain injury group ($p = 0.004$), and mixed-handedness was significantly over-represented in the mild traumatic brain injury group ($p = 0.02$).**

Conclusion: **In this study, children with mild traumatic brain injury did not differ from the norm in terms of fine- or gross-motor proficiency compared with a control group of uninjured children, but a difference in balance skill ($p = 0.03$), mixed-handedness ($p = 0.02$) and tremor ($p = 0.004$) was detected, to the injured children's detriment.**

Key words: motor function; mild TBI; children; control study.

J Rehabil Med 2013; 45: 729–733

Correspondence address: Ingrid Emanuelson, Habilitering och Hälsa, Näverlursgatan 38, SE-42144 Västra Frölunda, Sweden. E-mail: ingrid.emanuelson@vgregion.se

Accepted April 23, 2013

INTRODUCTION

Head injuries are common; one-third of all newborns world wide will experience a head injury before the age of 16 years and between 80–95% of the injuries are mild (1). In a recent World Health Organization (WHO) study, the mean annual incidence of mild traumatic brain injury (MTBI) at all ages is estimated to be at least 600 per 100,000 inhabitants (2). In a recently published study from Sweden, the annual incidence of MTBI in children (0–17 years) was found to be 468/100,000 (3), which is in agreement with, and comparable to, a Swedish adult population (16–65 years of age) (4).

However, definitions of MTBI vary considerably (5), and this makes it difficult to compare the severity and outcome for this group (6).

Several studies highlight the fact that post-traumatic complaints or post-concussion syndrome (PCS) exist after MTBI and, in some cases, persist for years (2, 6, 7). To date, there are no national guidelines for follow-up after MTBI that include motor function. In Sweden MTBI is regarded as a relatively harmless injury with complete recovery within a couple of weeks (6, 8–10).

Movement disorders after MTBI are usually described in the literature as mild and transient, and severe movement disorders are rare (6, 7, 10, 11). The term "movement disorder" is used to encompass tremors, hypokinetic syndromes and "extra-pyramidal" symptoms. Koller and co-workers (8) found post-traumatic movement disorders in 10% of patients after mild or moderate head injury, the majority of these patients had transient mild tremor, and persistent movement disorders were only rarely detected. No disabling transient low-amplitude postural/intention tremor was found in this group (8). However, Kuhtz-Buschbeck (12) reported that hand motor skills improve less than gait within 5 months after injury. Functional motor function and control are affected 1–2 years after TBI (12), whereas reaction time and movement duration are prolonged. Co-ordination deficits are also frequent (10).

Fine-motor skills are often included in neuropsychology tests, and several studies have been published in this area (2, 13). Only a few studies of gross- as well as fine-motor proficiency post-trauma for MTBI in children have been published (5, 6, 10, 14, 15).

Another complication after severe and moderate head injury is reduced dynamic balance, but this has been only sparsely studied after MTBI (15, 16). According to Rosenblum et al. (17), postural control/balance is defined as the ability to maintain the centre of body mass or a body part over a stable or moving base of support. Gagnon et al. (15) studied a group of injured children and a control group, and found that children with MTBI scored significantly worse than controls in the balance subtest.

Aim

The aim of this study was to assess general motor proficiency and movement disorders in a group of children over 4 years of age, 3–6 months after a MTBI, and compare their performance with an uninjured control group using the Bruininks-Oseretskys Test of Motor Proficiency.

PATIENTS AND METHODS

Series

The MTBI group consisted of children, age range 0–17 years, registered in a Brain Injury Register (BIR) at Boras Hospital in two different 6-month periods (in 1999 and 2000).

Inclusion criteria were: all children aged 0–17 years fulfilling the criteria for MTBI according to the American Congress of Rehabilitation Medicine (ACRM). MTBI is considered present if any of the following criteria are fulfilled: focal neurological deficit(s) that may not be transient; but where the severity of the injury does not exceed the following: any period of loss of consciousness (LOC) of 30 min or less; any loss of memory for events immediately before or after the accident lasting less than 24 h, or a Glasgow Coma scale (GCS) score of 13–15, 30 min after the injury (18).

Children living in provinces outside the County of South Alvsborg, and children with injuries more severe than MTBI, were excluded.

The study comprised 192 children, 54 of whom agreed to evaluation. Of these, 11 did not attend for evaluation. A total of 43 children were evaluated (a further one was excluded because of myelomeningocele). They were all offered a post-concussion examination (PCE) 3–6 months after injury. The PCE included a motor skills examination, the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) test for children older than 4 years. Of the remaining 42 children, 27 were older than 4 years of age and were eligible for this study.

Control group

A total of 294 children aged 0–17 years, from a school situated in Boras were asked by their parents to participate as a control group. Inclusion criteria were: healthy children with no known concussion or brain injury. Originally 99 children agreed to participate as controls, but 6 were excluded because of a previous concussion episode, thus 93 remained. Of these, 88 children attended the evaluation, 79 of whom were older than 4 years of age and were included in this study.

The study was approved by the ethics committee at Sahlgrenska University Hospital, Gothenburg, Sweden.

Measurements

The complete battery of the English version of the BOTMP (19) was used for the examination. This test is a standardized comprehensive battery of gross- and fine-motor measurements that produces standard scores for children in the age range 4–14 years. The BOTMP consists of 3 composites, and the reliability of these parts is tested using the coefficient alpha; gross-motor function ($r = 0.77$), fine-motor function ($r = 0.88$) and general-motor function ($r = 0.89$). The test is divided into 8 sub-tests: 4 gross-motor tasks, 3 fine-motor tasks, and 1 combined task, comprising 46 separate items and a test for hand and foot dominance. The sub-test standard score has a mean of 15 (standard deviation (SD) 5). Standard scores are interpreted as "below average performance" in groups with scores between 6 and 11, and as "low performance" for scores of less than 6. The composites are expressed as normalized standard scores with means of 50 (SD 10). Hand preference and foot dominance are recorded from one catching and one kicking item using a tennis ball. During the test, any changes in hand or foot preference are noted. Administration of the complete battery took between 45 and 60 min (19).

Any visible hand tremor during the activities was noted.

Mild traumatic brain injury group

The children in the MTBI group ($n = 27$) were all examined at the local habilitation centre. All examinations were performed by the same physiotherapist and the same child neurologist.

Control group

The children in the control group ($n = 79$) were examined in the same manner and by the same physiotherapist as the children with MTBI, but the examinations were carried out at their school during school hours.

Statistics

All statistical analyses were carried out using the SPSS®. Descriptive methods were used for the mean, median, age and gender. As the samples were small, non-parametric statistics were used for comparing the groups (Mann-Whitney U test and Pearson's χ^2 test). Statistical significance was set at $p \leq 0.05$. For comparisons between groups, a logistic regression model was used (Fisher's exact test), and for variances Levene's test for equality of variances was used.

RESULTS

This study is based on 27 children with MTBI, age range 4–17 years, mean age 8.6 years (SD 2.6, standard error (SE) ± 0.5), and a control group of 79 children in the same age range, mean age 8.7 years (SD 2.4, SE ± 0.3).

The MTBI group comprised 16 (59%) boys and 11 (41%) girls, and the control group comprised 41 (52%) boys and 38 (48%) girls. The groups were not initially matched by age and gender, although there were no significant differences between the groups (Table I) according to age and gender.

Bruininks-Oseretsky Test of Motor Proficiency

The mean standard score results for the BOTMP in both groups, were all within the range of normal performance (15 ± 5 points).

A significant difference between the groups (MTBI and controls) could be seen only in capacity for balance ($p = 0.03$) and a tendency towards a difference in fine-motor dexterity ($p = 0.07$). Complete results for the BOTMP are given in Table II.

The mean standard scores for each sub-test were within the range for normal performance. A significant difference between the groups ($p \leq 0.05$) was revealed only for balance ($p = 0.03$).

Tremor

Tremor was more common in the MTBI group; 8 children in the MTBI group ($n = 27$) had visible tremor in their hands during fine-motor activities, compared with 6 ($n = 79$) children in the control group ($p = 0.004$).

Table I. *Number and age distribution of all children examined by the Bruininks-Oseretsky Test of Motor Proficiency*

Group	Number	Mean age	SD	SE	CI
MTBI	27	8.6	2.6	0.5	–1.18 to 0.98
Controls	79	8.7	2.4	0.3	–1.2 to 1.0

MTBI: mild traumatic brain injury; SD: standard deviation; SE: standard error; CI: confidence interval.

Table II. *Bruininks-Oseretsky Test of Motor Proficiency results: the 4 subtests of gross-motor function and upper-limb co-ordination and the 3 subtests of fine-motor function*

	MTBI group $n=27$			Control group $n=79$			
	Mean (SD)	Median	Range	Mean (SD)	Median	Range	*p*-value
Gross-motor function							
Running speed and agility[a]	9.1 (4.9)	9	1–17	9.9 (3.9)	11	1–17	Ns
Balance	15.4 (4.4)	15	1–20	17.4 (4.7)	18	1–26	0.03
Bilateral co-ordination	17 (5.1)	17	1–19	18.4 (3.7)	19	1–19	Ns
Strength	16.3 (6.1)	17	1–28	17.1 (4.8)	17	1–21	Ns
Upper-limb co-ordination	16.2 (4)	17	1–17	17 (4.5)	17	1–24	Ns
Fine-motor function							
Response speed	16.9 (6.2)	16	1–22	19.1 (5.6)	19	1–24	Ns
Visio-motor control	17.2 (5)	18	1–22	18.3 (4.5)	19	1–25	Ns
Dexterity	11.9 (7)	10	1–25	13.7 (4.7)	14	1–23	Ns

[a]$n=78$.
Standard score [15 ± 5 points].
Ns: not significant; SD: standard deviation; MTBI: mild traumatic brain injury.

Handedness

Several children in the MTBI group used both hands (mixed-handed) in fine-motor activities, instead of having a left- or right-hand dominance (Table III).

There was a positive relationship between upper-limb speed and dexterity and hand dominance. It appears that right-handed children perform tasks more quickly than left or mixed-handed children (SE ± 5.2, $p=0.05$).

According to the above results a linear regression analysis (Fisher's exact test) was conducted between the groups' (dominators), handedness (right-handed and mixed-handed) balance, fine-motor control, dexterity and tremor (numerators). The results indicate that children with MTBI run an increased risk of developing tremor in their hands (relative risk (RR) = 0.068, SE ± 0.90, $p=0.03$) and developing balance problems (RR = 1.11, SE ± 0.06, $p=0.07$). The analysis also indicated an increased risk of being afflicted with MTBI if the child was mixed-handed compared with a dominant right-handedness (RR = 9.95, SE ± 0.82, $p=0.005$). Age or gender had no impact on the results.

Subgroups

Sub-groups were detected in both the MTBI group and the control group. The sub-groups consisted of the children who performed less than the standard norm in one or several subtests of the BOTMP. The sub-groups comprised 19 (70%) children from the MTBI group, 11 boys and 8 girls, mean age 9.0 years (SD 2.6, SE ± 0.6) and 45 (59%) controls, 21 boys and 24 girls, mean age 9.2 years (SD 2.4, SE ± 0.4). There were no significant differences in performance between MTBI and control groups, except for bilateral co-ordination ($p=0.05$) and strength ($p=0.05$) (Levene's test for equality of variances), but the results were still within the standard norms for age and gender (Table IV).

Table III. *Distribution of children with respect to handedness*

BOTMP	MTBI $n=27$	Controls $n=79$	*p*-value
Hand preference			
Right-handed	17 (63%)	68 (86%)	Ns
Left-handed	1 (4%)	0	Ns
Mixed-handed	9 (33%)	11 (14%)	**0.02**

Statistically significant result are marked in bold.
BOTMP: Bruininks-Oseretsky Test of Motor Proficiency; MTBI: mild traumatic brain injury; Ns: not significant.

DISCUSSION

The design of this study is prospective from a BIR. The children were encouraged by their parents, 3–6 months after the injury, to participate in the project.

Concussion is a common occurrence. The guidelines for follow-up after the injury have been inadequate, and there has been a tendency for both the healthcare system and the general public to play down any consequences. To ensure the reliability of our results, a control group was tested.

Table IV. *Distribution of standard scores for the mild traumatic brain injury (MTBI) and control groups*

	BOTMP		Controls $n=45$		
Subtest	Mean (SD)	SE	Mean (SD)	SE	*p*-value
Running speed and agility	7.6 (4.9)	1.1	7.7 (3.6)	0.55	0.19
Balance	14.7 (4.6)	1.05	17.4 (4.7)	0.74	0.54
Bilateral coordination	15.9 (5.3)	1.21	16.7 (3.9)	0.57	**0.05**
Strength	15.2 (6.8)	1.57	15.4 (4.2)	0.63	**0.05**
Upper limb coordination	15.6 (4.2)	0.97	15.6 (5.2)	0.78	0.38
Response speed	16.2 (6.6)	1.51	17.5 (5.6)	0.83	0.39
Visio-motor control	16.1 (5.3)	1.23	17.1 (5.1)	0.76	0.73
Fine-motor control and dexterity	9.2 (5.7)	1.30	12.0 (4.7)	0.70	0.79

Statistically significant result are marked in bold.
Standard score [15 ± 5 points].
BOTMP: Bruininks-Oseretsky Test of Motor Proficiency; SE: standard error; SD: standard deviation.

The BOTMP is useful as a test for comparing groups and evaluating differences between them (19, 20, 21). The test battery is easy to administer, giving instructions is straightforward, the items are independent of age and gender, and the children find the test interesting and enjoyable to perform. In our study we used the English version, as no Swedish version is available as yet, and our plan was not to validate it to Swedish conditions. We feel that there are no crucial differences between Swedish and Canadian children in terms of their motor activity and ability. At the time of our study only the first edition of the BOTMP was available (19). In this study we have not collected facts about the children's motor performance pre-injury and cannot, with absolute certainty, state whether their motor behaviour was changed post-injury.

Fine-motor control and balance

In the present study the BOTMP test in 27 children with acquired MTBI and 79 controls indicated that the MTBI group performed less well in sub-tests of fine-motor control and dexterity ($p = 0.07$), which agrees with the findings presented by Chaplin and co-workers (5). They evaluated 14 patients 16 months or later after injury using the BOTMP, and reported that upper-limb speed and dexterity were significantly poorer than the other fine-motor sub-tests.

In our study balance was significantly poorer in the MTBI group compared with the control group ($p = 0.03$), but it was still in the range of normality. In the literature to date, cognitive problems after MTBI are more frequently discussed than motor problems. However, several research teams have found that balance problems are frequently involved in both mild injuries and more serious TBI (20–24). Gagnon et al. (15, 16) have suggested that a significant number of children sustaining an MTBI present some form of postural instability during the first 3 months after the injury, and the risk of another injury will therefore increase.

Tremor

The results indicated that children with MTBI run an increased risk of developing tremor in their hands (RR = 0.068, SE ± 0.90, $p = 0.03$), and the occurrence of tremor in the MTBI group ($p = 0.004$) compared with the control group was significant. Hand tremor was not tested specifically, but it was noted in the clinical examination by both the physiotherapist and the child-neurologist independently of each another.

Tremor post-head injury is well-described in the literature, but it is rarely seen after MTBI (6, 11, 14). When it occurs it is often as a non-disabling, low-amplitude, postural and kinetic tremor and might be seen as a post-concussion symptom (11, 24–26). In our study, tremor was observed during fine-motor activities and had no impact on the child's fine-motor function.

Handedness

In the present study 9/27 children (33%) (mean age 7.8 years) in the MTBI group displayed mixed-handedness, compared with 11/79 (14%) (mean age 6.6 years) in the control group ($p = 0.02$). A stable hand preference can be expected at approximately 3 years of age (27). The literature describes changes in hand dominance after severe TBI, but this is rarely described after MTBI (28, 29). On the other hand, our analysis indicated an increased risk of having MTBI if the child was mixed-handed compared with a dominant right-handedness (RR = 9.95, SE ± 0.82, $p = 0.005$). Age or gender had no impact on the results. In a recent study, Domellöv et al. (28) suggested that left- and/or non-right-handedness is over-represented in children with a history of preterm birth associated with brain insult. The children in this study were all born at term with no previous history of brain injury of any kind.

Subgroups

A statistical analysis was conducted for children performing below norm in any of the BOTMP's sub-tests. A sub-group consisting of 19 children with MTBI (19/43) and 45 controls (45/79) was then detected. Significant differences were found between the injured children and the controls for the sub-tests of bilateral co-ordination and strength ($p = 0.05$). The problems with bilateral co-ordination are in agreement with the findings of Kusch-Buschbeck and co-workers from 2003 (12).

Study strengths and weaknesses

This study was initially designed as a prospective follow-up study, as described elsewhere (3). In order to compare motor proficiencies between the groups the BOTMP test was used. The BOTMP is internationally well known and validated and has been used in several studies for the purpose of testing motor proficiency in children with varying diagnoses (5, 19, 21). All the children in the MTBI group were examined between 3 and 6 months' post-injury by the same physiotherapist and the same child neurologist.

The drop-out rate was high, despite several reminders, and only 21% (27 of 130) in the MTBI group attended the follow-up. Although the drop-out rate was high, the patients did not differ from the whole group of children ($n = 192$) in terms of severity of injury, loss of consciousness and post-traumatic amnesia (3). We can only speculate about why so few parents with injured children wanted to participate in a follow-up post-injury. It may be that they did not consider it important, or that the children had no obvious or emerging problems or symptoms following trauma and a follow-up survey was therefore not a priority.

Conclusion

The results of this study indicate that children with MTBI do not differ from the norm in terms of fine- or gross-motor proficiency, compared with a control group of uninjured children. However, a difference in balance skill ($p = 0.03$), mixed-handedness ($p = 0.02$), and tremor ($p = 0.004$) was detected, to the injured children's detriment. The number of children included in the study was limited, however. Further studies are desirable in order to develop adequate follow-up routines for this group of patients.

ACKNOWLEDGEMENTS

This study was supported by grants from the Alice Svensson's Memorial Fund at The Hospital of South Alvsborg, SÄS, Sweden. The authors are especially grateful to the parents and their children who participated in the study.

REFERENCES

1. Yeates KO. Mild traumatic brain injury and postconcussive symptoms in children and adolescents. J Int Neuropsychol Soc 2010; 16: 953–960.
2. Carroll LJ, Cassidy JD, Peloso PM, Borg J, von Holst H, Holm L, et al. Prognosis for mild traumatic brain injury: results of the WHO collaborating centre task force on mild traumatic brain injury. J Rehabil Med 2004 Suppl 43: 84–105.
3. Dahl E, v Wendt L, Emanuelson I. A prospective, population based, follow-up study of mild traumatic brain injury in children. Injury 2006; 37: 402–409.
4. Andersson EH, Björklund R, Emanuelson I, Stålhammar D. Epidemiology of traumatic brain injury: a population based study in western Sweden. Acta Neurol Scand 2003; 107: 256–259.
5. Chaplin MS, Deitz J, Jaffe KM. Motor performance in children after traumatic brain injury. Arch Phys Med Rehabil 1993; 74: 16.
6. Dumas HM, Carey T. Motor skill and mobility recovery outcomes of children and youth with traumatic brain injury. Phys Occup Ther Pediatr 2002; 22: 444–459.
7. Jaffe KM, Polissar NL, Fay GC, Liao S. Recovery trends over three years following pediatric traumatic brain injury. Arch Phys Med Rehabil 1995; 76: 17–26.
8. Coller WC, Wong GF, Lang A. Posttraumatic movement disorders: a review. Mov Disord 1989; 4: 20–36.
9. De Kruijk JR, Leffers P, Menheere PPCA, Meerhoff S, Rutten J, Twijnstra A, et al. Prediction of post-traumatic complaints after mild traumatic brain injury: early symptoms and biomechanical markers. J Neurol Neurosurg Psychiatry 2002; 73: 727–732.
10. O'Flaherty SJ, Chivers A, Hannan TJ, Kendrick LM, McCartney LC, Wallen MA, et al. The Westmead Pediatric TBI Multidisciplinary Outcome Study: use of functional outcomes data to determine resource prioritization. Arch Phys Med Rehabil 2000; 81: 723–729.
11. Krauss JK, Tränkle R, Kopp K-H. Posttraumatic movement disorders after moderate or mild head injury. Mov Disord 1997; 12: 428–431.
12. Kuhtz-Buschbeck JP, Hoppe B, Gölge M, Dreesmann M, Damm-Stünitz U, Ritz A. Sensorimotor recovery in children after traumatic brain injury: analysis of gait, gross motor and fine motor skills. Dev Med Child Neurol 2003; 45: 821–828.
13. Knights RM, Ivan LP, Ventureya EC, Bentivoglio C, Stoddart C, Winogron W. The effects of head injury in children on neuropsychological and behavioural functioning. Brain Inj 1991; 5: 339–345.
14. Quinn B, Sullivan SJ. The identification by physiotherapists of the physical problems resulting from a mild traumatic brain injury. Brain Inj 2000; 14: 1063–1076.
15. Gagnon I, Friedman D, Swaine B, Forget R. Balance findings in a child before and after a mild head injury. J Head Trauma Rehabil 2001; 16: 595–602.
16. Gagnon I, Swaine B, Friedman D, Forget R. Children show decreased dynamic balance after mild traumatic brain injury. Arch Phys Med Rehabil 2004; 85: 444–452.
17. Rosenblum S, Josman N. The relationship between postural control and fine manual dexterity. Phys Occupat Ther Pediatr 2003; 23: 47–60.
18. Kay T, Harrington DE, Adams R, Andersen T, Berrol S, Cicerone K, et al. Definitions of mild traumatic brain injury. J Head Trauma Rehabil 1993; 8: 86–87.
19. Bruininks R. Bruininks-Oseretsky test of motor proficiency. 1978 American Guidance Service, Inc. 1401, Woodland Road Circle Pines, MN 55014-1798.
20. Guskiewicz KM, Ross SE, Marshall SW. Postural stability and neuropsychological deficits after concussion in collegiate athletes. J Athl Train 2001; 36: 263–273.
21. Crock RV, Horvat M, McCarthy E. Reliability and concurrent validity of the movement assessment battery for children. Percept Motor Skills 2001; 93: 275–280.
22. Keren O, Reznic J, Grosswasser Z. Combined motor disturbances following severe traumatic brain injury: an integrative long-term treatment approach. Brain Inj 2001; 15: 633–638.
23. Cohen JS, Gioia G, Atabaki S, Teach SJ. Sports-related concussions in pediatrics. Curr Opin Pediatr 2009; 21: 288–293.
24. Biary N, Cleeves L, Findley L, Koller WC. Post-traumatic tremor. Neurology 1989; 39: 103–106.
25. Bawden HN, Knights RM, Winogron HW. Speeded performance following head injury in children. J Clin Exp Neuropsychol 1985; 7: 38–54.
26. Wong GF, Lang A. Posttraumatic movement disorders: a review. Mov Disord 1989; 4: 20–36.
27. Rönnqvist L, Domellöv E. Quantitative assessment of right and left reaching movements in infants: A longitudinal study from 6–36 months. Dev Psychobiol 2006; 48: 444–459.
28. Domellöf E, Johansson AM, Rönnqvist L. Handedness in preterm born children: a systematic review and a meta-analysis. Neuropsychologia 2011; 49: 2299–2310.
29. O'Callaghan MJ, Burn YR, Mohay HA, Rogers Y, Tudehope DI, et al. The prevalence and origins of left hand preference in high risk infants, and its implications for intellectual, motor and behavioral performance at four and six years. Cortex 1993; 29: 617–627.

J Rehabil Med 2013; 45: 734–740

ORIGINAL REPORT

SEVERE TRAUMATIC BRAIN INJURY IN NORWAY: IMPACT OF AGE ON OUTCOME

Cecilie Røe, MD, PhD[1,2], Toril Skandsen, MD, PhD[3,4], Audny Anke, MD, PhD[6,7], Tiina Ader, MD[12], Anne Vik, MD, PhD[3,5], Stine Borgen Lund, MSc[5], Unn Manskow, MPH[6,7], Snorre Sollid, MD, PhD[8], Terje Sundstrøm, MD, PhD[9,10,11], Morten Hestnes, RN[13] and Nada Andelic, MD, PhD[1]

From the [1]Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval, [2]Faculty of Medicine, University of Oslo, Oslo, [3]Department of Neuroscience, Faculty of Medicine, Norwegian University of Science and Technology (NTNU), [4]Department of Physical Medicine and Rehabilitation and [5]Department of Neurosurgery, St Olavs Hospital, Trondheim University Hospital, Trondheim, [6]Department of Rehabilitation, University Hospital of North Norway, [7]Faculty of Health Sciences, Institute of Clinical Medicine, University of Tromsø, [8]Department of Neurosurgery, University Hospital of North Norway, Tromsø, [9]Department of Neurosurgery, Haukeland University Hospital, [10]Department of Biomedicine and [11]Department of Surgical Sciences, University of Bergen, [12]Department of Physical Medicine and Rehabilitation, Haukeland University Hospital, Bergen and [13]Trauma Registry, Oslo University Hospital, Ulleval, Oslo, Norway

Objective: **The aim of this study was to investigate the influence of age on mortality and 3-month outcome in a Norwegian cohort of patients with severe traumatic brain injury.**
Methods: **Norwegian residents ≥16 years of age who were admitted with a severe traumatic brain injury to the country's 4 major trauma centres in 2009 and 2010 were included, as were adults (16–64 years) and elderly patients (≥65 years).**
Results: **Half of the adult subjects and 84% of the elderly subjects were injured by falls. One-third of the adults and half of the elderly subjects were admitted to a local hospital before being transported to a regional trauma hospital. Subdural haematomas were more frequent in the elderly subjects. One-quarter of adults and two-thirds of the elderly subjects died within 3 months. At 3 months, 41% of the adult survivors were still in-patients, mainly in rehabilitation units (92%). Of the surviving elderly subjects, 14% were in-patients and none were in rehabilitation units. There was no difference in functional level for survivors at the 3-month follow-up.**
Conclusion: **Old age is associated with fall-induced severe traumatic brain injury and high mortality rates. Less intensive treatment strategies were applied to elderly patients in the present study despite high rates of haemorrhage. Few surviving elderly patients received rehabilitation at 3 months post-injury.**

Key words: traumatic brain injury; aged; treatment; outcome; prognosis.

J Rehabil Med 2013; 45: 734–740

Correspondence address: Cecilie Røe, Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval, Oslo, Norway. E-mail: e.c.t.roe@medisin.uio.no

Accepted April 23, 2013

INTRODUCTION

Traumatic brain injury (TBI) is recognized as a major health problem, with 15% of the patients with TBI admitted to trauma centres having severe TBI (1). These patients require intensive medical care and long-term rehabilitation (2). Mortality after TBI is higher than for other injuries and is nearly 30% for severe TBI (3). Some patients with severe TBI develop long-standing deficits that interfere with independent living, reduced levels of functioning and restrictions on activities (4). Several factors are associated with mortality and unfavourable outcome, with age and injury severity being the dominating determinants (5, 6).

Cardiac co-morbidity and coagulopathy are well-known risk factors that significantly increase overall mortality in elderly patients with TBI (7). With increasing age, autoregulatory capacity decreases, resulting in diminished cerebrovascular control (8). Moreover, as indicated by animal studies, there is prolonged acute oedema, increased permeability of the blood–brain barrier and increased neurodegeneration in the ageing brain following injury (9).

Evidence also suggests that elderly people are treated less aggressively than younger people (10), and that it would be beneficial to increase the treatment intensity for this large group of patients (11). However, treatment choices can be more difficult when treating elderly patients. An unconscious state may be interpreted by emergency staff as the result of a cardiovascular episode rather than a TBI. Treatment strategies may be influenced by the fear that rescuing elderly patients from death may result in a vegetative or very low functional status (12). To provide sound management guidelines for elderly patients, there is a need for more knowledge about the impact of age on injury characteristics and treatment choices.

The aim of this study was therefore to investigate the influence of age on mortality and 3-month outcome in a Norwegian cohort of patients with severe TBI.

MATERIAL AND METHODS

Design and study region

This project was a prospective, multicentre, cohort study, comprising patients admitted with severe TBI to the regional hospitals in all 4

health regions in Norway. Norway has a land area of 323,758 km^2 and an adult population (aged >16 years) of 3.8 million (Statistics Norway). There is a public, 3-level hospital structure, with local hospitals serving small areas, central hospitals serving larger areas (counties) and a total of 5 university hospitals serving these hospitals in a regional manner.

Inclusion

Norwegian residents ≥16 years of age who were admitted to their regional trauma centres within 72 h of a severe TBI were considered for inclusion in this study. Severe TBI was defined by International Classification of Diseases – 10th revision (ICD 10) criteria (S06.1–S06.9) and a Glasgow Coma Scale (GCS) score between 3 and 8 within the first 24 h after injury. The regional trauma centres were the University Hospital of North Norway for the northern region, St Olav's Hospital Trondheim University Hospital for the middle region, and Oslo University Hospital for the south-eastern region. In the western part of the country, patients are equally distributed between Haukeland University Hospital and Stavanger University Hospital. Unfortunately, Stavanger University Hospital was not able to participate. Exclusion criteria were chronic subdural haematomas (SDH), pre-injury cognitive disability, and severe psychiatric disease or drug abuse. This study was approved by the regional Committee for Medical Research Ethics, South-East Norway.

During the study period (January 2009 to January 2011), 276 patients were eligible for inclusion: 42 in the northern region, 40 in the middle, 16 in the west, and 178 in the south-east. Five patients did not consent to participate in the interviews at 3-month follow-up (4 from the south-east and 1 from the north) and were omitted from the analysis. Hence, 271 patients were included (Fig. 1).

Data collection

Data registration was based on a systematic review of hospital journals (paper and electronic records) and data from the trauma registries in the west and south-east. Trauma scores from the northern and middle regions were calculated by certified professionals. Supplementary information regarding demographic data and functional levels was collected from relatives of the patients or, preferably, from the patients themselves using a standardized telephone interview 3 months after the injury occurred.

Demographic and injury characteristics

The subjects were classified as adults (16–64 years) or elderly subjects (≥65 years), a dichotomization commonly employed for developed countries (www.who.int/healthinfo/survey/ageingdefnolder/en/index.html). The ICD-10 diagnoses of comorbid conditions were recorded and categorized anticoagulant status was defined by the use of warfarin or platelet inhibitors. The influence of alcohol or other substances at admission was categorized as yes or no, based on clinical judgement and blood or urine analysis, when available. Transport time from accident scene to the initial hospital was recorded. Intermediate stays at local hospitals prior to admittance to the trauma centre was recorded as yes or no.

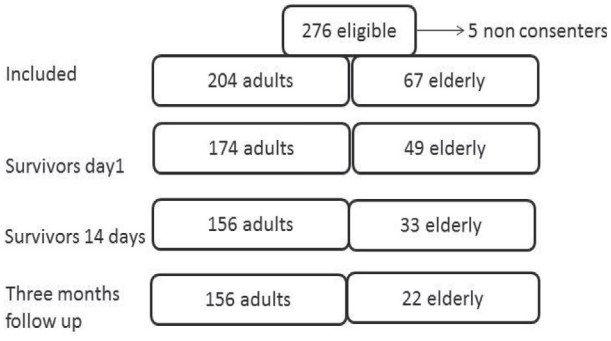


Fig. 1. Included and 3-month surviving adults and elderly patients.

Injury-related variables

The GCS score was assessed at the accident scene and at hospital admittance; we recorded the lowest GCS score recorded within the first 24 h. The duration of post-traumatic amnesia (PTA) was categorized as <7, 7–13, 14–20, 21–27 or >27 days (13). The Injury Severity Score (ISS) version 2008 was applied to indicate overall trauma severity.

The computed tomography (CT) findings were described according to the presence of contusions and haemorrhages (epidural, subdural and subarachnoid). These findings were also categorized according to the Rotterdam CT classification. The Rotterdam CT score is based on the compression of basal cisterns, midline shift, epidural mass lesion and intraventricular blood or subarachnoid hemorrhage and is scored from 1 (least severe) to 6 (most severe). The scan showing the greatest injury severity was used for scoring. The Rotterdam CT scores were interpreted by one neuroradiologist at each trauma centre for the northern and south-eastern regions, and a neurosurgeon for the western and middle regions.

Medical complications and interventions

Hypoxia was defined as at least one episode of oxygen saturation (SaO_2) <90% before or after admittance to a hospital. Hypotension was defined as at least 1 episode of systolic blood pressure (BP) <90 mmHg before or after admittance to a hospital. Cerebral perfusion pressure (CPP) was classified as reduced when it was <60 mmHg; an intracranial pressure (ICP) of >30 mmHg was categorized as elevated; and pyrexia was defined as 1 or more recordings of a body temperature (temp) of >38ºC. The ICD-10 diagnoses of medical complications were recorded and categorized for analytical purposes as present or absent. Patients who received any type of surgery, including ICP monitoring, cerebrospinal fluid (CSF drainage), craniotomy and craniectomy were registered as yes and others as no. The administration of mannitol, hypertonic saline, vasopressors, anti-epileptics or antipsychotics was also recorded as yes or no. The number of days on a respirator and number of days with active sedation were recorded. Treatment with tracheostomy and percutaneous endoscopic gastrostomy (PEG) was similarly dichotomized.

Early outcome

We registered all deaths within the first 3 months after injury. Residency at 3 months was categorized as "at home" or "not at home" (hospital, rehabilitation units, or nursing homes). The global functional outcome at 3 months was evaluated in survivors using a structured interview with the Glasgow Outcome Scale Extended (GOSE) (14).

Data analysis and statistics

Data are presented as the mean value with SD or the median value with 95% confidence intervals (CI) and range for skewed data. The χ^2 test for contingency tables was used to detect associations between categorical independent variables. Age was dichotomized into adults (16–64 years) and elderly subjects (≥65 years) for these analyses. Percentages or odds ratios (OR) and CI are presented for dichotomized variables across the age categories. Independent *t*-tests or the Mann-Whitney *U* test were applied to compare normally distributed and skewed values, respectively, in adults and elderly people.

Binary logistic regression was applied to investigate the effect of age (adult = 0/elderly = 1) on intubation (yes = 0/no = 1) at the accident scene, controlling for the GCS score at the accident scene (a log-transformed score value due to skewed distribution) and the injury mechanism (fall = 0, other injuries = 1).

Binary logistic regression analysis was applied to examine the effect of age on mortality (0 = dead, 1 = survival at 3 months), residence (0 = hospital, 1 = home) and GOSE score at 3 months. GOSE scores were dichotomized into unfavourable outcome (vegetative state or severe disability = 0) and favourable outcome (moderate disability or good recovery = 1). The independent variables were the GCS score (3–8), pupillary dilation (no = 0, yes = 1) and Rotterdam CT score (1–6), in addition to age.

Subsequently, we added comorbidity (no = 0, yes = 1), anticoagulant status (warfarin, platelet inhibitors) (no = 0, yes = 1) and intubation, hyperosmolar therapy and vasopressor medication (no = 0, yes = 1) and intracranial surgery (no = 0, yes = 1) to all models.

Adjusted OR with 95% CI were calculated using the highest values as references. Cox and Snell and Nagelkerke R squares are given. The possible multicollinearity of the independent variables was examined. The present sample size could capture a twice as high odds of mortality in the elderly group compared with the adult group, with a power of 90%.

A significance level of 5% was used. Statistical analyses were performed with SPSS 19.0 and IBM Sample Power 3 (SPSS Inc., Chicago, IL, USA).

RESULTS

Pre-injury characteristics

Three subjects lived in sheltered homes at the time of injury (two in the elderly group). Thirty-nine percent of adults and 58% of the elderly subjects were married or cohabitant (Table I). In addition, 15% of the adults and 3% of the elderly group were living with adults other than their spouses. Four percent of the elderly group were still working, whereas 60% of the adult subjects were working. Comorbidity was more common in the elderly subjects. Only 12% of adults had multiple diseases, whereas nearly half of the elderly subjects had several comorbid conditions. Half of the adults (46%) and 90% of the elderly subjects had comorbid disorders. No single condition was predominant among the adult group, whereas cardiovascular disorders dominated among the elderly subjects.

Injury mechanism and transportation to hospital

Fall is the leading cause of injury, with the highest frequency among elderly subjects (Table I). Forty percent of the injured patients were admitted to a local hospital prior to transport to a regional trauma hospital. The elderly subjects were significantly more frequently transported to a local hospital prior to transfer to the trauma centre (Table I). Even when injured in traffic accidents, 5 out of 8 elderly subjects were transported to the local hospital. The median time of transport to the first hospital was 60 min, ranging from 6 min to nearly 11 h, regardless of the injury mechanisms ($p = 0.48$) or age ($p = 0.56$).

Injury severity and complications

GCS score at the accident scene was significantly higher in older patients, while no difference was found between the age groups for the lowest GCS score within 24 h (Table II). Pupillary dilation was observed in the pre-hospital phase in 41% of adults and 33% of the elderly subjects ($\chi^2 = 0.30$, $p = 0.59$), and dilation was noted at admittance or during the hospital stay in 41% of adults and 42% of elderly subjects ($\chi^2 = 0.05$, $p = 0.82$).

The elderly subjects had significantly higher Rotterdam CT scores and significantly lower ISS scores (Table II). The type of intracranial lesions was equally distributed across age groups (Fig. 2), but the elderly subjects had an OR of 3.25 (CI 1.67–6.33, $\chi^2 = 12.80$, $p < 0.001$) for SDH compared with adults. Hypoxia and hypotension were frequent, with no differences between the age groups (Table III). These patients also had a wide variety of complications in general, which were of respiratory, cardiovascular, metabolic, hormonal and infectious origin, and no statistically significant differences between the groups in the overall frequency of these complications were observed (Table III).

Interventions

Fifty percent of the adult patients were intubated at the accident scene, compared with 18% of elderly subjects ($\chi^2 = 20.99$, $p < 0.001$, OR 0.22, CI 0.11–0.44). In a logistic regression controlling for GCS score and the injury mechanism, age remained a significant predictor of non-intubation at the accident scene (OR 0.32, CI 0.15–0.69, $p = 0.003$).

Table I. *Demographic characteristics and injury mechanisms of adult and elderly subjects*

	Adult subjects (16–64 years) ($n = 204$) % (n)	Elderly subjects (≥65 years) ($n = 67$) % (n)	χ^2	p-value
Male	82 (168)	63 ($n = 42$)	11.04	0.01
Married/cohabitant	39 (80)	58 ($n = 39$)	7.48	0.006
Comorbidity	45 (91)	90 ($n = 60$)	25.71	<0.001
Anticoagulant medication[b]	6 (12)	60 ($n = 40$)	91.81	<0.001
Injury mechanism				
Fall	49 (99)	84 (56)		
Transport	39 (80)	12 (8)		
Violence	7 (14)	1 (1)		
Sports/other	5 (11)	3 (2)	40.61	<0.001
Transport via local hospital	34 (70)	52 (35)	6.68	0.01
Substance influencea	38 (77)	16 (11)	10.80	0.005

[a]Clinical evaluation or results of blood test documented in medical record.
[b]Anticoagulation and platelet inhibitors.

Table II. *Injury severity in adult and elderly subjects. Proportion of patients with pupil dilation reported either pre- or during hospital stay*

	Adult subjects (16–64 years) ($n = 204$) % (n)	Elderly subjects (≥65 years) ($n = 67$) % (n)	p-value
GCS score accident scene, median (range)	6 (3–15)	8 (3–15)	<0.001
GCS score lowest, median (range)	5 (3–8)	5 (3–8)	0.54
Pupil dilation, %	41	45	0.82**
AIS head, median (range)	5 (2–5)	5 (2–5)	0.38
ISS, median (range)	28 (4–75)	25 (10–59)	0.02*
Rotterdam CT score, median (range)	4 (1–6)	5 (2–6)	<0.001

p-values from independent sample t-test and from Mann-Whitney U test when the distribution was skewed (*), and from χ^2 test for the presence or absence of pupillary dilation either before or during hospitalization (**).
GCS: Glasgow Coma Scale; AIS: American Spinal Injury Association Impairment Scale; ISS: Injury Severety Score; CT: computed tomography.

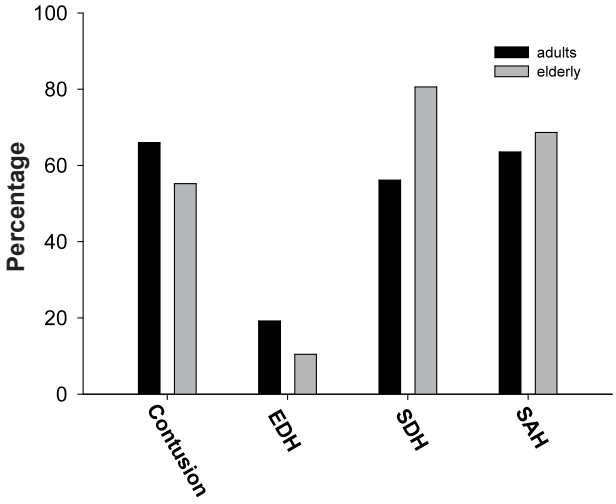


Fig. 2. Intracranial injuries in adults and elderly subjects expressed as the percentage of each age group: adults ($n=204$) (*black bars*), elderly subjects ($n=67$) (*grey bars*) (*$p<0.05$). EDH: epidural haematomas; SDH: subdural haematomas; SAH: subarachnoid hemorrhage.

Medication as well as monitoring of ICP varied between the adult and elderly subjects (Tables III and IV).

ICP and CPP were not monitored in 60% of the elderly subjects and 27% of the adults (Table III). Among those surviving at 3 months, 64% of elderly subjects and 88% of adult subjects had received ICP monitoring in the acute phase ($\chi^2=3.70$, $p=0.05$). In patients with ICP monitoring there were no statistically significant difference in the percentage of patients with ICP values > 30 mmHg in the two age groups (Table III).

The 178 surviving patients spent a mean of 10 (SD 12) days on a respirator and were sedated for a mean of 6 (SD 6) days, regardless of age group ($p>0.36$).

The percentage receiving tracheostomy or PEG was not different between the two age groups ($\chi^2=1.03$, $p=0.31$ and $\chi^2=0.08$, $p=0.77$), but the number of elderly subjects included in these analyses was low.

Table III. *Medical complications in adult and elderly subjects*

	Adults (16–64 years) ($n=204$) % (n)	Elderly (≥65 years) ($n=67$) % (n)	χ^2	p-value
Hypoxia (SaO_2 < 90%)	51 (104)	39 (26)	0.001	0.47
Hypotension (BP < 90 mmHg)	48 (97)	48 (32)	0.53	0.97
ICP/CPP not monitored	27 (55)	60 (40)	23.74	<0.001
ICP > 30 mmHg	32 (65)	12 (8)	1.84	0.21[a]
CPP< 60 mmHg	33 (67)	18 (12)	0.15	0.56[a]
Pyrexia (temperature >38ºC)	53 (109)	42 (28)	2.66	0.27
Other complications	66 (156)	81 (54)	0.43	0.51

[a]Comparison among adults and elderly receiving ICP/CPP monitoring. BP: blood pressure; CPP: cerebral perfusion pressure; ICP: intracranial pressure.

Table IV. *Medical and surgical interventions in adults and elderly receiving vasopressor and osmotic medication, cerebrospinal fluid (CSF) drainage, and intracranial surgery. χ^2 test and* p*-values for the difference between adult and elderly subjects*

	Adult subjects (16–64 years) ($n=204$) % (n)	Elderly subjects (≥65 years) ($n=67$) % (n)	χ^2	p-value
Vasopressor medication	77 (156)	55 (37)	11.05	0.001
Hyperosmolar therapy	38 (77)	25 (17)	3.33	0.08
CSF drainage	18 (37)	10 (7)	2.00	0.16
Craniotomy	23 (47)	30 (20)	1.41	0.24
Craniectomy	14 (28)	2 (1)	7.95	0.005

Mortality

The overall 3 months mortality was 34%, corresponding to 24% in the adult group and 67% in the elderly group. Eighty-six percent of the deaths occurred within 2 weeks (Fig 1) and the median time from the accident to death was within 1 day in the adult subjects and 2 days in the elderly subjects.

There was significantly higher mortality in the elderly subjects after adjusting for injury severity (GCS score, Rotterdam score and pupillary dilation) (Table V). Comorbidity and treatment factors did not contribute to the model or change the effect of age.

Three-month outcome

At 3 months, 41% of the adult survivors were still in-patients, mainly in rehabilitation units (92%). Of the surviving elderly

Table V. *Binary logistic regression analysis exploring the effect of age on survival (all patients), home residence and favourable outcome (Glasgow Outcome Scale Extended) (survivors at 3-month follow-up). The independent variables were Glasgow Coma Scale (GCS) (3–8), pupillary dilation (yes/no) and Rotterdam score (1–6), in addition to age (adult/elderly). Adjusted odds ratios (ORs) with 95% confidence intervals (95% CI) and Cox & Snell and Nagelkerke R squares are given*

Model	OR	95% CI	p-value	R^2 Nagelkerke (Cox and Snell)
Survival ($n=271$)				0.59 (0.42)
GCS score	1. 57	1.27–1.95	<0.001	
Pupil dilation	0.57	0.27–1.19	0.13	
Rotterdam	0.28	0.18–0.43	<0.001	
Age	0.09	0.04–0.21	<0.001	
Home residence ($n=178$)				0.22 (0.16)
GCS	1.17	0.98–1.39	0.09	
Pupil dilation	0.41	0.21–0.81	0.01	
Rotterdam	0.64	0.45–0.92	0.01	
Age	2.18	0.79–6.03	0.13	
Favorable outcome ($n=178$)				0.11 (0.08)
GCS	1.25	1.04–1.52	0.02	
Pupil dilation	0.67	0.33–1.37	0.27	
Rotterdam	0.79	0.54–1.13	0.20	
Age	0.46	0.17–1.22	0.39	

subjects, 14% were in-patients and none were in rehabilitation units. Six percent of adult subjects and 18% of elderly subjects stayed in nursing homes or adapted living units. Thus, 53% of adult subjects and 68% of elderly subjects had returned to their own home. For survivors, the mean GOSE score at 3-month follow-up was 5.00 (SD 1.52), and statistically significant differences in distribution between the age groups were not observed ($\chi^2 = 11.43$, $p = 0.08$) (Fig. 3). Elderly subjects were more likely to be discharged to their home at 3 months after adjusting for injury severity (GCS score, Rotterdam score and pupillary dilation) (Table V); the logistic regression with dichotomized GOSE scores indicated a tendency toward more unfavourable outcomes for the elderly subjects, although the results did not reach statistical significance. Low level of comorbidity was a significant predictor of favourable outcome ($p = 0.03$), but did not add unique explanatory value to the model (R^2 Nagelkerke = 0.42), whereas intubation, medication and surgery did not contribute to the models or change the effect of age.

DISCUSSION

The present study adds to the huge amount of evidence of TBI associated with high mortality in elderly subjects. In the present study, mortality was also higher in elderly subjects after adjusting for injury severity. Elderly subjects had a higher burden of comorbidity, but the treatment also differed between the two age groups. Elderly subjects were less frequently intubated and more often admitted to care via local hospitals. ICP and CPP were measured in less than half of the elderly subjects. At 3 months, two-thirds of elderly subjects had returned to their homes, whereas a larger number of adult subjects remained in hospital, mainly due to sustained rehabilitation. Injury severity, as evaluated by GCS, was the single best predictor of unfavourable outcome, and more so in elderly subjects.

Falls are the main cause of TBI in elderly subjects (15). Several actions are effective in fall prevention, including better control of medication, adapted environments, adjustments for reduced vision and hearing, as well as activity and exercises, even though ageing and comorbidity itself may not be prevented (16). Alcohol may also be less well tolerated in elderly subjects, and result in falls, although the overall percentage of injuries associated with alcohol was lower in elderly subjects than adult subjects in the present study. Hence, attention should be paid to the prevention of falls, including better monitoring of medication and interventions to improve mobility and balance (17).

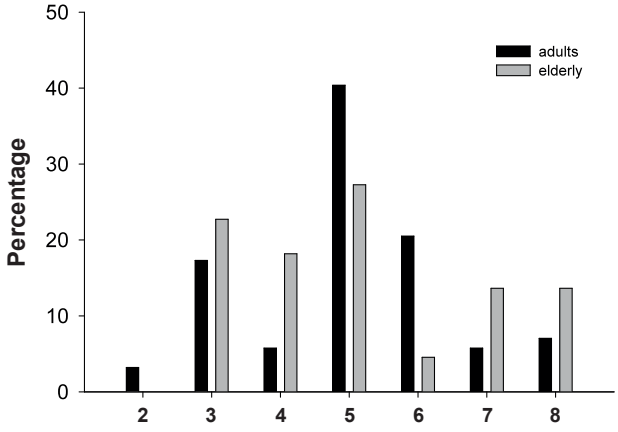


Fig. 3. Distribution of Glasgow Outcome Scale Extended (GOSE) score expressed as the percentage of survivors in each age group: adults ($n = 156$) (black bars) and elderly subjects ($n = 22$) (grey bars).

The present study also shows that elderly subjects were more often transported to a local hospital, which is a negative predictor of outcome (18, 19). The high number of falls resulting in unconsciousness without information on the trauma mechanisms may lead to a suspicion of a cardiovascular disorder or other medical conditions. However, the lower rate of intubation in patients with reduced levels of consciousness is less likely to be influenced by such factors. Thus, there may be potential for improvement in the pre-hospital treatment of elderly subjects, possibly with improved survival rates for these patients.

The elderly group had higher GCS scores at the accident scene, whereas pupillary dilation in the pre-hospital phase was equally frequent in both age groups. However, the worst GCS score within 24 h was similar across age groups. The elderly subjects had slightly more extensive intracranial injuries as evaluated by the Rotterdam score. These differences may be partially explained by more frequent SDHs in the elderly subjects, with gradually developing haemorrhages causing clinical deterioration as well as intracranial findings on CT (20, 21). Improved diagnostic evaluation and direct and swift transport to a trauma centre may improve the prognosis in elderly patients (19).

In hospitals, a case fatality rate between 20% and 40% for severe TBI is reported in most European countries (22). TBI is still the major cause of death and disability in young adults in developed countries (23). However, a 50% reduction in the mortality rate due to severe TBI over the last 150 years has been reported (24). Safer cars and roads and improved pre-hospital and emergency management have contributed to this trend (3, 25). However, in Western countries in the most recent decades, there is an increasing incidence of falls among elderly citizens (16), resulting in severe TBI (26) that are associated with poor outcomes (27, 28). Similar results have emerged from the Nordic countries, with increases in the mortality rates for elderly people, particularly women, and an increase in the mean age of TBI casualties from 45 to 53 years of age for men and 54 to 65 years of age for women (29). Although the overall mortality was approximately 30% in the present study, only one-third of the present patients ≥ 64 years of age survived.

The relationship between age and probability of death is a subject of debate, with some studies showing a linear association and other studies showing an association only in patients > 40 years of age (30, 31). However, the marked shift in injury mechanisms is a feature of patients aged above 60–65 years, with a steep increase in the incidence of falls (32). The influence of age on treatment choices, controlling for all other injury variables, is a difficult topic. The increased morbidity associated with aggressive management of TBI in some studies

has been interpreted as support for a more conservative treatment policy in the elderly status (12). However, recent studies clearly show an overall benefit of aggressive treatment in older patients (11), and even the most severely injured elderly people may recover (33). Higher mortality in elderly people may have influenced the recorded rate of osmotic and vasopressor medication, ICP and CSF drainage in the present study. However, a clear tendency to lower rate of ICP monitoring in elderly people was also found among the surviving patients. It is worth noting that less aggressive monitoring and treatment may also cause higher mortality (11). The major improvement in outcome over the last years reflects the use of protocols to guide all phases of treatment for these patients, with focus on certain groups now recognized as being at greater risk, in particular elderly people, and anti-coagulated patients (34). Thus, the lack of national guidelines for hospital treatment of severe TBI in Norway adapted to elderly people is a major challenge.

The high number of elderly people receiving anti-coagulation and anti-thrombotic medications is worth noting. Although they did not influence the mortality or crude measurements of early outcome in the present study, these medications may contribute to minor falls that result in severe TBI, and interact with complications and treatment results (34). Anti-thrombotic medication may, in particular, contribute to the high frequency of SDH in elderly people, where prompt intervention and craniotomy are of particular importance (35). The lack of significant differences in craniotomy frequency between adults and elderly people in the present study may therefore indicate a less aggressive treatment approach towards the elderly population.

In this study, the GOSE scale was dichotomized between severe and moderate disability, according to the customary procedures in the literature (36). However, recent evidence indicates that the application of the GOSE as an ordinal dependent variable markedly increases the sensitivity of the analysis (37). However, with only 22 surviving patients in the elderly group, this method was not applied in the present study. Outcome measurement focusing in more detail on activities and participation tasks would probably be more sensitive, but also more difficult to apply comparing patients still in rehabilitation units with patients discharged to their homes (38). This multicentre study design did not allow for a more detailed registration of pre-injury morbidity and functional status. Such information, if available, could also have contributed to a more sensitive prediction of outcomes (39).

The modified predictive factors from the impact study (38) are well adapted to describe mortality in the present study, and additional injury variables and treatments did not contribute significantly to the results. However, these models performed more poorly in predicting functional outcome at 3-month follow-up when only surviving patients were included.

The relatively low proportion of elderly subjects in nursing homes and the high proportion residing at home 3 months post-injury is worth noting. This represents a challenge to the healthcare system in municipalities as well as to families and other caregivers. In contrast, nearly 40% of the adults were still receiving rehabilitation at this time point. Given the information regarding rehabilitation in elderly stroke patients, the importance of placing elderly patients with TBI in rehabilitation units should be reconsidered.

Although this study included all severe TBIs in Norway (except for Stavanger County) over a 2-year period, the number of patients surviving and eligible for follow-up in each age group was relatively low. The strength of the study is that it used a representative cohort because all severe trauma patients in Norway that were admitted to regional trauma referral centres are referred to further care in public hospitals or rehabilitation units (40). Despite this, a multicentre study will always be flawed by differences between study centres that are not documented and by biases in registration procedures. The present study was based on registrations of crude measurements and procedures. For example, a more detailed monitoring of ICP also covering levels between 20 and 30 mmHg would be preferred. Our results may also be influenced by the choice of cut-off between adult and elderly subjects at 65 years. Subgrouping the elderly subjects further was difficult in the present study as there was a low number of elderly survivors. This limited number of surviving elderly subjects also flaws the ability of the study to detect differences in outcome. The power of the study to capture the large age-related differences in mortality was high. However, the present differences in favourable outcome between the age groups render the power for these analyses down to 30%.

By studying patients admitted to the trauma referral centres, patients dying in the pre-hospital phase or at the local hospital were not included. Hence, overall mortality from severe TBI cannot be assessed in the present study, and may possibly exaggerate the age differences.

In conclusion, old age is associated with fall-induced severe TBI and high mortality rates. Less intensive treatment strategies were applied to elderly patients in the present study despite high rates of haemorrhages. Few surviving elderly patients received rehabilitation at 3 months post-injury. Recent evidence suggests that this patient group would benefit from a more intensive treatment strategy, and guidelines are needed for this purpose.

ACKNOWLEDGEMENTS

The authors would like to thank the Trauma Registry at Oslo University Hospital, Ulleval and Haukeland University Hospital for providing data regarding injury severity. We also thank Cand. Med. Tone Jerstad for her effort in analysing the majority of CT scans and providing the Rotterdam scores.

REFERENCES

1. Ingebrigtsen T, Mortensen K, Romner B. The epidemiology of hospital-referred head injury in northern Norway. Neuroepidemiology 1998; 17: 139–146.
2. Polinder S, Meerding WJ, van Baar ME, Toet H, Mulder S, van Beeck EF. Cost estimation of injury-related hospital admissions in 10 European countries. J Trauma 2005; 59: 1283–1290.
3. Masson F, Thicoipe M, Aye P, Mokni T, Senjean P, Schmitt V, et al. Epidemiology of severe brain injuries: a prospective population-based study. J Trauma 2001; 51: 481–489.

4. Andelic N, Hammergren N, Bautz-Holter E, Sveen U, Brunborg C, Roe C. Functional outcome and health-related quality of life 10 years after moderate-to-severe traumatic brain injury. Acta Neurol Scand 2009; 120: 16–23.
5. Lingsma HF, Roozenbeek B, Steyerberg EW, Murray GD, Maas AI. Early prognosis in traumatic brain injury: from prophecies to predictions. Lancet Neurol 2010; 9: 543–554.
6. Utomo WK, Gabbe BJ, Simpson PM, Cameron PA. Predictors of in-hospital mortality and 6-month functional outcomes in older adults after moderate to severe traumatic brain injury. Injury 2009; 40: 973–977.
7. Thompson HJ, Dikmen S, Temkin N. Prevalence of comorbidity and its association with traumatic brain injury and outcomes in older adults. Res Gerontol Nurs 2012; 5: 17–24.
8. Czosnyka M, Steiner L, Balestreri M, Schmidt E, Smielewski P, Hutchinson PJ, et al. Concept of "true ICP" in monitoring and prognostication in head trauma. Acta Neurochir Suppl 2005; 95: 341–344.
9. Onyszchuk G, He YY, Berman NE, Brooks WM. Detrimental effects of aging on outcome from traumatic brain injury: a behavioral, magnetic resonance imaging, and histological study in mice. J Neurotrauma 2008; 25: 153–171.
10. Munro PT, Smith RD, Parke TR. Effect of patients' age on management of acute intracranial haematoma: prospective national study. Br Med J 2002; 325: 1001.
11. Whitmore RG, Thawani JP, Grady MS, Levine JM, Sanborn MR, Stein SC. Is aggressive treatment of traumatic brain injury cost-effective? J Neurosurg 2012; 116: 1106–1113.
12. Patel HC, Bouamra O, Woodford M, Yates DW, Lecky FE. Clinical article: mortality associated with severe head injury in the elderly. Acta Neurochir (Wien) 2010; 152: 1353–1357.
13. Brown AW, Malec JF, Mandrekar J, Diehl NN, Dikmen SS, Sherer M, et al. Predictive utility of weekly post-traumatic amnesia assessments after brain injury: A multicentre analysis. Brain Inj 2010; 24: 472–478.
14. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. J Neurotrauma 1998; 15: 573–585.
15. Majdan M, Mauritz W, Brazinova A, Rusnak M, Leitgeb J, Janciak I, et al. Severity and outcome of traumatic brain injuries (TBI) with different causes of injury. Brain Inj 2011; 25: 797–805.
16. World Health Organization. WHO global report on falls prevention in older age. WHO Library; 2007. Available from: http://www.who.int/ageing/publications/Falls_prevention7March.pdf.
17. Gillespie LD, Robertson MC, Gillespie WJ, Lamb SE, Gates S, Cumming RG, et al. Interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev 2009; CD007146.
18. Sollid S, Sundstrom T, Kock-Jensen C, Juul N, Eskesen V, Bellander BM, et al. [Scandinavian guidelines for prehospital management of severe traumatic brain injury.] Tidsskr Nor Laegeforen 2008; 128: 1524–1527 (in Norwegian).
19. Joosse P, Saltzherr TP, van Lieshout WA, van EP, Ponsen KJ, Vandertop WP, et al. Impact of secondary transfer on patients with severe traumatic brain injury. J Trauma Acute Care Surg 2012; 72: 487–490.
20. Depreitere B, Meyfroidt G, Roosen G, Ceuppens J, Grandas FG. Traumatic brain injury in the elderly: a significant phenomenon. Acta Neurochir Suppl 2012; 114: 289–294.
21. Moore MM, Pasquale MD, Badellino M. Impact of age and anticoagulation: need for neurosurgical intervention in trauma patients with mild traumatic brain injury. J Trauma Acute Care Surg 2012; 73: 126–130.
22. Andriessen TM, Horn J, Franschman G, van der Naalt J, Haitsma I, Jacobs B, et al. Epidemiology, severity classification, and outcome of moderate and severe traumatic brain injury: a prospective multicenter study. J Neurotrauma 2011; 28: 2019–2031.
23. Willemse-van Son AH, Ribbers GM, Verhagen AP, Stam HJ. Prognostic factors of long-term functioning and productivity after traumatic brain injury: a systematic review of prospective cohort studies. Clin Rehabil 2007; 21: 1024–1037.
24. Stein SC, Georgoff P, Meghan S, Mizra K, Sonnad SS. 150 years of treating severe traumatic brain injury: a systematic review of progress in mortality. J Neurotrauma 2010; 27: 1343–1353.
25. Hartl R, Gerber LM, Iacono L, Ni Q, Lyons K, Ghajar J. Direct transport within an organized state trauma system reduces mortality in patients with severe traumatic brain injury. J Trauma 2006; 60: 1250–1256.
26. Gerber LM, Ni Q, Hartl R, Ghajar J. Impact of falls on early mortality from severe traumatic brain injury. J Trauma Manag Outcomes 2009; 3: 9.
27. Perel P, Arango M, Clayton T, Edwards P, Komolafe E, Poccock S, et al. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. Br Med J 2008; 336: 425–429.
28. Hukkelhoven CW, Steyerberg EW, Rampen AJ, Farace E, Habbema JD, Marshall LF, et al. Patient age and outcome following severe traumatic brain injury: an analysis of 5600 patients. J Neurosurg 2003; 99: 666–673.
29. Sundstrom T, Sollid S, Wentzel-Larsen T, Wester K. Head injury mortality in the Nordic countries. J Neurotrauma 2007; 24: 147–153.
30. Mushkudiani NA, Engel DC, Steyerberg EW, Butcher I, Lu J, Marmarou A, et al. Prognostic value of demographic characteristics in traumatic brain injury: results from the IMPACT study. J Neurotrauma 2007; 24: 259–269.
31. McMillan TM, Teasdale GM, Weir CJ, Stewart E. Death after head injury: the 13 year outcome of a case control study. J Neurol Neurosurg Psychiatry 2011; 82: 931–935.
32. Andelic N, Sigurdardottir S, Brunborg C, Roe C. Incidence of hospital-treated traumatic brain injury in the Oslo population. Neuroepidemiology 2008; 30: 120–128.
33. Brazinova A, Mauritz W, Leitgeb J, Wilbacher I, Majdan M, Janciak I, et al. Outcomes of patients with severe traumatic brain injury who have Glasgow Coma Scale scores of 3 or 4 and are over 65 years old. J Neurotrauma 2010; 27: 1549–1555.
34. Protheroe RT, Gwinnutt CL. Early hospital care of severe traumatic brain injury. Anaesthesia 2011; 66: 1035–1047.
35. Leitgeb J, Mauritz W, Brazinova A, Janciak I, Majdan M, Wilbacher I, et al. Outcome after severe brain trauma due to acute subdural hematoma. J Neurosurg 2012; 117: 324–333.
36. Weir J, Steyerberg EW, Butcher I, Lu J, Lingsma HF, McHugh GS, et al. Does the extended Glasgow Outcome Scale add value to the conventional Glasgow Outcome Scale? J Neurotrauma 2012; 29: 53–58.
37. McHugh GS, Butcher I, Steyerberg EW, Marmarou A, Lu J, Lingsma HF, et al. A simulation study evaluating approaches to the analysis of ordinal outcome data in randomized controlled trials in traumatic brain injury: results from the IMPACT Project. Clin Trials 2010; 7: 44–57.
38. Hall KM, Bushnik T, Lakisic-Kazazic B, Wright J, Cantagallo A. Assessing traumatic brain injury outcome measures for long-term follow-up of community-based individuals. Arch Phys Med Rehabil 2001; 82: 367–374.
39. Stocchetti N, Paterno R, Citerio G, Beretta L, Colombo A. Traumatic brain injury in an aging population. J Neurotrauma 2012; 29: 1119–1125.
40. Magnussen J, Hagen TP, Kaarboe OM. Centralized or decentralized? A case study of Norwegian hospital reform. Soc Sci Med 2007; 64: 2129–2137.

J Rehabil Med 2013; 45: 741–748

ORIGINAL REPORT

DISORDERS OF CONSCIOUSNESS AFTER SEVERE TRAUMATIC BRAIN INJURY: A SWEDISH–ICELANDIC STUDY OF INCIDENCE, OUTCOMES AND IMPLICATIONS FOR OPTIMIZING CARE PATHWAYS

Alison K. Godbolt, MBChB, MD[1,2], Catharina Nygren DeBoussard, MD, PhD[1], Maud Stenberg, MD[3], Marie Lindgren, MD[4], Trandur Ulfarsson, MD[5] and Jörgen Borg, MD[1]

From the [1]Department of Clinical Sciences, Karolinska Institute and University Department of Rehabilitation Medicine Stockholm, Danderyd Hospital, Stockholm, [2]formerly of Department of Rehabilitation Medicine, University Hospital Uppsala and Uppsala University, Uppsala, [3]Department of Rehabilitation Medicine, Norrlands University Hospital, Umeå, [4]Clinical Department of Rehabilitation Medicine, County Council of Östergötland, Linköping and [5]Department of Rehabilitation Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden

Background: **Very severe traumatic brain injury may cause disorders of consciousness in the form of coma, unresponsive wakefulness syndrome (also known as vegetative state) or minimally conscious state. Previous studies of outcome for these patients largely pre-date the 2002 definition of minimally conscious state.**

Objectives: **To establish the numbers of patients with disorder of consciousness at 3 weeks, 3 months and 1 year after severe traumatic brain injury, and to relate conscious state 3 weeks after injury to outcomes at 1 year.**

Design: **Multi-centre, prospective, observational study of severe traumatic brain injury. Inclusion criteria: lowest (non-sedated) Glasgow Coma Scale 3–8 during the first 24 h; requirement for neurosurgical intensive care; age 18–65 years; alive 3 weeks after injury. Diagnosis of coma, unresponsive wakefulness syndrome, minimally conscious state or emerged from minimally conscious state was based on clinical and Coma Recovery Scale Revised assessments 3 weeks, 3 months and 1 year after injury. One-year outcome was measured with Glasgow Outcome Scale Extended (GOSE).**

Results: **A total of 103 patients was included in the study. Of these, 81% were followed up to 1 year (76% alive, 5% dead). Three weeks after injury 36 were in coma, unresponsive wakefulness syndrome or minimally conscious state and 11 were anaesthetized. Numbers of patients who had emerged from minimally conscious state 1 year after injury, according to status at 3 weeks were: coma (0/6), unresponsive wakefulness syndrome (9/17), minimally conscious state (13/13), anaesthetized (9/11). Outcome at 1 year was good (GOSE > 4) for half of patients in minimally conscious state or anaesthetized at 3 weeks, but for none of the patients in coma or unresponsive wakefulness syndrome. These differences in outcome were not revealed by prognostic predictions based on acute data.**

Conclusion: **Patients in minimally conscious state or anaesthetized 3 weeks after injury have a better prognosis than patients in coma or unresponsive wakefulness syndrome, which could not be explained by acute prognostic models.**

Key words: traumatic brain injury; prognosis; vegetative state; minimally conscious state; outcome; care pathways.

J Rehabil Med 2013; 45: 741–748

Correspondence address: Alison K. Godbolt, Department of Clinical Sciences, Karolinska Institute and University Department of Rehabilitation Medicine Stockholm, Danderyd Hospital, Stockholm, Sweden. E-mail: alison.godbolt@ki.se

Accepted February 19, 2013

INTRODUCTION

Some patients survive severe traumatic brain injury (S-TBI) and emerge from coma to a state with preserved sleep-wake cycles, but no evidence of awareness of self or environment, and, as such, no evidence of consciousness. The description of this state as "vegetative state" (1), proposed 40 years ago, has in recent years been seen as derogatory to patients. A new term, "unresponsive wakefulness syndrome" (UWS) (2) has recently been proposed for the same condition and will be used here.

After S-TBI, patients may alternatively show clearly discernible, but inconsistent, signs of consciousness; for example, sustained visual tracking, localization of painful stimuli, and/or attempts at communication, without these reaching a functional level. This state is described as minimally conscious state (MCS) (3).

Brain-injured patients may or may not recover from UWS to consciousness, and the time-course for this recovery may vary from hours or days (in which case it may not be meaningful to describe the clinical progression in terms of UWS) to years (4). Patients pass through MCS for a shorter or longer period, before sometimes emerging from the minimally conscious state (EMCS).

An understanding of the natural history of recovery from S-TBI is a prerequisite for optimizing care for these patients. Care pathways for patients in UWS after S-TBI typically involve several transfers between healthcare and other facilities, at various time-points after injury, but there is a lack of consensus on what is optimal. Rehabilitation interventions may or may not begin as early as in the neurointensive care unit (5). Admission to neurorehabilitation units in some countries

requires that the patient is able to participate actively in rehabilitation interventions, and therefore this may, by definition, exclude patients in UWS.

Although there are no such formal barriers to access to rehabilitation in Sweden, there is a lack of consensus regarding the appropriateness of rehabilitation admission for patients in UWS (6). Health insurance is universal, with decisions on admission to rehabilitation units, and on length of stay, made largely by rehabilitation physicians, according to local criteria. However, there are no defined care-pathways or national guidelines regarding the care of patients with impaired consciousness after S-TBI, in-patient beds for acquired brain injury rehabilitation are limited, and (with the exception of a single two-bed unit in one centre) S-TBI patients with disorders of consciousness receive rehabilitation within the same services as patients with less severe acquired brain injury. Experience is that, when beds are limited, patients with disorders of consciousness compete for admission with patients who may more obviously benefit from rehabilitation, and in practice may have difficulties accessing services. Implementation of specific rehabilitation interventions (medication, sensory stimulation programmes, orthotics, physiotherapy) may be according to a structured programme in some units, but otherwise may be largely up to the interest and experience of healthcare personal involved.

Integral to decisions on care pathways is an understanding of the natural course of UWS after S-TBI. A 1994 meta-analysis performed by the Multi-Society Task Force on persistent vegetative state, synthesized data on recovery from UWS in 434 patients reported in 6 articles (7). Outcomes were expressed in terms of the relatively crude Glasgow Outcome Scale, with the method of assessment either not stated (8–11) or based on standard neurological examination and interview with the family (12). Information on participation rates was incomplete in some studies. Of those in UWS (then "vegetative state") 1 month after traumatic brain injury, 33% recovered consciousness by 3 months, 46% by 6 months, and 52% by 1 year. However, this report pre-dated the definition of MCS in 2002 (3), with probable inclusion of some patients who would today be diagnosed as being in MCS and not UWS.

Since publication of the Task Force study, it has been shown that misdiagnosis of UWS (VS) may occur in up to 40% of patients (13), when standardized assessment instruments are not used. Developments in neurosurgical intensive care and neurorehabilitation during the past 20 years may also impact on recovery.

This study was based on a subset of data from a prospective observational study of S-TBI (the "PROBRAIN" study). The objective was to provide updated data on the rates of occurrence of coma, UWS and MCS after S-TBI, and to assess the extent to which state of consciousness 3 weeks after injury is related to outcome at 1 year. It is hoped that these data will inform the planning and provision of acute, rehabilitation and social care for patients suffering S-TBI, and inform discussions with relatives.

METHODS

We performed a prospective, multicentre, observational study of patients with severe traumatic brain injury. Inclusion criteria were: (*i*) severe, non-penetrating, traumatic brain injury, with a lowest non-sedated Glasgow Coma Score (GCS) score of 3–8 or Reaction Level Scale (14) score (RLS) of 4–8 in the first 24 h after injury; (*ii*) age at injury 18–65 years; (*iii*) injury requiring neurosurgical intensive care, or collaborative care with a neurosurgeon in another intensive care unit.

Exclusion criteria were: death or expected death within 3 weeks of injury.

The 8-point RLS (Table I) is widely used in Sweden, and in some emergency departments and neurosurgical units is used instead of the GCS: RLS criteria were therefore necessary to allow recruitment of patients from those centres using this scale, and thus to avoid selection bias. Scores on the GCS of 3–8 and on the RLS of 8–4 reflect similar severity of injury (15), the RLS having been shown to have somewhat better inter-rater reliability than the GCS (16). RLS scoring is in the opposite direction to GCS scoring, with the highest RLS score of 8 reflecting the most severe injuries.

Patients were recruited prospectively by rehabilitation physicians from January 2010 until June 2011, with extended recruitment until December 2011 at 2 centres. Results from the main recruitment period until June 2011 are reported here. The participating centres provide neurosurgical care to more than 80% of the population of Sweden, and the population of Iceland (total approximately 4.7 million adults aged 18–65 years). Neurosurgical intensive care units at 6 (out of a possible 7) centres in Sweden and Iceland were contacted on a weekly basis to identify eligible patients. The patient gave informed consent in cases where he/she had capacity. In the majority of cases the patient lacked capacity and the patient's nearest relative gave consent to inclusion. The study was reviewed by the regional ethics review board in Stockholm.

After inclusion, acute data were obtained from medical records. Patients were then assessed prospectively, at 3 time-points, 3 weeks (18–24 days), 3 months (75–105 days) and 1 year (350–420 days) after injury. Assessments took place in the patient's current care setting where possible (which in some cases was in the patient's home), or in a local out-patient department. Inclusion and follow-up was therefore designed to be independent of any decisions regarding care-pathways and admission to in-patient rehabilitation.

Assessments were performed by rehabilitation physicians with assistance from rehabilitation nurses, psychologists, physiotherapists and occupational therapists. Assessments at each of the 3 time-points included both clinical examination and a battery of standardized instruments, allowing description of the patient's condition according to the framework of the International Classification of Functioning, Disability and Health (ICF): bodily structure and function, activities and participation.

Table I. *Reaction level scale (RLS)*

1	Alert, with no delay in response (responds without stimulus).
2	Drowsy or confused, but responds to light stimulation.
3	Very drowsy or confused, but responds to strong stimulation.
4	Unconscious; localizes (moves a hand towards) a painful stimulus but does not ward it off.
5	Unconscious; makes withdrawing movements following a painful stimulus.
6	Unconscious; stereotypic flexion movements following painful stimuli
7	Unconscious; stereotypic extension movements following painful stimuli.
8	Unconscious; no response to painful stimuli.

Patients with RLS > 3 are unconscious.

Instruments relevant to this sub-study included the Coma Recovery Scale Revised (CRS-R) (17), and the Glasgow Outcome Scale Extended (GOSE) (18). The CRS-R was recently recommended by the American Congress of Rehabilitation Medicine for the assessment of possible disorders of consciousness (DOC), has good reliability and validity (19), and was administered in all patients where a DOC was suspected on the basis of lack of functional communication and/or functional object use, with the exception of patients who remained sedated or anaesthetized. The GOSE has good inter-rater reliability (18) and validity (20), and is an established measure of global outcome after traumatic brain injury.

Patient age and acute markers of injury severity are known to impact on outcome, and possible differences in outcome according to conscious state 3 weeks after injury would be of lesser interest if different outcomes could already have been predicted using acute data. The CRASH acute prognostic model (21) is an externally validated acute prognostic model, based on data from 10,008 patients worldwide. CRASH incorporates 10 acute variables: age, pupil reaction, acute GCS, country, presence or absence of major extracranial injury, presence or absence of 5 specified acute CT-brain findings. We used the online calculator for the CRASH prognostic model (available at: http://www.crash2.lshtm.ac.uk/Risk%20calculator/index.html) to calculate percentage risk of an unfavourable outcome (equivalent to GOSE 1–4) at 6 months, for each patient, after conversion of RLS scores for those patients not assessed with the GCS. Conversion used was RLS8 = GCS3, RLS7 = GCS4, RLS6 = GCS5, RLS5 = GCS6, RLS4 = GCS7. Ordering of severity with the RLS and GCS has been shown to be consistent (22), the RLS and GCS are highly correlated ($r = -0.94$), and assess similar behavioural features reflecting consciousness (15).

Data were analysed with SPSS version 20.

Table II. *Patient characteristics*

Age at injury, years, median, (range)	41 (17–65)
Worst un-sedated GCS (3–15) first 24 h ($n = 58$)	5 (3–8)
Or Worst un-sedated RLS (8–1) first 24 h in patients not assessed with GCS ($n = 42$)	5 (8–4)
Cause of injury, %	
Transport accident	42
Fall	44
Other	11
Missing data	4
Length of stay in intensive care, days, median (range)	17.5 (1–54)
Duration of ventilation, days, median (range)	13 (range 0–36, with 1 outlier at 101 days)
Economic support at time of injury, %	
Employed/self-employed	50
Study grant	7
Unemployment benefit or social support	8
Sick pay	17
Other	7
Unknown	12
Previous brain injury requiring hospitalization, %	15
Known drug or alcohol misuse at time of injury, %	26
Gender, men/women/missing, *n*	69/25/9

GCS: Glasgow Coma Score; RLS: Reaction Level Scale.

RESULTS

A total of 103 patients were recruited from 6 neurosurgical intensive care units in Sweden and Iceland, and acute data entered for 102 patients (one patient withdrew consent). Three weeks after injury 102 patients continued in the study. Three months after injury, 3 (3%) patients had died, 4 (4%) had withdrawn from the study and 96 continued (93%). One year after injury 5 (5%) patients had died, 18 (17%) had withdrawn, 78 (76%) continued, and data on study status was missing for one. Patients who withdrew were similar to those who continued in terms of median age (34 compared with 42 years, Mann-Whitney test, $p = 0.55$) and median acute GCS or RLS-derived GCS (4 compared with 5, Mann-Whitney U test, $p = 0.18$). Demographic details and summary statistics on severity of injury are given in Table II.

For acute assessment of level of consciousness, the GCS alone was available for 27 patients, RLS alone for 43, both scales for 30 patients, data was missing for 2 patients: where both scales were available the GCS is reported. The median lowest GCS of 5 ($n = 57$) and median lowest RLS of 5 ($n = 43$), median duration of artificial ventilation of 13 days and median length of intensive care of 17.5 days reflect that, as a group, these patients had brain injuries towards the more "severe" end of the group generally defined as having S-TBI. Most injuries were due to transport accidents and falls. Due to a minor protocol violation one patient was included shortly before their 18th birthday.

Outcomes one year after injury

GOSE 1 year after injury was 1 (dead, $n = 5$), 2 (vegetative state, $n = 6$), 3 (lower severe disability, $n = 22$), 4 (upper severe disability, $n = 6$), 5 (lower moderate disability, $n = 10$), 6 (upper moderate disability, $n = 0$), 7 (lower good recovery, $n = 19$), 8 (upper good recovery, $n = 12$), missing ($n = 3$). Data on the relationship between conscious state at 3 weeks and outcome at 1 year is given in Fig. 1.

Disorders of consciousness

Three weeks after injury 17 patients were in UWS, 13 in MCS, 6 in coma and 11 sedated/anaesthetized. Outcomes are sum-

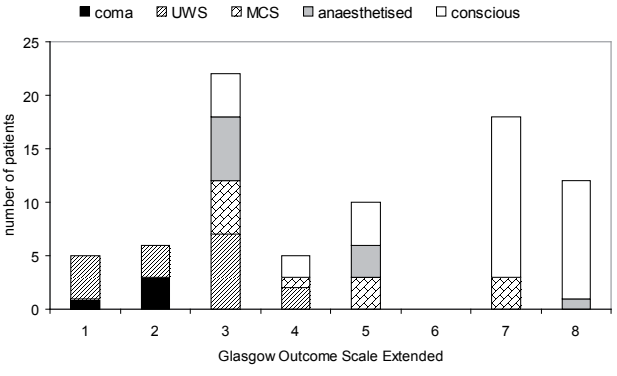


Fig. 1. Outcome at one year in relation to conscious state 3 weeks after injury. Each bar shows the number of patients with each Glasgow Outcome Scale Extended level 1 year after injury. Within each bar, the conscious level of patients 3 weeks after injury is shown by different patterns of shading, as indicated below the figure title. 1: dead; 2: vegetative state; 3: lower severe disability; 4: higher severe disability; 5: lower moderate disability; 6: upper moderate disability; 7: lower good recovery; 8: upper good recovery.

marized in Table III. Trajectories of recovery are summarized in Table IV.

Patients in unresponsive wakefulness syndrome 3 weeks after injury. Of the 17 patients in UWS at 3 weeks, by 3 months, 5 remained in UWS, 6 had improved to MCS, 4 had emerged from MCS, and 2 were dead. One year after injury, 2 remained in UWS, 1 was in MCS, 9 had emerged from MCS, 4 were dead, and data on 1 was missing.

Outcome 1 year after injury for these patients, according to the GOSE, was 1 (dead, $n=4$), 2 (vegetative state, $n=3$), 3 (lower severe disability, $n=7$), 4 (upper severe disability, $n=2$), missing data ($n=1$). Note, that GOSE level 2, associated with the description "vegetative state", includes in fact some patients in MCS, explaining the apparent discrepancy.

Scores on the CRS-R (maximum 23) at first assessment, 3 weeks after injury, for patients found to be in UWS, ranged from 0 to 7. Correlation between CRS-R score at 3 weeks and outcome at 1 year for these patients, according to the GOSE, was poor ,with a correlation co-efficient of 0.29.

Patients in minimally conscious state 3 weeks after injury. Of those in MCS at 3 weeks, all 13 had emerged from MCS at 3 months. These patients had scored a median of 12 points (range 6–19 of a possible maximum 23 points) on the CRS-R at 3 weeks.

GOSE 1 year after injury for these 13 patients was 1 (dead, $n=0$), 2 (vegetative state, $n=0$), 3 (lower severe disability, $n=5$), 4 (upper severe disability, $n=1$), 5 (lower moderate disability, $n=3$), 6 (upper moderate disability, $n=0$), 7 (lower good recovery, $n=3$), 8 (upper good recovery, $n=0$), missing data ($n=1$). Correlation between CRS-R score at 3 weeks and outcome at 1 year for these patients, according to the GOSE, was also weak, with a correlation co-efficient of –0.19.

One year after injury, 4 of these patients were living at home without assistance, 8 were at home with assistance, and 1 was in a nursing home. One patient was working full-time (and also driving).

Patients in coma or sedated/anaesthetized, 3 weeks after injury. Of the 6 patients in coma (i.e. not sedated, but no eye opening) at 3 weeks, by 3 months, 4 were in UWS, 1 was in MCS, none were better than MCS, and 1 was dead. These figures were unchanged at follow-up 1 year after injury.

Table IV. *Recovery for patients with low levels of consciousness 3 weeks after injury*

Status 3 weeks after injury	Follow-up status	Three months after injury *n*	One year after injury *n*
UWS ($n=17$)	EMCS	4	9
	MCS	6	1
	UWS	5	2
	Dead	2	4
	Missing data	0	1
MCS ($n=13$)	EMCS	13	13
Coma ($n=6$)	UWS	4	4
	MCS	1	1
	EMCS	0	0
	Dead	1	1
	Withdrawn	0	0
Anaesthetized/sedated ($n=11$)	UWS	1	0
	MCS	3	2
	EMCS	7	9
	Dead	0	0
	Withdrawn	0	0

EMCS: emerged from the minimally conscious state; MCS: minimally conscious state; UWS: unresponsive wakefulness syndrome.

At the 3-week assessment, rehabilitation physicians recorded whether patients were sedated/anaesthetized, after review of the current drug regime. Of the 11 patients who were sedated/anaesthetized 3 weeks after injury, by 3 months, 1 was in UWS, 3 were in MCS, and 7 were better than MCS. One year after injury none of these initially sedated patients remained in UWS, 2 were in MCS, and 8 were better than MCS (Table IV).

Consideration of possible confounders

We considered whether the better one-year outcome of patients in MCS compared with UWS (3 weeks after injury) could have been predicted from acute variables of prognostic significance. There was no significant difference in the percentage risk of an unfavourable outcome at 6 months, as assessed with the CRASH model, between patients in UWS 3 weeks after injury compared with those in MCS (median risk of unfavourable outcome 81% for patients in UWS (range 47–98%) and 75% for patients in MCS (range 47–97%), Mann-Whitney *U* test not

Table III. *Outcome one year after injury related to conscious state 3 weeks after injury*

	Conscious state 3 weeks after injury					
GOSE, 1 year after injury	Conscious	Anaesthetized	Coma	UWS	MCS	Not assessable/missing data
1=dead	0	0	1	4	0	0
2=vegetative state	0	0	3	3	0	0
3=lower severe disability	4	6	0	7	5	0
4=upper severe disability	2	0	0	2	1	1
5=lower moderate disability	4	3	0	0	3	0
6=upper moderate disability	0	0	0	0	0	0
7=lower good recovery	15	0	0	0	3	*1*
8=upper good recovery	11	1	0	0	0	0
Grand total	36	10[a] (+1)	4[a] (+2)	16 (+1)	12 (+1)	2

[a]GOSE data at 1 year missing for 5 patients. Number of additional patients in each category with missing GOSE data is given in brackets.
GOSE: Glasgow Outcome Scale Extended; UWS: unresponsive wakefulness syndrome (i.e. vegetative state); MCS: minimally conscious state.

significant, $p = 0.81$), showing that the differences in outcome between these groups could not have been predicted using existing acute prognostic models.

The need to derive GCS scores from RLS score for those patients not assessed with GCS could have introduced some error, with possible overestimation of the risk of unfavourable outcome as calculated with CRASH for patients with RLS 4, for whom it can be debated where an appropriate conversion is to GCS 7 (as initially performed) or GCS 8 (16). To exclude any impact of this possible error on the above finding, the CRASH-risk was re-calculated using an alternative conversion of RLS4 = GCS8. This resulted in unchanged median risk of unfavourable outcome for both UWS and MCS groups, but with a slightly modified range for UWS of 43–98% (previously 47–98%).

Outcome predictions with CRASH are relatively crude: unfavourable outcome is defined as death, vegetative state (UWS) or severe disability according to the earlier Glasgow Outcome Scale (corresponding to GOSE 1–4). By this definition of unfavourable outcome, all of our study patients in UWS at 3 weeks, but only half ($n = 6$) of the patients in MCS at 3 weeks, had an unfavourable outcome at one year. This difference in outcome between UWS and MCS was statistically significant (Fisher's exact test, $p = 0.01$).

Medication use in patients with UWS or MCS. Some evidence has existed for many years regarding beneficial effects of amantadine (with dopaminergic and NMDA effects) in aiding recovery of consciousness after profound acquired brain injury (including traumatic injury). Recently, a large, well-performed, multicentre, randomized controlled trial demonstrated a clear effect of amantadine in speeding improvement in patients with disorders of consciousness after S-TBI (23). There is also some, less robust, support for the use of other dopaminergic agents. It is therefore relevant to consider medication use in study patients when interpreting our findings.

Very few patients were treated with dopaminergic drugs at the time of study assessments. Of patients in UWS at any point during the study, none were receiving such drugs at the 3-week assessment; at the 3-month assessment 1 patient (in UWS at 3 weeks, MCS at 3 months, and EMCS at one year) was receiving Madopar (levodopa/benserazide combination), and one patient (coma at 3 weeks, UWS at 3 months, UWS at 1 year) was receiving amantadine at 3 months but not at 1 year. One further patient (UWS at all study time-points) was receiving amantadine at the 1-year assessment, but not earlier. One patient initially in MCS had emerged from MCS at 3 months, before later receiving Madopar, which was noted at the 1-year assessment. In summary, the impact of drug use in altering patterns of recovery from post-traumatic disorders of consciousness in study patients is probably minimal.

There are practical barriers to the use of amantadine in Sweden, which may explain the low rates of its use: it is not registered with the national Medical Products Agency, and physicians are required to apply for a special license before it can be prescribed. The period of recruitment to this study was also before the publication of the most robust study on amantadine (23).

Possible confounding from other treatments. To our knowledge, no attempt has been made in Sweden to use deep brain stimulation to treat patients in UWS or MCS. Despite promising case reports (24), and case series (25), there has been no randomized controlled trial, and in Sweden the evidence has not been considered strong enough to support introduction into routine clinical practice.

Admission to specialized rehabilitation units. Of the 15 patients in UWS at 3 weeks who survived at least to 3 months, 14 were admitted to an inpatient specialized rehabilitation unit (missing data for 1 patient). Rehabilitation admission occurred a mean of 62 days after injury (standard deviation (SD) 46, range 26–198 days). All of the 13 patients in MCS 3 weeks after injury were admitted to inpatient rehabilitation units, a mean of 44 days after injury (SD 18, range 17–78).

Participation rates. The number of patients recruited corresponds to an assumed annual incidence of S-TBI, with survival of at least 3 weeks, of 14 per million, had all eligible patients had been identified and recruited. This is very similar to the reported incidence of approximately 15 per million population (26) from a previous retrospective study based on review of medical records of patients with S-TBI treated at 3 centres in Sweden, and suggests that participation rates were sufficiently high that the sample can be considered representative.

DISCUSSION

Rates of recovery from post-traumatic UWS in this study are, at first sight, remarkably similar to those reported in the Multi-Society Task Force study nearly 20 years ago. Our first assessment was slightly earlier than that in the original task force (3 weeks rather than 1 month), and despite this study spanning 80% of the population of Sweden and 100% of the population of Iceland, patient numbers were relatively small, necessitating some caution in interpretation.

Comparing figures from the current study with those from the 1994 Task Force (given in brackets), 24% (33%) of patients in UWS 3 weeks (1 month) after injury had emerged to full consciousness (EMCS) at 3 months, and 53% (52%) at 1 year.

However, MCS had not been defined at the time of the Task Force report, and it is likely that most MCS patients would have been included in the vegetative state group in the Task Force report. Neither did the original studies behind the Multi-Society task force use standardized scales in diagnosis of vegetative state/UWS, which have been shown to improve diagnostic accuracy (13). If, instead, one compares outcomes for all patients with either UWS (vegetative state) or MCS early after injury, 57% (Task Force 33%) of patients in UWS/MCS 3 weeks (1 month) after injury had recovered consciousness (EMCS) at 3 months, and 73% (52%) at 1 year. This is probably a fairer reflection of developments in neurosurgical and neurorehabilitative care in the past decades.

Long-term outcome for patients in UWS 3 weeks after injury was, however, poor, with the best GOSE level being upper severe disability. Such patients, according to the GOSE can,

however, be left alone, unsupervised, for some periods during the day. Definitions of poor outcomes are always relative. Outcomes were similarly poor for patients who showed no eye opening at 3 weeks, as such classified as being in coma.

Reports have recently appeared in the literature on outcomes for selected groups of patients with disorders of consciousness from the point at which they are admitted to specialized rehabilitation programmes. Katz et al. (27) reported a retrospective review of outcomes in 36 patients admitted to a slow-to-recover rehabilitation unit, of whom the 22 with traumatic injuries (8 in UWS at admission, 14 in MCS) were admitted a mean of 37 days after injury. Seven of the 8 UWS patients improved to MCS and 45% (number not stated) later emerged from MCS. Although follow-up periods differ, the figure of 45% improving to better than MCS is not dissimilar to our figure of 53% 1 year after injury. It should be emphasized that such estimates are, of necessity, based on small numbers of patients and some margin of error is to be expected.

Outcome was better for patients in MCS 3 weeks after injury, suggesting that it is important to distinguish between UWS and MCS when considering prognosis. This distinction is not easy, with reports of misdiagnosis in 40% of patients even in the hands of teams experienced in the assessment of patients in low responsive states (13). More than one-third of patients in MCS 3 weeks after injury were living independently at home 1 year after injury. One patient had returned to work and had regained their driving licence. Katz et al. (27) reported similar findings for MCS patients: all of their patients admitted in MCS after TBI emerged from MCS during rehabilitation. Identification of patients in MCS rather than UWS, via standardized assessment of conscious level at 3 weeks post-injury, gave additional prognostic information that was not apparent from acute-stage predictions using the CRASH-model.

Outcome was also better for patients who were sedated/anaesthetized at 3 weeks. Our data do not allow analysis of the possible reasons for this, but is could be that sedation is continued when treatable factors, such as raised intracranial pressure, are present, which, if successfully controlled, result in a better outcome than for patients for whom sedation was not judged appropriate, probably due to the absence of such treatable factors.

It is encouraging that all patients with UWS or MCS 3 weeks after injury were later admitted to inpatient rehabilitation units. We cannot exclude that contact with study personnel had some impact on this: rehabilitation medicine in Sweden is a relatively small profession, and physicians involved in the study are also clinically active, with admitting rights to rehabilitation units. However, the extended time before admission is suboptimal. Recent evidence from Norway (5) has shown that early initiation of an unbroken chain of rehabilitation improves outcomes after S-TBI. The Norwegian study involved rehabilitation physicians integrated into the intensive care unit, a model with at present does not exist in Sweden. Cardiovascular instability and other medical complications in the post-acute phase after S-TBI may preclude earlier transfer to specialized rehabilitation units, which are often geographically distant from neurosurgical intensive care units. Integrating rehabilitation physicians and paramedical staff into the intensive care team would seem to offer a solution.

Study limitations

Confirming a diagnosis of UWS or MCS requires repeated assessments over a period of time (19), which were not possible within the study design, given that patients were assessed in whichever care setting was current at the study time-points. In some cases this required study personal to travel long distances to the patient, which made repeated assessments over time impossible. However, the use of the CRS-R is a strength, and has been shown to improve diagnostic accuracy (13). A degree of misclassification is, however, possible, but is probably of a much lesser degree than that in the original Task Force report.

Our follow-up rate of 81% patients (76% living, 5% dead), 1 year after injury, is satisfactory, considering that of necessity patients were initially included in the study with the consent of the nearest relative, as S-TBI causes patients to lack capacity in the acute phase after injury. In this context, it is noteworthy that only 18% of patients withdrew consent to further follow-up.

Some degree of error is possible due to derivation of acute GCS scores from RLS scores for those patients not assessed with GCS. This could have caused some slight overestimation of injury severity, particularly for patients with RLS 4–5. Proponents of the RLS in Sweden highlight its superior inter-rater reliability compared with the GCS, and the avoidance of the GCS's problems with scoring for intubated patients. However, the exclusive use of the RLS does complicate application of established prognostic models, such as CRASH, and hampers direct application of evidence from studies of patients assessed with the GCS.

Another possible source of error is the use of radiology reports to assess the CT-criteria for the CRASH model. If certain features were not reported, there is some uncertainty as to whether they were absent or simply not reported. However, it is unlikely that major abnormalities will have been omitted from radiology reports. The protocol for the CRASH study (28) did not state how or by whom the CT criteria should be assessed, and it is reasonable to assume similar errors would have been possible during that study. We consider our use of radiology reports to be a reasonable, although imperfect, method. A re-review of CT-brain images by independent neuro-radiologists is currently underway in order to assess the degree to which this could have impacted on predictions using the CRASH model.

The CRASH prognostic model predicts outcome 6 months after injury. We assessed outcome 1 year after injury, as recovery may continue at least until this time-point in severely injured patients. These differing time-frames could explain why differences in outcome between patients in UWS and MCS 3 weeks after injury were not predicted by CRASH. However, it seems unlikely that new acute prognostic models will be developed considering outcome at 1 year, given the practical difficulties involved in longer-term follow-up of the very large numbers of patients needed.

Implications for application of Swedish law

In Sweden, patients with severe cognitive and physical disability after S-TBI in adulthood have rights defined in law to suitable, specified, support in the community, including 24-h care at home, if desired, with a higher level of support for those with cognitive impairments equivalent to learning disability ("The law on support and service for certain people with disabilities", LSS). However, the law requires that impairments are permanent, and certified as such by doctors and psychologists. Statements of permanence have, by tradition, not been considered possible until 6 months after injury, with the consequence that optimal care placement is often not possible before this time. Our data show that patients in UWS 3 weeks after injury will have, at best, severe disability at 1 year, and early certification that severe disability will persist at least for 1 year after injury is justified.

Conclusion

The approximate annual incidence of post-traumatic disorders of consciousness (PT-DOC) persisting for at least 3 months, was 3 per million working age people a year (based on 20 patients in our study, recruited over 18 months, from a population of 4.7 million). More transient PT-DOC occurred in 5 per million working-age people (present 3 weeks after injury, but not at 3 months) and longer lasting PT-DOC, persisting 1 year after injury had an incidence of 1.4 per million working age people per year.

With these small numbers of patients spread throughout a geographically large country, development of national standards for post-acute and rehabilitation care for these patients is necessary to ensure a good standard of care for all. Such standards already exist in some European countries (e.g. Scotland (29)). Some centralization of care and/or development of a disorders of consciousness network should be considered to enable dissemination of expertise, implementation of standards, and to promote further research.

Based on our figures, one can further calculate that each year, in Sweden, approximately 14 patients of working age will develop coma or UWS in the post-acute phase after S-TBI, and that all of these patients can be expected to have severe disability 1 year after injury, even if approximately half of them will recover consciousness.

Development of a continuous chain of rehabilitation after S-TBI, which has been shown to improve outcomes, but was not in place for any patients in this study, should be prioritized.

ACKNOWLEDGEMENTS

The authors would like to thank the patients and their relatives, the PROBRAIN collaborators*, the clinical staff of our units, and our neurosurgical colleagues for allowing recruitment of their patients. This study was supported by grant 060833 from AFA insurance. The funders had no access to data and no input to study design or data analysis. AKG has received support from ALF-grants from Uppsala University Hospital and Danderyd Hospital. We also thank Dr Anna Tölli, Danderyd Hospital and Karolinska Institute, Dr Kristina Lindgren, Karlstad Hospital, Dr Björn Johansson, University Hospital Uppsala and Dr Christer Tengvar, University Hospital Uppsala, who assisted in assessment of patients. Paramedical staff contributing to the study included Stina Gunnarsson and Marina Byström Odhe, (Linköping), Anna-Lisa Nilsson (Umeå), Marie Sandgren (Stockholm), Staffan Stenson (Uppsala), and Siv Svensson (Gothenburg). Seija Lund was nurse coordinator in Stockholm and Ingrid Morberg in Gothenburg. Lisbet Broman gave advice on statistical aspects.

*PROBRAIN collaborators: the authors, together with Dr Britt-Marie Stålnacke, Department of Rehabilitation Medicine, Norrlands University Hospital, Umeå, Sweden, Dr Marianne Lannsjö, Department of Rehabilitation Medicine, Sandviken Hospital and Institute of Neuroscience, Uppsala University Hospital, Sweden, Dr Gudrun Karlsdottir, Department of Rehabilitation Medicine, Landspitalinn, University Hospital, Reykjavik, Iceland.

REFERENCES

1. Jennett B, Plum F. Persistent vegetative state after brain damage. A syndrome in search of a name. Lancet 1972; 1: 734–737.
2. Laureys S, Celesia GG, Cohadon F, Lavrijsen J, Leon-Carrion J, Sannita WG, et al. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. BMC Med 2010; 8: 68.
3. Giacino J, Ashwal S, Childs N, Cranford R, Jennett B, Katz DJ, et al. The minimally conscious state: Definition and diagnostic criteria. Neurology 2002; 58: 349–353.
4. Estraneo A, Moretta P, Loreto V, Lanzillo B, Santoro L, Trojano L. Late recovery after traumatic, anoxic, or hemorrhagic long-lasting vegetative state. Neurology 2010; 75: 239–245.
5. Andelic N, Bautz-Holter E, Ronning P, Olafsen K, Sigurdardottir S, Schanke AK, et al. Does an early onset and continuous chain of rehabilitation improve the long-term functional outcome of patients with severe traumatic brain injury? J Neurotrauma 2012; 29: 66–74.
6. Godbolt AK, Tengvar C, Johansson B, Stenson S, Borg J. Opportunity for inpatient brain injury rehabilitation for persons in a vegetative state: survey of Swedish physicians. Am J Phys Med Rehabil 2011; 90: 482–489.
7. The Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (2). N Engl J Med 1994; 330: 1572–1579.
8. Sazbon L, Groswasser Z. Outcome in 134 patients with prolonged posttraumatic unawareness. Part 1: Parameters determining late recovery of consciousness. J Neurosurg 1990; 72: 75–80.
9. Groswasser Z, Sazbon L. Outcome in 134 patients with prolonged posttraumatic unawareness. Part 2: Functional outcome of 72 patients recovering consciousness. J Neurosurg 1990; 72: 81–84.
10. Alberico AM, Ward JD, Choi SC, Marmarou A, Young HF. Outcome after severe head injury. Relationship to mass lesions, diffuse injury, and ICP course in pediatric and adult patients. J Neurosurg 1987; 67: 648–656.
11. Ingvar DH. Cerebral blood flow and metabolism in complete apallic syndromes, in states of severe dementia, and in akinetic mutism. Acta Neurol Scand 1973; 49: 233–244.
12. Levin HS, Saydjari C, Eisenberg HM, Foulkes M, Marshall LF, Ruff RM, et al. Vegetative state after closed-head injury. A Traumatic Coma Data Bank Report. Arch Neurol 1991; 48: 580–585.
13. Schnakers C, Vanhaudenhuyse A, Giacino J, Ventura M, Boly M, Majerus S, et al. Diagnostic accuracy of the vegetative and minimally conscious state: clinical consensus versus standardized neurobehavioral assessment. BMC Neurol 2009; 9: 35.
14. Starmark JE, Stalhammar D, Holmgren E. The Reaction Level Scale (RLS85). Manual and guidelines. Acta Neurochir (Wien) 1988; 91: 12–20.
15. Starmark JE, Stalhammar D, Holmgren E, Rosander B. A comparison of the Glasgow Coma Scale and the Reaction Level Scale (RLS85). J Neurosurg 1988; 69: 699–706.
16. Walther SM, Jonasson U, Gill H. Comparison of the Glasgow Coma Scale and the Reaction Level Scale for assessment of

cerebral responsiveness in the critically ill. Intensive Care Med 2003; 29: 933–938.
17. Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. Arch Phys Med Rehabil 2004; 85: 2020–2029.
18. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. J Neurotrauma 1998; 15: 573–585.
19. Seel RT, Sherer M, Whyte J, Katz DI, Giacino JT, Rosenbaum AM, et al. Assessment scales for disorders of consciousness: Evidence-based recommendations for clinical practice and research. Arch Phys Med Rehabil 2010; 91: 1795–1813.
20. Levin HS, Boake C, Song J, Mccauley S, Contant C, Diaz-Marchan P, et al. Validity and sensitivity to change of the extended Glasgow Outcome Scale in mild to moderate traumatic brain injury. J Neurotrauma 2001; 18: 575–584.
21. MRC CRASH Trial Collaborators, Perel P, Arango M, Clayton T, Edwards E, Poccock S, Roberts I, et al. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008; 336: 425–429.
22. Tesseris J, Pantazidis N, Routsi C, Fragoulakis D. A comparative study of the Reaction Level Scale (RLS85) with Glasgow Coma Scale (GCS) and Edinburgh-2 Coma Scale (modified) (E2CS(M)). Acta Neurochir (Wien) 1991; 110: 65–76.
23. Giacino JT, Whyte J, Bagiella E, Kalmar K, Childs N, Khademi A, et al. Placebo-controlled trial of amantadine for severe traumatic brain injury. N Engl J Med 2012; 366: 819–826.
24. Schiff ND, Giacino JT, Kalmar K, Victor JD, Baker K, Gerber M, et al. Behavioural improvements with thalamic stimulation after severe traumatic brain injury.(Erratum appears in Nature. 2008 Mar 6; 452:120. Note: Biondi, T (added)). Nature 2007; 448: 600–603.
25. Yamamoto T, Katayama Y, Kobayashi K, Oshima H, Fukaya C, Tsubokawa T. Deep brain stimulation for the treatment of vegetative state. Eur J Neurosci 2010; 32: 1145–1151.
26. Krakau K, Hansson A, Karlsson T, de Boussard CN, Tengvar C, Borg J. Nutritional treatment of patients with severe traumatic brain injury during the first six months after injury. Nutrition 2007; 23: 308–317.
27. Katz DI, Polyak M, Coughlan D, Nichols M, Roche A. Natural history of recovery from brain injury after prolonged disorders of consciousness: outcome of patients admitted to inpatient rehabilitation with 1–4 year follow-up. Amsterdam: Elsevier; 2009, p. 73–88.
28. The CRASH trial protocol (Corticosteroid randomisation after significant head injury) (ISRCTN74459797). BMC Emerg Med 2001; 1: 1.
29. NHS Scotland, Acquired Brain Injury National Managed Clinical Network. Traumatic Brain Injury (TBI) in Adults, Standards [Internet]. 2009 [Accessed 10 Oct 2012]. (standard 5 on vegetative and minimally conscious state). Available from: http://www.sabin.scot.nhs.uk/files/standards.pdf.

J Rehabil Med 2013; 45: 749–757

ORIGINAL REPORT

SEX DIFFERENCES IN SYMPTOMS, DISABILITY AND LIFE SATISFACTION THREE YEARS AFTER MILD TRAUMATIC BRAIN INJURY: A POPULATION-BASED COHORT STUDY

Johan Styrke, MD, PhD[1], Peter Sojka, MD, PhD[2], Ulf Björnstig, MD, PhD[1], Per-Olof Bylund, PhD[3] and Britt-Marie Stålnacke, MD, PhD[4]

From the [1]Division of Surgery, Department of Surgical and Perioperative Sciences, Umeå University, Umeå, [2]Department of Health Sciences, Mid Sweden University, Östersund, [3]Emergency and Disaster Medical Centre, Umeå University Hospital, [4]Department of Community Medicine and Rehabilitation, Rehabilitation Medicine, Umeå University, Umeå, Sweden

Objective: **To investigate sex differences in symptoms, structure of symptoms, disability and life satisfaction 3 years after mild traumatic brain injury. Secondary aims were to find risk factors for adverse outcome.**
Design: **Population-based cohort study.**
Patients: **The cohort comprised 137,000 inhabitants at risk in a defined population served by a single hospital in northern Sweden. Patients attending the emergency department following a mild traumatic brain injury in 2001 were included.**
Methods: **Of 214 patients aged 18–64 years, 163 answered a questionnaire on symptoms, disability, and life-satisfaction 3 years post-injury. The instruments were analysed with descriptive statistics. A principal component analysis of the Rivermead Post-Concussion Symptoms Questionnaire was conducted. Risk factors were identified using logistic regression.**
Results: **Post-concussion syndrome was found in 50% of the women and 30% of the men. Disability was found in 52% of the women and 37% of the men, and 57% of the women and 56% of the men were satisfied with their lives. For both genders, high frequency of symptoms was a risk factor for disability and low life satisfaction. Back pain was a risk factor for disability. Living alone was a risk factor for low levels of life satisfaction. The principal component analysis revealed differences between the sexes.**
Conclusion: **There are sex differences in outcome 3 years after mild traumatic brain injury. Women and men should be analysed separately.**

Key words: traumatic brain injury; minor head injury; sex differences; post-concussion syndrome; follow-up studies; quality of life; principal component analysis; odds ratio.

J Rehabil Med 2013; 45: 749–757

Correspondence address: Johan Styrke, Division of Surgery, Department of Surgical and Perioperative Sciences, Umeå University, SE-901 85 Umeå, Sweden. E-mail: johan.styrke@surgery.umu.se

Accepted July 16, 2013

INTRODUCTION

Traumatic brain injury (TBI) is defined as "an alteration in brain function, or other evidence of brain pathology, caused by an external force" (1). The incidence of TBI in Europe has been found to vary between 91/100,000/year and 546/100,000/year (2). In addition to these cases of TBI registered at hospitals, 30–40% of persons who sustain an MTBI do not seek medical care (3).

Approximately 90% of treated TBI are mild (MTBI) (2). The definition of MTBI varies in different studies, but often includes patients presenting at the emergency department (ED) with a Glasgow Coma Scale score (GCS) (4) of 13–15 and/or a history of loss of consciousness (LOC) not exceeding 30 min and/or a history of post-traumatic amnesia (PTA) not exceeding 24 h (5).

The literature on consequences following MTBI is extensive. Patient symptoms are often divided into 3 subgroups: physical, cognitive or behavioural/emotional (5). Carroll et al. conducted a systematic review of the prognosis for MTBI, and concluded that symptoms and cognitive deficits are common immediately following MTBI, but most often resolve within 3–12 months (6). There is, however, a significant minority of patients whose symptoms persist. In hospital-based cohort studies with follow-up extending over a 1-year period symptoms or disabilities are found in approximately 10–50% of cases (7–9).

Men are at higher risk than women of sustaining a TBI (9). Sex differences in outcome following MTBI have been addressed in a number of studies, of which some found women to have an unfavourable outcome compared with men (10, 11). The evidence, however, is limited and some studies on cognitive symptoms found no difference between women and men, or even found men to have a worse outcome (12, 13). A lack of age matching and other baseline data between women and men, as well as the possibility that women and men report subjective symptoms differently have been known to bias the research of TBI gender studies (14).

The point prevalence of low back pain varies between 12% and 33% in the general population, and pain can confound results from studies of MTBI outcome because pain correlates with cognitive difficulties (15, 16). Zhang et al. (17) recently included neck/shoulder pain and low back pain in a regression analysis of factors contributing to poor perceived general health 6 weeks after MTBI, and found that presence of neck/shoulder pain and low back pain were associated with worse outcome.

Few studies have addressed long-term sex-related outcome after MTBI. The aim of this study was therefore to analyse symptoms, structure of symptoms, disability, and life satisfaction from this perspective in our hospital-based MTBI cohort 3 years after injury. Secondary aims were to investigate the frequency of neck, thoracic and lumbar back pain among the patients, and to find risk factors for adverse outcome of disability and life satisfaction.

MATERIAL AND METHODS

Participants and setting

Umeå is a mid-sized Swedish city located approximately 400 km south of the Arctic Circle. The city has only one hospital, serving a defined population of 137,000 inhabitants (2001 census). The distance to the next nearest hospital is 110 km. The study cohort originates from prospectively collected data in the Umeå University Hospital's (UUH) injury register from 2001. This ED-based register describes all injuries that necessitate inpatient or outpatient treatment at the hospital. An extraction of data from the register was conducted in 2003. The data was re-evaluated and additional data added by retrospective analysis of medical records.

Inclusion criteria

In 2001, 485 patients with TBI were included in the injury register, 214 of whom met the inclusion criteria for the current study, listed below:

- injury event within the primary catchment area of UUH;
- arrival at the ED within 24 h after the injury event;
- presence of TBI, defined as a brain trauma causing any degree of disturbed consciousness (e.g. LOC, disorientation), PTA, neurological deficit, severe headache, nausea, or vomiting;
- GCS assessed as 13–15 at the ED;
- age 18–64 years at the time of follow-up (working age population).

Follow-up

Of the 214 MTBI patients, 200 could be contacted, as shown in Fig. 1. In 2004 they were sent a set of postal questionnaires; a mean of 3 years and 3 months after the injury incident. Non-responders were contacted by telephone and reminded to complete the questionnaires. A total of 163 persons (81%) responded and were further analysed. Data on sex, age, type of injury event, presence of alcohol inebriation at the time of the injury, PTA, LOC, and presence of intracranial bleeding (ICB) were tested for differences in mean values between responders and non-responders.

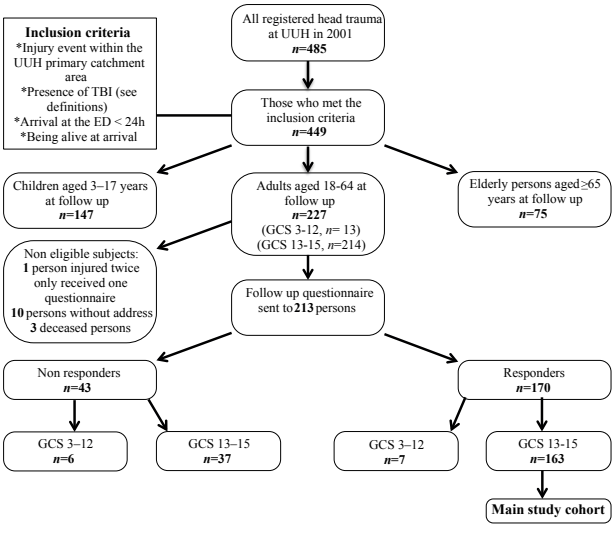


Fig. 1. Study flow chart. UUH: Umeå University Hospital; TBI: traumatic brain injury; ED: emergency department; GCS: Glasgow Coma Scale.

Severity classification

Our definition of MTBI falls within the American Congress of Rehabilitation Medicines definition of MTBI, with some exceptions (5). We did not, at the time of the primary data analysis in 2003, exclude patients with LOC exceeding 30 min or PTA exceeding 24 h from the MTBI group, because data on LOC and PTA could not be determined in approximately 40% of the patients. When answering the questionnaires in 2004, the patients responded to questions about the length of LOC and PTA. Five of the patients with GCS 13–15 at arrival claimed that the length of LOC had exceeded 30 min, and 3 of the patients stated that PTA had lasted for more than 24 h. These 8 patients are included in the study even though they could have been classified as moderate TBI in retrospect.

Definition of post-concussion syndrome

We used the definition of post-concussion syndrome (PCS) given by the International Classification of Diseases – 10th revision (ICD-10) (18). Hence 3 of the following symptoms (score 2–4) on the Rivermead Post-Concussion Symptoms Questionnaire *(*RPQ) were required: headache, dizziness, fatigue, poor memory, poor concentration, irritability, or sleep disturbance.

Statistical analysis

All data were analysed using SPSS 19 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel 2011 (Microsoft Corp., Redmond, WA, USA). Contingency tables were analysed with Pearson's χ^2 test or Fisher's exact test if any value was below 5. When comparing mean and median values, Student's *t*-test (*t*-test) or the non-parametric Mann-Whitney *U* test (*U*-test) was used. Interquartile ranges (IQR) were used as measures of variability. Effect sizes were calculated for *t*-tests (d) (Cohen's *d*) and *U*-tests (r) ($r = z/\sqrt{n}$). Statistical significance was set at $p < 0.05$. A principal component analysis (PCA) was performed to explore patterns in the RPQ data for women and men, respectively. Scree tests were used to determine the number of components to be included. These components also had eigenvalues > 1. No rotation was used. We investigated how to interpret the first 2 components by plotting the female component scores on the x-axis and the male component scores on the y-axis. We also graphically explored the relationship between the components and the presence of PCS, presence of disability and low levels of life satisfaction. To do this, we extracted the component scores and plotted them on scatterplots, coloured for the outcome measures. Finally, the component scores were included in multiple logistic regressions. These regressions were conducted to analyse the relationship between the dependent factors Rivermead Head Injury Follow-Up Questionnaire (RHFUQ) (presence of any disability) and life satisfaction checklist (LiSat-11) (</>median) vs some independent demographic and injury-related factors, along with the mean values of back pain and the RPQ component scores for each component. The tested demographic and injury-related risk factors were: age ≥40 years, traffic injury, presence of amnesia, presence of LOC, presence of ICB, living alone, unemployment, less than university-level education, TBI before 2001, TBI after 2001, and on-going insurance claim. An initial screening was conducted with χ^2 tests and Mann-Whitney *U* tests, thereby ruling out risk factors with a *p*-value > 0.3. All remaining risk factors were included in the regression models and the models were subsequently simplified by the exclusion of risk factors with a *p*-value > 0.1. Nagelkerke R^2 was used as a measure of goodness of fit for the models.

Follow-up instruments

RPQ. The RPQ is a frequently used questionnaire consisting of 16 symptoms commonly exhibited after MTBI (19). The patient is asked to rate symptoms exhibited during the last 24 h on a scale from 0 to 4, where 0 means no experience of the symptom, and 4 means that the

symptom is a severe problem. The answers were dichotomized into 0–1 = no symptom experienced or 2–4 = symptom experienced. We added 3 questions regarding symptoms of back pain: During the last 24 h did you experience: 1, neck/cervical pain; 2, thoracic pain; or 3, lumbar pain? The total score from all 3 types of back pain is referred to as "back pain score".

RHFUQ. The RHFUQ is an instrument aimed at describing outcome of mild to moderate TBI in terms of disability (20). The 10 items cover social and domestic activities, work, and relations with friends and family. The participants are asked to rate changes in their abilities compared with prior to the injury. The answers range from 0 = no change to 4 = a very marked change. The RHFUQ was dichotomized into 0 = no disability and 1–4 = presence of disability.

LiSat-11. Life satisfaction was assessed using the LiSat-11 (21). The instrument uses a 6-grade scale (from 1 = very dissatisfying to 6 = very satisfying). The LiSat-11 scale was dichotomized into satisfied (5–6) or dissatisfied (1–4).

Reference populations

The RPQ answers were compared with a 2007 reference group consisting of 461 18–64-year-old consecutive blood donors at the Blood Centre of UUH (the only blood donor site in the area) (Nilsson Sojka & Sojka, unpublished, anonymously collected data). The LiSat-11 reference population comprised 2,533 Swedes, aged 18–64 years, who answered the questionnaire in 1996 (21).

Ethics

The regional ethics committee approved the study (04-097M).

RESULTS

Characteristics of the patients, non-responders and reference groups

Some demographic and injury-related characteristics are shown in Table I. There were no significant differences between women and men, except that men more often had presence of LOC and were less often university-educated. No significant differences in proportions were found between responders and non-responders, with the exceptions that alcohol inebriation at the time of the injury was more common among the non-responders, and LOC was more common among the responders. There was no significant difference in sex distribution between the RPQ reference population and the study population. The references were older than the study population: median 35 years (IQR 24) vs 25 years (IQR 23) ($p < 0.001$, *U*-test, $r = 0.25$). Previous TBI was reported by 116 of the references. When comparing the LiSat-11 reference population with the study population, the distribution of women and men was similar. The mean age of the LiSat-11 references was unknown.

Rivermead Post-Concussion Symptoms Questionnaire and back pain

The scores for all symptoms on the RPQ in women and men, with the addition of back pain, are shown in Table II. Women had a significantly higher median RPQ score than men: 13 (IQR 21) vs 6 (IQR 16) ($p = 0.006$, *U*-test, $r = 0.22$). PCS according to the ICD-10 was found in 50% of the women and 30% of the men ($p = 0.008$). When comparing presence of symptoms (score 2–4), the share of women who exhibited symptoms of headache, dizziness, nausea/vomiting, noise sensitivity, fatigue, feelings of depression, and taking longer to think were significantly higher than the share of men claiming to have those symptoms (Table III). Feelings of depression were reported by 41% of the women and 22% of the men among the patients, but only by 5% and 4% among the references. In the reference group, fewer differences between women and men were found (Table III).

Presence of almost all RPQ symptoms was significantly more frequent in the MTBI group than in the reference group (Table III). The median RPQ score was higher among the patients of this study than among the references: 9 (IQR 18) vs 2 (IQR 5) ($p < 0.001$, *U*-test, $r = 0.31$). This was also true for women: 13 (IQR 21) vs 3 (IQR 6) ($p < 0.001$, *U*-test, $r = 0.26$) and

Table I. *Demographic and injury-related characteristics*

	Women ($n = 68$)	Men ($n = 95$)	*p*-value	Responders ($n = 163$)	Non-responders ($n = 37$)	*p*-value
Male, %	–	–	–	58	58	0.97
Age ≥40 years, %	24	33	0.21	29	32	0.74
Age, years, median (IQR)	25 (19)	25 (27)	0.90 (*U*-test)	25 (23)	29 (22)	0.22 (*U*-test)
Injured in traffic, %	37	32	0.49	34	37	0.72
PTA present, %	38	47	0.25	44	45	0.90
PTA, min, median (IQR)	15 (115)	30 (236)	0.31 (*U*-test)	–	–	–
LOC present, %	40	57	**0.031**	50	26	**0.009**
LOC, min, median (IQR)	5 (I28)	5 (22)	0.97 (*U*-test)	–	–	–
ICB present, %	3	5	0.70	4	3	0.53
Alcohol inebriation, %	18	27	0.15	23	42	**0.019**
Living alone, %	34	32	0.76	–	–	–
Unemployed, %	27	26	0.98	–	–	–
Not university-educated, %	52	78	**< 0.001**	–	–	–
TBI before year 2001, %	44	40	0.60	–	–	–
TBI after year 2001, %	12	12	0.97	–	–	–
Insurance process present, %	32	34	0.86	–	–	–

Significant *p*-values are shown in **bold**.
PTA: post-traumatic amnesia; LOC: loss of consciousness; ICB: intracerebral bleeding; TBI: traumatic brain injury; IQR: interquartile range.

Table II. *Number of post-concussion symptoms (RPQ) and back pain in women/men*

RPQ score[a]	0	1	2	3	4	Missing value
Headache	27/53	7/18	18/13	10/7	6/4	
Dizziness	29/67	15/9	15/13	7/6	2/0	
Nausea, vomiting	47/78	10/11	9/2	2/3	0/1	
Noise sensitivity	33/74	13/5	11/8	8/7	2/1	1/0
Sleep disturbance	36/59	7/12	4/7	14/12	7/5	
Fatigue	27/49	9/18	15/15	7/10	10/3	
Irritability	31/56	16/16	7/14	10/5	4/4	
Feeling depressed	29/57	11/17	15/12	7/4	6/5	
Feeling frustrated	30/55	15/17	15/16	4/4	4/3	
Poor memory	31/46	13/23	7/15	12/4	4/7	1/0
Poor concentration	35/57	9/14	10/14	10/6	4/4	
Taking longer to think	41/65	10/18	7/5	6/4	4/3	
Blurred vision	42/71	12/11	10/6	3/3	1/4	
Sensitivity to light	42/68	9/9	5/9	8/7	4/2	
Double vision	57/86	8/4	1/4	0/1	1/0	1/0
Restlessness	40/62	10/19	6/7	11/5	1/2	
Back pain						
Cervical spine	29/56	6/10	15/10	10/11	6/8	2/0
Thoracic spine	38/69	7/8	11/3	8/10	2/4	2/1
Lumbar spine	31/60	10/15	10/5	8/10	8/5	1/0

[a]0: not experienced; 1: no longer a problem; 2: a mild problem; 3: a moderate problem; 4: a severe problem.
RPQ: Rivermead Post-Concussion Symptoms Questionnaire.

men: 6 (IQR 16) vs 2 (IQR 5) ($p < 0.001$, *U*-test, $r = 0.40$). The symptoms with the highest difference of occurrence between the patients and the references in women were: headache, poor concentration, and feeling depressed, whereas in men the affective symptoms feeling frustrated and irritability accompanied headache and poor memory.

Neck pain (score 2–4) was found in 37%, lumbar back pain in 28%, and thoracic back pain in 24% of the patients. Women reported these symptoms significantly more frequently than men (Table III). Women also had a significantly higher median back pain score than men: 3 (IQR 6) vs 1 (IQR 4) ($p = 0.015$, *U*-test, $r = 0.19$).

Rivermead Head Injury Follow-Up Questionnaire

Presence of any disability was reported by 52% of the women and 37% of the men. The most frequently reported disability items were tiredness at work (23%), difficulty in sustaining previous workload (18%), and difficulty in ability to enjoy previous leisure activities (18%). Women had a significantly higher median RHFUQ score than men: 2 (IQR 11) vs 0 (IQR 4) ($p = 0.040$, *U*-test, $r = 0.16$). Women scored higher on all disability items, however, only significantly higher on 3 items: conversation with 2 or more people, tiredness at work, and family expectations (Table IV).

LiSat-11

For most items, the proportion of persons indicating satisfied or very satisfied on the LiSat-11 was significantly lower in the MTBI-group compared with the reference population. Exceptions were partner relationship and family life, where no significant differences were found (Table V). Fifty-seven percent of the women and 56% of the men were satisfied with their life as a whole. There were no significant differences in

Table III. *Comparison between the frequencies of post-concussion symptoms (RPQ-score 2–4) and back pain (score 2–4) exhibited by respondents of the present study and a reference group of blood donors*

	Present study		Reference					
	Women ($n = 68$) % a	Men ($n = 95$) % b	Women ($n = 179$) % c	Men ($n = 282$) % d	*p*-value a–b	c–d	a–c	b–d
Headache	50	25	7	4	**0.001**	0.25	**< 0.001**	**< 0.001**
Dizziness	35	20	8	2	**0.029**	**0.002**	**< 0.001**	**< 0.001**
Nausea, vomiting	16	6	0	0.7	**0.042**	0.52	**< 0.001**	**0.004**
Noise sensitivity	31	17	7	3	**0.035**	**0.047**	**< 0.001**	**< 0.001**
Sleep disturbance	37	25	10	10	0.11	0.97	**< 0.001**	**< 0.001**
Fatigue	47	30	28	18	**0.022**	**0.017**	**0.004**	**0.023**
Irritability	31	24	5	3	0.34	0.15	**< 0.001**	**< 0.001**
Feeling depressed	41	22	5	4	**0.009**	0.62	**< 0.001**	**< 0.001**
Feeling frustrated	34	24	8	3	0.18	**0.015**	**< 0.001**	**< 0.001**
Poor memory	34	27	7	6	0.38	0.49	**< 0.001**	**< 0.001**
Poor concentration	35	25	6	5	0.17	0.90	**< 0.001**	**< 0.001**
Taking longer to think	25	13	2	3	**0.042**	0.32	**< 0.001**	**< 0.001**
Blurred vision	21	14	3	4	0.24	0.42	**< 0.001**	**0.001**
Sensitivity to light	25	19	6	3	0.35	0.082	**< 0.001**	**< 0.001**
Double vision	3	5	0	0.4	0.70	1.0	0.075	**0.005**
Restlessness	27	15	3	3	0.063	0.81	**< 0.001**	**< 0.001**
Cervical spine pain	47	31			**0.034**			
Thoracic spine pain	32	18			**0.044**			
Lumbar spine pain	39	21			**0.014**			
Any spinal pain	62	37			**0.002**			

Significant *p*-values are shown in **bold**.
RPQ: Rivermead Post-Concussion Symptoms Questionnaire.

Table IV. *Disability (RHFUQ score 1–4) in comparison between women and men*

	Women ($n=68$) %	Men ($n=95$) %	*p*-value
Conversation 1 person	6	4	0.72
Conversation ≥2 persons	24	11	**0.025**
Domestic work	10	5	0.24
Social activities	16	8	0.13
Leisure activities	24	14	0.11
Workload	24	14	0.11
Tired at work	32	17	**0.021**
Relationship with previous friends	19	9	0.076
Relationship with partner	13	5	0.13
Family demands	18	6	**0.023**

Significant *p*-values are shown in **bold**.
RHFUQ: Rivermead Head Injury Follow-Up Questionnaire.

any of the items or the mean LiSat-11 score between men and women: 46.0 (IQR 16) vs 46.7 (IQR 15) ($p=0.70$; difference 0.7, 95% CI –4.1–2.7, t-test, d = 0.06) (Fig. 2).

Principal component analysis

In women, we found 3 significant components (eigenvalues 8.0, 1.5 and 1.1) explaining 50 + 10 + 7=66% of the total variance and in men 2 significant components (eigenvalues 8.0 and 1.7) explaining 50 + 11 = 61% of the total variance. In both women and men, all symptoms of the RPQ highly contributed to component 1, and those symptoms that also highly contributed to component 2 were mainly vision-related symptoms, whereas, for example, frustration and restlessness were low contributors. Differences between women and men existed; for example, noise sensitivity and headache were slightly more prominent symptoms on component 1 in men, while noise sensitivity and poor memory scored high in women but not in men on component 2 (Fig. 3). To reach a 1-component solution in men, the 3 vision-related symptoms plus dizziness, nausea/vomiting, and sleep disturbance had to be excluded. To reach a 2-component solution in women, the vision-related symptoms had to be removed, and to further reach a 1-factor solution, noise sensitivity also had to be eliminated.

The first component was a strong indicator for PCS and when graphically investigating the importance of the first and second components for the outcome (disability and life satisfaction), the first component, but not the second, indicated whether the patients had an unfavourable outcome (Fig. 4). Women and men did not differ in this matter. In conclusion, vision-related factors and other factors scoring high on the second component are of less importance for disability and life satisfaction than are the other RPQ symptoms. The first component in women and men also predicted worse outcome in the multiple logistic regressions (Table VI).

Table V. *LiSat-11: comparison between the patients of this study and the Swedish general population reference group (Fugl-Meyer et al. [21]) for the answers "very satisfied" or "satisfied" on all items*

	Present study ($n=163$) %	Reference ($n=2,533$) %	*p*-value
Life as a whole	56	70	**<0.001**
Closeness			
Sexual life	46	56	**0.011**
Partner relationship	80	82	0.65
Family life	81	81	0.98
Health			
ADL	90	95	**0.003**
Somatic health	43	77	**<0.001**
Psychological health	60	81	**<0.001**
Spare time			
Leisure	45	57	**0.002**
Contacts	54	65	**0.003**
Provision			
Vocation	42	54	**0.001**
Economy	25	39	**<0.001**

Significant *p*-values are shown in **bold**.
ADL: activities of daily living.

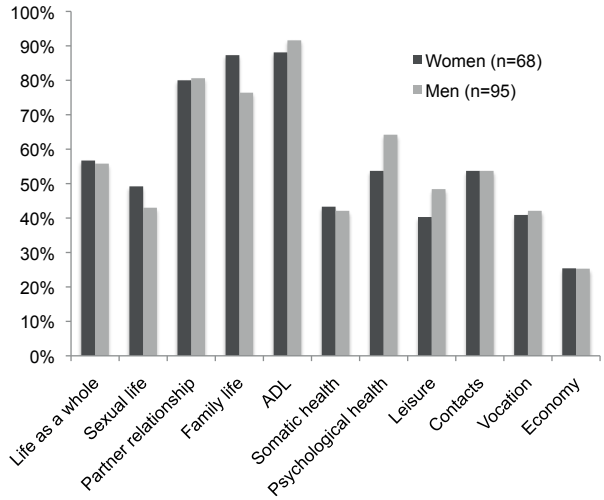


Fig. 2. Frequency of persons being satisfied or very satisfied (score 5–6) with different aspects of life measured on the LiSat-11. ADL: activities of daily living.

Multiple logistic regression analysis

The multiple logistic regression analysis is summarized in Table VI. This revealed some possible risk factors for having any disability, as measured with RHFUQ, or life satisfaction less than the median, as measured with LiSat-11:

- significant risk factors for disability in women were being injured in traffic, having a high first component score of the RPQ, and having a high back pain score.
- significant risk factors for disability in men were having a high first component score of the RPQ and having a high back pain score.
- significant risk factors for impaired life satisfaction for both genders were living alone and having a high first component score of the RPQ.

Table VI. *Multiple logistic regression analysis of the relationship between disability and life satisfaction vs possible demographic and injury-related risk factors, the RPQ-components and mean back pain score in women and men*

	RHFUQ (disability/no disability)				LiSat-11 (<median/>median)			
	B	OR	95% CI	*p*-value	B	OR	95% CI	*p*-value
Women								
Injured in traffic	1.5	4.5	1.2–17	**0.029**[a]	1.2	3.3	0.91–12	0.069
Living alone	–	–	–	–	2.0	7.1	1.9–110	**0.006**[e]
TBI after 2001	2.5	12	0.89–150	0.061	–	–	–	–
RPQ: Female Component 1[b]	0.17	1.2	1.1–1.3	**0.006**[c]	0.2	1.2	1.1–1.4	**0.001**[f]
Back pain[b]	0.26	1.3	1.0–1.6	**0.026**[d]	–	–	–	–
Constant	–1.4	1.4		0.33	–0.71	0.49		0.36
	Nagelkerke R^2 0.52				Nagelkerke R^2 0.46			
Men								
Living alone	–	–	–	–	1.7	5.2	1.9–14	**0.001**[i]
TBI after 2001	1.8	5.9	0.86–41	0.070	–	–	–	–
RPQ: Male Component 1[b]	1.1	1.1	1.0–1.2	**0.003**[g]	1.0	1.1	1.0–1.1	**0.004**[j]
Back pain[b]	0.52	1.7	1.2–2.3	**0.002**[h]	–	–	–	–
Constant	1.1	0.01		0.25	–0.52	0.59		0.24
	Nagelkerke R^2 0.64				Nagelkerke R^2 0.25			

Significant *p*–values are shown in **bold**. A positive value on B indicates that the patients with the potential risk factor had unfavourable outcome.
[a]Women injured in traffic had 4.5 times the odds of having disability than those who were not injured in traffic.
[b]Continuous variables.
[c]For every 1-point increase in RPQ: female component 1, the women had 1.2 times higher odds of having disability.
[d]For every 1-point increase in the mean back pain score, the women had 1.3 times higher odds of having disability.
[e]Women living alone had 7.1 times the odds of having a life satisfaction below median than those who lived with someone.
[f]For every 1-point increase in RPQ: female component 1, the women had 1.2 times higher odds of having a life satisfaction below median.
[g]For every 1-point increase in RPQ: male component 1, the men had 1.1 times higher odds of having disability.
[h]For every 1-point increase in the mean back pain score, the men had 1.7 times higher odds of having disability.
[i]Men living alone had 5.2 times the odds of having a life satisfaction below median than those who lived with someone.
[j]For every 1-point increase in RPQ: male component 1, the men had 1.1 times higher odds of having a life satisfaction below median.
RPQ: Rivermead Post-Concussion Symptoms Questionnaire; RHFUQ: Rivermead Head Injury Follow-Up Questionnaire; TBI: traumatic brain injury; OR: odds ratio; CI: confidence interval; RPQ components: the component scores.

DISCUSSION

The present study addresses long-term consequences after MTBI. Similar studies have been conducted previously, but not presented from a gender-perspective. It is important to recognize and study differences between women and men because this might lead to future development of separate management strategies for the different sexes following MTBI. The main findings were that significant unfavourable outcome for women

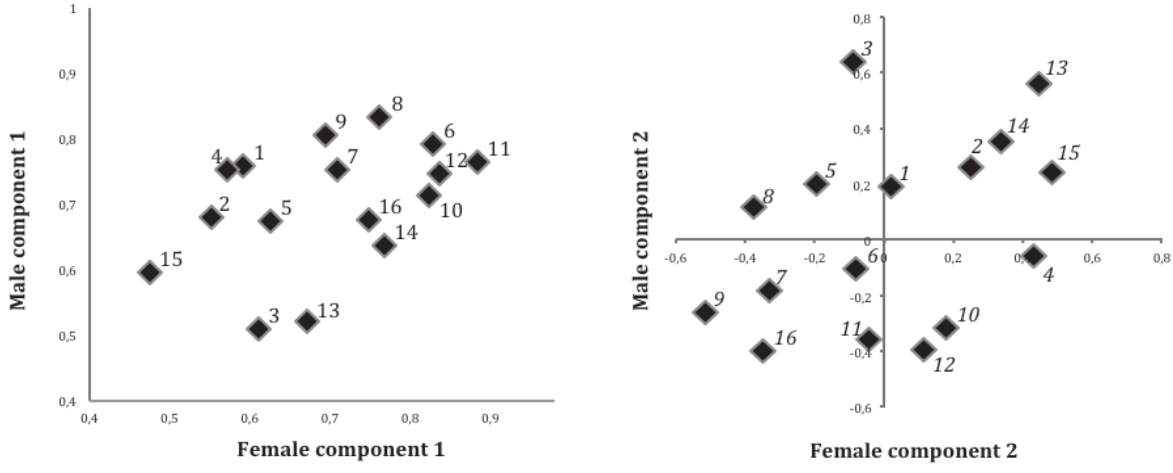


Fig. 3. First and second component scores in women and men. 1, Headache; 2, Dizziness; 3, Nausea, vomiting; 4, Noise sensitivity; 5, Sleep disturbance; 6, Fatigue; 7, Irritability; 8, Feeling depressed; 9, Feeling frustrated; 10, Poor memory; 11, Poor concentration; 12, Taking longer to think; 13, Blurred vision; 14, Sensitivity to light; 15, Double vision; 16, Restlessness.

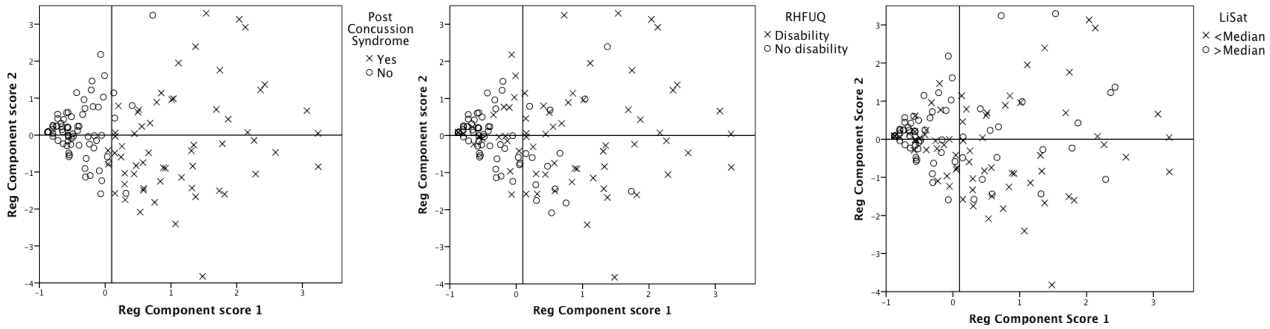


Fig. 4. Scatterplots of the component scores of components 1 and 2 in all patients coloured by post-concussion syndrome (PCS), Rivermead Head Injury Follow-Up Questionnaire (RHFUQ) and LiSat-11 scores.

in comparison with men was found in the total RPQ score, back pain score, and RHFUQ score, but not in the LiSat-11 score reported 3 years post-MTBI. The MTBI group reported higher prevalence of symptoms and lower life satisfaction compared with the reference groups. PCS was found in 50% of the women and 30% of the men. Disability was found in 52% of the women and 37% of the men and satisfaction with life as a whole was found in 57% of the women and 56% of the men. In the PCA, the structure of RPQ differed between women and men, thus giving different numbers of components. In the multiple regression analysis, living alone or having a high value on the first RPQ-component were the most significant risk factors for low life satisfaction regardless of gender. Having a high value on the first RPQ component or a high back pain score were the most significant risk factors for disability in women and men.

Regarding sex differences, the general impression from our cohort is that females had more symptoms and disability compared with males, although significance was reached in only 3 of 10 RHFUQ items and 6 of 16 RPQ items. Effect sizes were small. Long-term evaluations of sex-specific outcome after MTBI have been conducted previously and the females appear to be at risk of unfavourable outcome in most studies. Regarding outcome 3 months post-MTBI, Bazarian et al. (10) concluded that adult females are at greater risk than males for having a high RPQ score. Several other studies support that females are at greater risk for adverse outcome (7, 22, 23). There are, however, also studies in which no sex differences are found (13, 24–26). Bay et al. (11) noted more depression, stress and symptoms in women up to 6 months after mild and moderate TBI. After 12 months, no sex differences remained. In the RPQ-items dizziness, noise sensitivity, fatigue, and feeling frustrated we found sex differences to be significant among the references. This is important to be aware of because it suggests that at least some differences found in our cohort could be normal rather than a result of MTBI.

Post-concussion symptoms were frequently reported. The 3 most prominent symptoms in women were headache (50%), fatigue (47%), and feeling depressed (41%); whereas in men, fatigue (30%), poor memory (27%), and headache/sleep disturbance/poor concentration (25%) were most common. Lannsjö et al. (27) investigated the prevalence of symptoms reported by 2,523 Swedes at 3 months post-MTBI. They found that fatigue (23%), headache (22%), dizziness (16%), and poor memory (16%) were the most commonly reported symptoms (27). Their figures were clearly lower than ours; however, they included children over the age of 6 years and elderly persons over 65 years of age, thus comparison is difficult. In other studies, the prevalence of the most commonly reported symptoms varies between 12% and 63% (7, 9, 24, 26, 28, 29). When synthesized, other studies report the following symptoms to be most common: 1, headache; 2, fatigue; 3, dizziness; 4, poor memory; 5, poor concentration; 6, irritability; and 7, sleep disturbance (7, 9, 24, 26, 27, 29).

The frequencies of PCS were within the span of previous findings (24, 26, 28, 30).

Presence of any disability was more common in women than in men. The answers to the RHFUQ revealed that tiredness at work, leisure activities, and workload were the domains where women and men most frequently reported problems. In both genders, a high frequency of RPQ symptoms predicted disability. Unfortunately, disability was not assessed in the reference population, thus it is difficult to evaluate the importance of the MTBI to the disability. Other studies have shown frequencies of disability using various measurements between < 10% and approximately 50% of the patients (7, 9, 22, 29–31). The association that more symptoms give more disability has also previously been shown (7, 30).

The patients of the present study had significantly lower life satisfaction on most of the LiSat-11 items compared with the references. Similar results on LiSat-11 from our area were found by Stålnacke et al. (31). Petchprapai et al. (32) in a review found the literature on quality of life (QoL) to be inconclusive; however, several studies have found MTBI patients to have adverse outcome on various measures of QoL (17, 33). The finding of no differences between women and men regarding life satisfaction, despite the fact that women had more symptoms and disability than men, were interesting. It might suggest that women and men have different patterns in translating symptoms and disability to life satisfaction.

The frequencies of back pain seem to correspond with previous studies (34, 35) and back pain was associated with disability. As previously suggested by Zhang et al. (17), if chronic back pain in MTBI patients leads to impaired life satisfaction, then treatment for back pain should be given.

Previous PCA, factor analysis, and Rasch analysis have found multiple factor-solutions when analysing the RPQ (27, 30, 36–38). Our PCA showed different number of components in women and men. On the other hand, with a few exceptions, both genders had similar distributions of the RPQ symptoms when graphically examined. Lannsjö et al.(36) concluded that sex did not affect their results. We conclude that the issue needs further clarification and we suggest that future factor analysis within the field of MTBI should be conducted separately on women and men.

This study's strength is that it covers symptoms, disability and life satisfaction in women and men from a defined population seeking medical attention for MTBI during a 1-year period at the only hospital within a 100 km radius. Given these circumstances, we can describe the burden and consequences of hospital-registered MTBI with accuracy in our community. The major disadvantage of this type of cohort study, however, is it does not catch the 30–40% of MTBI cases not seen at the ED (3). It is reasonable to believe that persons not seeking medical attention because of their MTBI have less severe injuries and/or are less worried about their injuries than the others. This would create a selection bias that theoretically might enhance the frequency of symptoms and disability being reported.

Men had more LOC and less education than women. However, LOC is not considered an important risk factor for outcome after MTBI (7, 25), and both LOC and education were included in the multiple regression analysis and thereby controlled for. We did, however, not control for PTSD, which has been reported to be an important confounding factor (39).

Do symptoms like those in the RPQ reflect MTBI? Questions have been raised about their specificity. A review by Fayol et al. (39) states that PCS is reported in healthy subjects, general trauma patients, psychiatric patients, neurology patients, pain patients, patients with minor medical issues, and insurance claimants. Overestimation of the pre-injury health status along with symptom over-endorsement can also bias the results of questionnaires (40). It is also possible that life events during the 3-year follow-up influenced the answers to the questionnaires. However, we clearly show that our MTBI patients are bothered by more symptoms and have lower life satisfaction than the reference groups. Because we simultaneously analysed RPQ, RHFUQ, and LiSat-11, causal conclusions cannot be made.

In conclusion, this study of sex differences in late outcome following MTBI shows that symptoms, structure of symptoms, disability, and risk factors for adverse outcome differs between women and men. These aspects should be considered in future studies of MTBI. As much as 50% of the women and 30% of the men met the definition of PCS 3 years post-injury and almost all symptoms were reported more frequently in our cohort than in a reference population. Life satisfaction was also inferior in comparison with references. A high frequency of symptoms was independently associated with worse outcome in terms of disability and life satisfaction. These aspects need to be taken into consideration in the management of patients with MTBI.

ACKNOWLEDGEMENTS

The authors would like to thank Gabriel Granåsen for assisting in the statistical analysis and Asta Strandberg for helping us to administer the questionnaires. This work was supported by grants from the Swedish Association of Brain Injured and Families and the Department of Research and Development, Västernorrland County Council.

REFERENCES

1. Menon DK, Schwab K, Wright DW, Maas AI. Position statement: definition of traumatic brain injury. Arch Phys Med Rehabil 2010; 91: 1637–1640.
2. Tagliaferri F, Compagnone C, Korsic M, Servadei F, Kraus J. A systematic review of brain injury epidemiology in Europe. Acta Neurochir (Wien) 2005; 148: 255–268.
3. Demakis GJ, Rimland CA. Untreated mild traumatic brain injury in a young adult population. Arch Clin Neuropsychol 2010; 25: 191–196.
4. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
5. Kay T, Harrington DE, Adams R, Anderson T, Berrol S, Cicerone K, et al. Definition of mild traumatic brain injury. J Head Trauma Rehabil 1993; 8: 86–87.
6. Carroll L, Cassidy JD, Peloso P, Borg JXR, Holst von H, Holm L, et al. Prognosis for mild traumatic brain injury: results of the who collaborating centre task force on mild traumatic brain injury. J Rehabil Med 2004; 36: 84–105.
7. Edna TH. Disability 3–5 years after minor head injury. J Oslo City Hosp 1987; 37: 41–48.
8. Whitnall L, McMillan TM, Murray GD, Teasdale GM. Disability in young people and adults after head injury: 5–7 year follow up of a prospective cohort study. J Neurol Neurosurg Psychiatr 2006; 77: 640–645.
9. Rickels E, Wild von K, Wenzlaff P. Head injury in Germany: a population-based prospective study on epidemiology, causes, treatment and outcome of all degrees of head-injury severity in two distinct areas. Brain Inj 2010; 24: 1491–1504.
10. Bazarian JJ, Blyth B, Mookerjee S, He H, McDermott MP. Sex differences in outcome after mild traumatic brain injury. J Neurotrauma 2010; 27: 527–539.
11. Bay E, Sikorskii A, Saint-Arnault D. Sex differences in depressive symptoms and their correlates after mild-to-moderate traumatic brain injury. J Neurosci Nurs 2009; 41: 298–309, quiz 310–311.
12. Covassin T, Bay E. Are there gender differences in cognitive function, chronic stress, and neurobehavioral symptoms after mild-to-moderate traumatic brain injury? J Neurosci Nurs 2012; 44: 124–133.
13. Tsushima WT, Lum M, Geling O. Sex differences in the long-term neuropsychological outcome of mild traumatic brain injury. Brain Inj 2009; 23: 809–814.
14. Farace E, Alves WM. Do women fare worse: a metaanalysis of gender differences in traumatic brain injury outcome. J Neurosurg 2000; 93: 539–545.
15. Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J Spinal Disord 2000; 13: 205–217.
16. Nicholson K. Pain, cognition and traumatic brain injury. Neuro-Rehabilitation 2000; 14: 95–103.
17. Zhang S, Carroll L, Cassidy J, Paniak C. Factors influencing self-rated health in traffic-related mild traumatic brain injury. J Rehabil Med 2009; 41: 1062–1067.
18. World Health Organisation (WHO). International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) version, 2010 [Internet]. 2010 [cited 2012 Oct 8]. Available from: URL: http://apps.who.int/classifications/icd10/browse/2010/en#/F07.2.

19. King NS, Crawford S, Wenden FJ, Moss NE, Wade DT. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. J Neurol 1995; 242: 587–592.
20. Crawford S, Wenden FJ, Wade DT. The Rivermead head injury follow up questionnaire: a study of a new rating scale and other measures to evaluate outcome after head injury. J Neurol Neurosurg Psychiatr 1996; 60: 510–514.
21. Fugl-Meyer AR, Melin R, Fugl-Meyer KS. Life satisfaction in 18- to 64-year-old Swedes: in relation to gender, age, partner and immigrant status. J Rehabil Med 2002; 34: 239–246.
22. Thornhill S, Teasdale GM, Murray GD, McEwen J, Roy CW, Penny KI. Disability in young people and adults one year after head injury: prospective cohort study. BMJ 2000; 320: 1631–1635.
23. Bazarian JJ, Wong T, Harris M, Leahey N, Mookerjee S, Dombovy M. Epidemiology and predictors of post-concussive syndrome after minor head injury in an emergency population. Brain Inj 1999; 13: 173–189.
24. Hou R, Moss-Morris R, Peveler R, Mogg K, Bradley BP, Belli A. When a minor head injury results in enduring symptoms: a prospective investigation of risk factors for postconcussional syndrome after mild traumatic brain injury. J Neurol Neurosurg Psychiatr 2012; 83: 217–223.
25. Jacobs B, Beems T, Stulemeijer M, van Vugt AB, van der Vliet TM, Borm GF, et al. Outcome prediction in mild traumatic brain injury: age and clinical variables are stronger predictors than CT abnormalities. J Neurotrauma 2010; 27: 655–668.
26. Roe C, Sveen U, Alvsåker K, Bautz-Holter E. Post-concussion symptoms after mild traumatic brain injury: influence of demographic factors and injury severity in a 1-year cohort study. Disabil Rehabil 2009; 31: 1235–1243.
27. Lannsjö M, Geijerstam J-LA, Johansson U, Bring J, Borg J. Prevalence and structure of symptoms at 3 months after mild traumatic brain injury in a national cohort. Brain Inj 2009; 23: 213–219.
28. Sigurdardottir S, Andelic N, Roe C, Jerstad T, Schanke A-K. Post-concussion symptoms after traumatic brain injury at 3 and 12 months post-injury: a prospective study. Brain Inj 2009; 23: 489–497.
29. Johansson E, Rönnkvist M, Fugl-Meyer AR. Traumatic brain injury in northern Sweden. Incidence and prevalence of long-standing impairments and disabilities. Scand J Rehabil Med 1991; 23: 179–185.
30. Lundin A, de Boussard C, Edman G, Borg J. Symptoms and disability until 3 months after mild TBI. Brain Inj 2006; 20: 799–806.
31. Stålnacke B-M, Björnstig U, Karlsson K, Sojka P. One-year follow-up of mild traumatic brain injury: Post-concussion symptoms, disabilities and life satisfaction in relation to serum levels of S-100B and neurone-specific enolase in acute phase. J Rehabil Med 2005; 37: 300–305.
32. Petchprapai N, Winkelman C. Mild traumatic brain injury: determinants and subsequent quality of life. A review of the literature. J Neurosci Nurs 2007; 39: 260–272.
33. Ponsford J, Cameron P, Fitzgerald M, Grant M, Mikocka-Walus A. Long-term outcomes after uncomplicated mild traumatic brain injury: a comparison with trauma controls. J Neurotrauma 2011; 28: 937–946.
34. Zumstein MA, Moser M, Mottini M, Ott SR, Sadowski-Cron C, Radanov BP, et al. Long-term outcome in patients with mild traumatic brain injury: a prospective observational study. J Trauma Inj Infect Crit Care. 2011; 71: 120–127.
35. Hoge CW, McGurk D, Thomas JL, Cox AL, Engel CC, Castro CA. Mild traumatic brain injury in U.S. Soldiers returning from Iraq. N Engl J Med 2008; 358: 453–463.
36. Lannsjö M, Borg J, Björklund G, af Geijerstam L, Lundgren-Nilsson Å. Internal construct validity of the Rivermead Post-Concussion Symptoms Questionnaire. J Rehabil Med 2011; 43: 997–1002.
37. Herrmann N, Rapoport MJ, Rajaram RD, Chan F, Kiss A, Ma AK, et al. Factor analysis of the Rivermead Post-Concussion Symptoms Questionnaire in mild-to-moderate traumatic brain injury patients. J Neuropsychiatry Clin Neurosci 2009; 21: 181–188.
38. Potter S, Leigh E, Wade D, Fleminger S. The Rivermead Post Concussion Symptoms Questionnaire – a confirmatory factor analysis. J Neurol 2006; 253: 1603–1614.
39. Fayol P, Carrière H, Habonimana D, Dumond JJ. Preliminary questions before studying mild traumatic brain injury outcome. Ann Phys Rehabil Med 2009; 52: 497–509.
40. Iverson GL, Lange RT, Brooks BL, Lynn Ashton Rennison V. "Good old days" bias following mild traumatic brain injury. Clin Neuropsychol 2010; 24: 17–37.

J Rehabil Med 2013; 45: 758–764

ORIGINAL REPORT

LONG-TERM FOLLOW-UP OF PATIENTS WITH MILD TRAUMATIC BRAIN INJURY: A MIXED-METHODS STUDY

Sara Åhman, MD[1], Britt-Inger Saveman, RNT, PhD[2], Johan Styrke, MD, PhD[3], Ulf Björnstig, MD, PhD[3] and Britt-Marie Stålnacke, MD, PhD[1]

From the [1]Department of Community Medicine and Rehabilitation, Rehabilitation Medicine, [2] Department of Nursing and [3]Division of Surgery, Department of Surgical and Perioperative Sciences, Umeå University, Umeå, Sweden

Objective: **To characterize the long-term consequences of mild traumatic brain injury regarding post-concussion symptoms, post-traumatic stress, and quality of life; and to investigate differences between men and women.**

Design: **Retrospective mixed-methods study.**

Subjects/patients and methods: **Of 214 patients with mild traumatic brain injury seeking acute care, 163 answered questionnaires concerning post-concussion symptoms (Rivermead Post-concussion Symptoms Questionnaire; RPQ), post-traumatic stress (Impact of Event Scale; IES), and quality of life (Short Form Health Survey; SF-36) 3 years post-injury. A total of 21 patients underwent a medical examination in connection with the survey. The patients were contacted 11 years later, and 10 were interviewed. Interview data were analysed with content analysis.**

Results: **The mean total RPQ score was 12.7 (standard deviation; SD 12.9); 10.5 (SD 11.9) for men and 15.9 (SD 13.8) for women ($p = 0.006$). The 5 most common symptoms were fatigue (53.4%), poor memory (52.5%), headache (50.9%), frustration (47.9%) and depression (47.2%). The mean total IES score was 9.6 (SD 12.9) 7.1 (SD 10.3) for men and 13.0 (SD 15.2) for women ($p = 0.004$). In general, the studied population had low scores on the Short Form Health Survey (SF-36). The interviews revealed that some patients still had disabling post-concussion symptoms and consequences in many areas of life 11 years after the injury event.**

Conclusion: **Long-term consequences were present for approximately 50% of the patients 3 years after mild traumatic brain injury and were also reported 11 years after mild traumatic brain injury. This needs to be taken into account by healthcare professionals and society in general when dealing with people who have undergone mild traumatic brain injury.**

Key words: traumatic brain injury; brain concussion; post-concussion symptoms; post-traumatic stress disorder.

J Rehabil Med 2013; 45: 758–764

Correspondence address: Britt-Marie Stålnacke, Department of Community Medicine and Rehabilitation (Rehabilitation Medicine) Bldg 9A, Umeå University Hospital, Umeå University, SE-901 85 Umeå, Sweden. E-mail: brittmarie.stalnacke@rehabmed.umu.se

Accepted April 23, 2013

INTRODUCTION

Traumatic brain injuries (TBIs) are a major health problem worldwide. Mild traumatic brain injury (MTBI) is by far the most common, representing 70–90% of all TBIs. The incidence of MTBI is between 100–300/100,000 inhabitants/year (1). The natural course after MTBI is resolution of symptoms within 3 months, which is the outcome for the majority of patients (2–4). However, a considerable proportion of patients (~7–45%) experience post-concussion symptoms for a prolonged period after the injury (5–7). These symptoms may include headache, dizziness, fatigue, irritability, poor memory, concentration difficulties, and depression. Although MTBIs are more prevalent among men than women (1), it has been shown that more women than men experience post-concussion symptoms and complications. In addition, female sex is suggested as one of several risk factors for prolonged symptoms (8–10). Other prognostic factors for persistent symptoms after MTBI are litigation/compensation-seeking, prior head injuries, psychiatric problems, and age over 40 years (11). Furthermore, the prevalence of MTBI is highest among young adults (1). Since they are more likely to be in the process of completing education and entering the labour market, the injury may have serious consequences for their work and future. Several studies have shown that post-concussion symptoms can decrease working ability and negatively affect leisure-time and social life (6, 12).

Following traumatic experiences such as MTBI, psychological disturbances, such as post-traumatic stress-related symptoms and post-traumatic stress disorder (PTSD), can occur. Diagnosis of PTSD comprises a combination of intrusive, avoidance, and arousal symptoms. In a study conducted 6 months after MTBI, it was found that 20% of patients had developed PTSD (13), whereas another study reported that 10% of patients exhibited 3 or more post-traumatic stress-related symptoms 1 year after MTBI (14). The quality of life of people who have experienced MTBI may further decrease (15).

Many studies of post-concussion symptoms and complications after MTBI have follow-ups of 3 months, 6 months, or 1 year (4, 12, 16–20). However, fewer studies have investigated the long-term effects and consequences several years after MTBI (21–24). Self-perceived limitations in psychosocial

function with low levels of life satisfaction have been reported in patients 3 years after MTBI (21). It has been shown that MTBI patients report significantly more post-concussion symptoms than control subjects 5–7 years after the injury (22). MTBI can further result in sequelae that significantly reduce quality of life, even 10 years later (23). In a follow-up study, patients with MTBI were evaluated 10 years after participating in a rehabilitation programme, and life satisfaction had decreased in the intervention group, but not among the controls (24).

Most studies on MTBI have used a quantitative design with validated questionnaires. Only a minority of studies have used a qualitative approach. A metasynthesis of 23 different qualitative studies has been published as a review (25). Collectively, these studies represent the views of 263 persons with mild to very severe TBI, ranging in age from 17 to 60 years. The main summary of the available research was the expression of a deep sense of loss associated with TBI. Key issues highlighted for persons who had survived TBI were loss and reconstruction of personal identity, loss of connection with, and control of, one's body, emotional sequelae following injury, and loss and reconstruction of one's place in the world.

Because there have been few long-term follow-up or qualitative studies of the consequences of MTBI, the aims of the present study were: (*i*) to follow up persons 3 years after MTBI regarding post-concussion symptoms, post-traumatic stress, and quality of life, and regarding differences between men and women; and (*ii*) to determine the long-term consequences for an individual level 11 years after MTBI.

METHODS

Patients and data

The baseline data originates from Umeå University Hospital's injury database. Since 1985, all cases of injury from the defined population of Umeå have been registered upon arrival at the emergency department (ED). Our data-set was derived from the database from 2001, when 137,000 inhabitants lived in Umeå University Hospital's catchment area. Inclusion criteria were: patients with a MTBI, which led to any degree of disturbed consciousness, amnesia, neurological deficit, severe headache, nausea, or vomiting, and who also arrived at the ED within 24 h of the brain injury. The severity of the TBI was classified according to the Glasgow Coma Scale (GCS) (26) at the time of arrival at the ED. GCS 13–15 represents MTBI. A more thorough description of the registration procedure for this study has been published (27).

Follow-ups were conducted by questionnaire in 2004 and by interview in 2012. Of 214 MTBI patients who, in 2001, sought care within 24 h of injury at the ED of Umeå University Hospital, 200 aged 18–64 years were contacted 3 years post-injury. Altogether, as shown in Fig. 1, 163 individuals (81%) (68 women and 95 men) responded. Demographic variables are shown in Table I. Responders were compared with non-responders. No significant differences in proportions were found between responders and non-responders with the exceptions that alcohol inebriation at time of the injury was more common among the non-responders ($p = 0.019$) and that loss of consciousness was more common among the responders ($p = 0.009$). All persons participating in the follow-up study in 2004 answered a question regarding their wish for further follow-up, giving 21 positive responses. They all had a medical examination in connection with the survey, and some were referred for additional investigation or treatment. As a group, these patients rated their symptoms according to the RPQ as significantly more severe than the rest of the patients ($p < 0.001$). They also had higher total scores on the IES ($p < 0.001$). For the qualitative part of the present study, these persons were again contacted. Of those, 10 gave their informed consent and were assured of anonymity and confidentiality. Six were women and 4 were men, ranging in age from 31 to 70 years. Four were injured

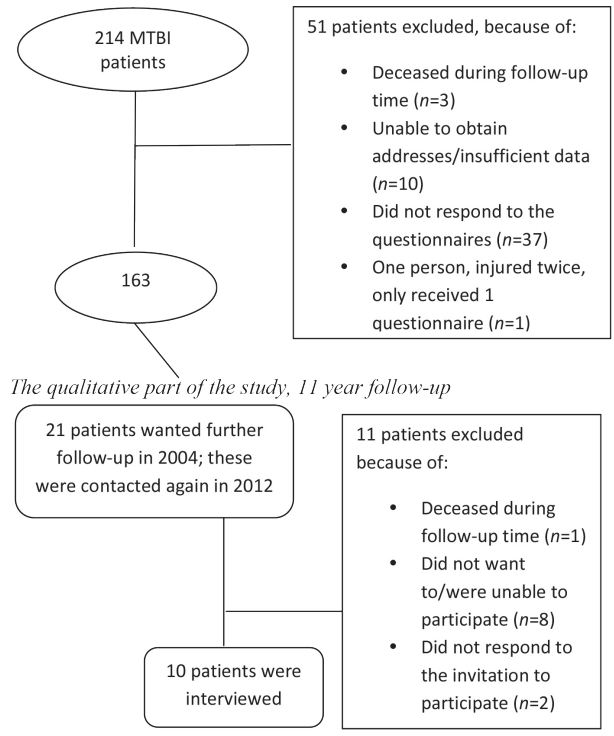


Fig. 1. Process for inclusion of patients in the 3-year and 11-year follow-ups.

Table I. *Demographic and injury characteristics*

Characteristics	
Gender, *n* (%)	
Male	95 (58.3)
Female	68 (41.7)
Age, years, mean (SD)	30.8 (14.3)
Education, *n* (%)	
9 years	19 (11.7)
10–12 years	90 (55.2)
13–21 years	54 (33.1)
Previous head trauma, *n* (%)	
Yes, once	44 (27.0)
Yes, more than once	24 (14.7)
No	79 (48.5)
Unknown	16 (9.8)
Cause of injury, *n* (%)	
Indoors fall	16 (9.8)
Outdoors fall	33 (20.3)
Falls from height	10 (6.1)
Bicycle	25 (15.3)
Horseback riding	5 (3.1)
Assault	9 (5.5)
Vehicle-related	37 (22.7)
Sports-related	23 (14.1)
Other	5 (3.1)

SD: standard deviation.

by falls, 3 in vehicle-related injury events, 1 by horse-back riding, and 2 by other causes. Eleven years after the injury, 3 persons were on sick leave, and 1 was receiving disability pension. They were interviewed and answered the same questionnaires as in 2004. Fig. 1 illustrates the process of inclusion to the study, and Table II the subjects' demographics.

Questionnaires

The Rivermead Post-Concussion Symptoms Questionnaire (RPQ) is a self-report symptom questionnaire consisting of 16 common symptoms following MTBI (7). The patients rate symptoms by degree of severity, on a scale of 0–4. The total RPQ score is the sum of the 16 ratings. Possible scores are 0–64. In this study, scores 1–4 were equivalent to having the symptom.

The Short Form Health Survey (SF-36) is an instrument developed to measure physical and mental health and quality of life. It consists of 36 questions and measures 8 health domains. For each domain the possible score is 0–100, where higher scores indicate better health. For comparison, there are age- and gender-matched control groups (28).

The Impact of Event Scale (IES) is a self-report questionnaire developed to measure anxiety and stress-reactions resulting from a specific event. The total score can vary from 0 to 75 and can be divided into 4 grades of stress reactions: sub-clinical (0–8), mild (9–25), moderate (26–43) and severe (44–75). The scale also provides ratings of avoidance and intrusion (29).

The questionnaires also contained questions about education levels and previous head trauma.

Qualitative interviews

Data were collected with semi-structured interviews. An interview guide was used during the interviews, making sure that the following areas were covered: thoughts about the injury event and the time immediately following the MTBI, general well-being and limitations in everyday life after the injury event, changes in occupational and family situation after the incident, and thoughts and feelings about the future. The interviews were audio-taped and transcribed verbatim.

The interviews were analysed using qualitative content analysis (30). The interviews were read and the text extracted to meaning units. The meaning units were condensed and coded, then divided into categories and subcategories. During the process, which went back and forth between the text (meaning units) and the emerging categories to ensure internal validity, the first author and two others continuously discussed and reached a consensus on the final categories and subcategories.

Ethics

The study was approved by the Regional Ethics Committee of Umeå University, Sweden (number 04-097M and 2012-48-32M).

Statistics

All statistical analysis was carried out using SPSS 18.0.0. Data are mean values (standard deviations; SD) unless otherwise indicated. As some samples were rather small and/or not normally distributed, a statistical evaluation was performed with non-parametric tests. Thus, Mann-Whitney *U* test was used for comparison between responders and non-responders, and for comparison between participants in the further follow-up and those who participated in the follow-up only through questionnaires. Wilcoxon signed-rank test was used to compare individual questionnaire scores from 2004 and 2012. Gender comparisons were made by χ^2 test and Mann-Whitney *U* test. Statistical significance was set at $p < 0.05$.

Table II. *Demographic and injury characteristics for the qualitative part of the study*

Patient	Gender/ age, years	Cause of injury	Current occupation
1	F/70	Outdoor fall	Retired
2	F/36	Fall from height	Sick leave
3	M/49	Other	Sick leave
4	F/64	Indoor fall	Government employee
5	M/59	Other	Farmer
6	M/67	Fall from height	Retired
7	F/34	Horseback riding	Sick leave
8	F/34	Vehicle-related	Teacher
9	M/31	Vehicle-related	Lorry driver
10	F/48	Vehicle-related	Disability-pension

F: female; M: male.

RESULTS

Symptoms and their severity 3 years after MTBI

Three years after MTBI, the RPQ total score was 12.7 (SD 12.9). For men, the total score was 10.5 (SD 11.9), and for women 15.9 (SD 13.8) ($p = 0.006$). The 5 most commonly found symptoms among the patients were fatigue (53.4%), poor memory (52.5%), headache (50.9%), frustration (47.9%), and depression (47.2%). Women reported a significantly higher prevalence of headaches (60.3%) and depression (47.2%) in comparison with men (44.2%, 47.2%, $p = 0.043$ and $p = 0.029$, respectively). The mean severity score of the 5 most disturbing symptoms of the RPQ is shown in Table III. Women reported significantly more problems than men with all symptoms, except poor memory and sleep disturbance.

Post-traumatic stress

The mean total stress score on the IES was 9.6 (SD 12.9). Women reported significantly higher scores (13.0; SD 15.2) in comparison with men (7.1; SD 10; $p = 0.004$).) Of all the patients, 65.4% had intrusion symptoms and 59.5% had avoidance symptoms. There were no significant differences between men and women regarding the prevalence of intrusion and avoidance symptoms. The mean intrusion score was 4.5 (SD 6.2). For men it was 3.2 (SD 4.7) and for women 6.2 (SD 7.5) ($p = 0.002$). The mean avoidance score was 5.0 (SD 7.7). For men it was 3.8 (SD 7.0) and for women 6.6 (SD 8.5) ($p = 0.024$). Regarding post-traumatic stress grades, moderate to severe stress was reported by 10% of men and 14% of women.

Quality of life

The scores for the 8 different scales of the SF-36 are shown in Table IV. Women had significantly lower scores than men in Role Physical, Role Emotional, and Mental Health ($p = 0.049$, 0.002 and 0.025). The scores in the studied patient material

Table III. *Mean severity of the 5 most disturbing symptoms according to the Rivermead Post-Concussion Symptoms Questionnaire (RPQ)*

Symptom	Total Mean (SD)	Men Mean (SD)	Women Mean (SD)	*p*-value
Fatigue	1.2 (1.3)	1.0 (1.2)	1.5 (1.5)	0.013
Headache	1.1 (1.3)	0.9 (1.2)	1.4 (1.4)	0.006
Poor memory	1.1 (1.3)	1.0 (1.2)	1.2 (1.4)	0.326
Depression	1.0 (1.3)	0.8 (1.2)	1.3 (1.4)	0.012
Sleep disturbance	1.0 (1.4)	0.9 (1.3)	1.3 (1.5)	0.082

SD: standard deviation.

Table IV. *Mean scores in the 8 different domains of the SF-36. Data represent mean (standard deviation)*

SF-36 domain	All (n=163) Mean (SD)	Men (n=95) Mean (SD)	Women (n=68) Mean (SD)	p-value
PF	88.9 (18.7)	89.9 (17.8)	87.6 (19.9)	0.442
RP	72.9 (38.7)	77.9 (35.1)	65.8 (42.5)	0.049
BP	49.8 (17.2)	49.2 (16.8)	50.6 (17.9)	0.616
GH	51.9 (16.1)	51.3 (15.4)	52.7 (17.1)	0.585
VT	44.1 (17.3)	45.6 (17.1)	42.0 (17.5)	0.199
SF	51.5 (8.6)	51.6 (8.5)	51.3 (8.7)	0.780
RE	70.4 (40.3)	78.5 (34.4)	59.2 (45.3)	0.002
MH	64.8 (9.4)	66.1 (9.4)	62.8 (9.0)	0.025

SD: standard deviation; PF: physical functioning; RP: role physical; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role emotional; MH; mental health.

were significantly lower (p<0.05) than in the Swedish general population (n=8930) in all of the 8 domains in SF-36, except Physical Functioning (31) (Fig. 2).

Symptoms, post-traumatic stress, and quality of life 11 years after the injury

In the small group of interviewed persons there were no statistically significant differences 11 years after the MTBI in comparison with 3 years after the injury on the total RPQ (from 27.7 (SD 20.3) to 24.3 (SD 19.7); p=0.123), the total IES score (from 30.3 (SD 18.6) to 25.2 (SD 20.6); p=0.241), and on all domains on the SF-36.

Experiences 11 years after MTBI

The patients described a spectrum of life situations, and 3 distinct groups of patients emerged. There were patients who had never given the injury event leading to MTBI any thought. These patients had no complications after the injury, but were positive to follow-up. On the other hand, there were patients whose lives were altered by the MTBI and were disabled to some degree by it; physically or mentally, or both. A third group of patients had developed other diseases during the 11 years since the MTBI, and were disabled because of them. These 3 patient groups contributed to the developed categories and subcategories found during the analysis process, as shown in Table V.

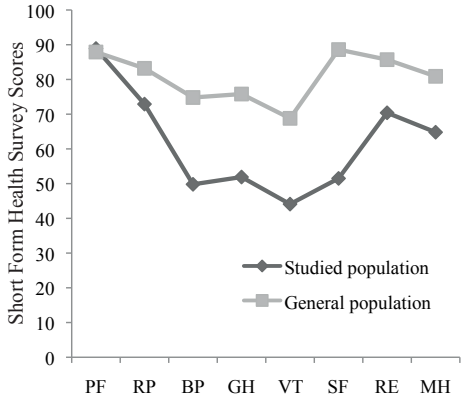


Fig. 2. Studied population's scores on the Short Form Health Survey compared with general Swedish population's scores. PF: physical functioning; RP: role physical; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role emotional; MH: mental health.

The first category, "Personal consequences" of the injury event was, to a large extent, physical and mental limitations. There were patients who described physical limitations immediately after the injury event, such as exhaustion, debilitation, dizziness, severe headache, and neck pain. The mental limitations described included nervousness and fear.

"It was unpleasant, I had a terrible headache."

"Pain. Nervous, I was afraid."

Shortly after the injury event, and continuing to the present, patients described many remaining physical and mental consequences. They were commonly tired and had sleep disturbances. The fatigue was described as both physical and mental. The term "*lack of energy"* was also specifically used. Pain was also frequently described, both directly after the injury event and in the present.

"I want so much more than I feel I am capable of, that's what has been tough."

"I don't know if it comes from the neck, but I've got more headache too."

The mental limitations stemming from the injury event and its complications were described as emotions, such as anger and irritation. The patients, furthermore, described fear of things that they associated with the injury event; for example, travelling by bus or watching television programmes where cars were driven at high speeds. Aside from the negative feelings, there was also a search for some positive consequences of the injury.

"*Well, you're pissed off the day it happened, I still am."*

"There's nothing bad that doesn't bring something good with it; maybe it stopped me from working as I did."

Cognitive limitations were expressed in terms of having impaired memory, difficulties concentrating and becoming easily stressed and irritable. The important role of scheduling daily life was highlighted.

"I have a hard time remembering things. I get annoyed easily. I just want to be alone sometimes. Have difficulties concentrating. If I'm going anywhere I'm really stressed out."

Some patients had impaired memory, were bothered by fatigue, or had other physical, mental or cognitive problems, which they had never directly connected with the injury event.

Table V. *Categories and subcategories*

Personal consequences	Social consequences	Dealing with the injury today
Physical limitations	Effects on work life	Thoughts about the injury event
Mental effects	Effects on family life	Thoughts about the time after the injury event
Cognitive limitations	Effects on social life	Thoughts about the future

They still believed that it was possible that the injury could be the cause of their problems, but other factors, such as ageing, were also considered.

"Well, I don't have any limitations from that brain injury. I get dizzy easily, but that could be for some other reason… I don't know."

The second category was comprised of consequences for work life, family life, and social life. In a broader context, social life included thoughts and perceptions about healthcare. Work performance consequences were described, and it was found that some patients were still on sick leave and did not think they could return to work. Others had been on sick leave and were returning to work. For some patients, the injury event never affected their work.

"I'm still sick, I'm on sick leave. I haven't gotten over it."

"I feel that I want to go back to my old job, but I feel, I don't think I'm going to make it."

Participants also described effects on family life. The patients sometimes felt that demands from family and friends were greater than what they could achieve or manage, both in terms of housework and in relationships with others. They also thought that the consequences of the injury event affected their family members and that the whole situation was difficult for the family. On the other hand, some experienced no effects on the same areas of life.

"You have your hands full only being a family father when you're home with the kids and there – you're sometimes not enough either."

Socially, the patients had a sense of alienation because of the effects of MTBI. This was described as feeling worthless or abnormal because of limited energy compared with healthy people or because of sick leave and not being able to have a job. People also experienced an uncomprehending society, and felt that people might begin to gossip if they related their difficulties.

"Just being understood, that's what I think is the hardest part in everyday life."

"Then you have to deal with the children; why aren't you working mom? You have to work like everybody else, and yes of course I have to be like all the other moms."

Thoughts about healthcare were dichotomized. Participation in a rehabilitation programme was described as positive and as having helped lead to improvement. However, it also gave a patient stigma, contributing to a feeling of alienation and abnormality in society. Some patients wished that all the physical consequences of the injury event had been examined properly from the beginning. Gratitude was also expressed for healthcare, and patients said that, without healthcare, return to an acceptable life would have been much more difficult.

"I've been very lucky to meet understanding persons because I don't think it is that known, brain tiredness, as you think it is; it isn't."

"Nobody prepared me for the fact that I was going to have cognitive difficulties or I mean brain tiredness, what's that?"

The third category, "Dealing with the injury today" showed great diversity concerning thoughts about the past. Some of the patients, as previously mentioned, had never given the injury event any thought. Others described a drastic change between life before and after the injury because of physical, mental and cognitive limitations.

"I haven't thought about the brain injury, I have many other things to think about instead."

"It was drastic, you just wanted to bury your head in the sand, let it all blow over."

Overall, the patients' prevailing thoughts about the future were positive or indifferent. The central attitude was to take one day at a time and to avoid thinking too much about the future. Strategies for coping with the consequences of MTBI mainly involved avoiding pondering about the future too much and learning how to live with the consequences of the injury event. Another strategy was for subjects to try to do the things they wanted to do on those days when energy and motivation were present. Drugs, such as analgesics and antidepressants, also made life easier, or acceptable, for some.

"I just take 1 day at a time because in my life now, anything could happen, you can't chew on that. You have to look forward."

"Well, it has been tough, but thanks to medication I've been able to find, like a balance in everyday life between activity and rest and so."

DISCUSSION

The main findings of this study were that symptoms and consequences of MTBI may still be present both 3 and 11 years after the injury event. During the process of interviewing patients 11 years after the injury event, it became clear that symptoms and disabilities continued for some of the patients. They experienced physical, mental, and cognitive limitations as well as the feeling of alienation and lack of societal understanding. On the other hand, several of the MTBI patients had fully recovered.

In the present study, fatigue was the most common symptom 3 years after MTBI. This finding is in accordance with previous studies shortly after the injury (4, 15, 17, 20). Fatigue has also been reported as the most common symptom 10 years after MTBI (23). It seems that fatigue is the most frequent persistent symptom, both early and late after a MTBI. During the interviews with patients 11 years after injury, it was also stated that fatigue, both mental and physical, was one of the major difficulties in everyday life. Fatigue was described as a road-block affecting daily life, forcing the patients to plan all their activities. Mental fatigue after MTBI is a well-known phenomenon, and studies show that severe fatigue is highly associated with limitations in daily functioning and lower levels of life satisfaction (32). This was also illustrated clearly by the interviewed patients. Headache and poor memory were also among the most frequent symptoms reported by the patients 3 years after the injury. This is in accordance with previous research (17, 20), and it is possible that

these symptoms are connected with fatigue. It seems likely that having headaches for longer periods could lead to fatigue. Fatigue may also contribute to cognitive symptoms, e.g. poor memory.

The 5 most disturbing symptoms, reported after 3 years, differed from the 5 most common symptoms. Although frustration was more common, sleep disturbance was more of an issue. It seems reasonable to assume that there was a relationship between sleep disturbances and fatigue.

In a previous study, which also used the RPQ to measure post-concussion symptoms after MTBI (33), 1 year after the injury a total RPQ score of 15.1 was reported. Because our results were in the same range, this could suggest that not much changes in terms of post-concussion symptoms between 1 and 3 years after MTBI. The symptoms persist, although slightly less frequently.

A minority of the patients had scores on the IES corresponding to moderate or severe post-traumatic stress reaction. This finding is consistent with the results from another study in which the IES was used 1 year after MTBI (14). Nevertheless, in some previous studies, patients with MTBI were examined for PTSD, and 17–20% of the studied patients met criteria for PTSD at 6 months after the injury (13, 34).

The present findings suggest that post-traumatic stress-related symptoms were not much of a problem for the patients 3 years after MTBI, although a substantial part of the patients may have had post-traumatic stress closer to the injury date. In a previous study of the same patient population the presence of post-concussion symptoms was shown to correlate with low levels of life satisfaction (21). This relationship is in accordance with a previous Swedish study conducted 3 months and 1 year post-injury (35).

In the present study, quality of life was compared between the subjects and the average population. Because patients reported significantly lower scores on all domains of the SF-36, these findings indicate that MTBI can result in sequelae that significantly reduce quality of life.

The majority of persons who answered the questionnaires in 2004 were men, but, in agreement with previous research (9), the women demonstrated more symptoms and, at more severe levels, higher grades of post-traumatic stress, and lower grades of life satisfaction.

In the qualitative part of the study, it was obvious that the patients whose symptoms or difficulties continued felt alienated by society. These feelings manifested because of patient limitations and because other people often did not understand their problems. Our findings regarding the patients' feelings of alienation are in accordance with previous research (36). In order to address this problem, more public education about MTBI and its long-term symptoms and limitations are required. For some patients the symptoms and consequences of the injury event continued to affect areas such as family life and work. In line with previous research (37), patients in the present study had to restructure their lives and adapt to their current situation.

Previous studies have shown that people with TBI of all grades experience a sense of loss of self, and a void, which is filled by the patients reconstructing stories about the injury and the recovery (25, 38, 39). Although we only included MTBI, some patients reported similar feelings. These experiences were demonstrated more frequently among the group with persistent symptoms.

Some limitations of this study should be noted. There was no control group, although that would have been illustrative. Post-concussion symptoms were commonly reported, but these symptoms are not exclusively encountered after MTBI, as they are also reported in the general population (40). On the other hand, the strength of this study is that it is based on one year of material from an injury database; hence it is genuinely epidemiological and representative for people with MTBI in a well-defined population and geographical area. The response rate was high, at 81%, and the questionnaires that were used in the study are validated and have often been used with persons with MTBI. Of the 21 patients who participated in the further follow-up with medical examination, 10 were included in the qualitative study 11 years after the injury. Because these patients belonged to the group with significantly more symptoms than the other 3 years after the injury, they seem to be representative of patients with more problems after the injury.

The process of interviewing patients and comparing their answers with the questionnaires elucidated a notable divergence between some of the patients' own stories and how they answered the questionnaires. The questionnaires did not give a fair picture of their life situations and difficulties. Their life stories gave an image of a troubled life. However, from the answers to the questionnaires, their lives did not seem to be so troubled. This difference could have had varying causes. It may have been that, due to cognitive impairment, they were unable to answer the questionnaires adequately, implying that information may be lost when conducting research on symptoms and personal difficulties in a quantitative manner with questionnaires. Another interpretation might be that commonly used instruments, such as the SF-36, even with a large number of questions, might not provide a true picture of an individual's experiences.

In conformity with other studies performed many years after the injury event, it can be difficult to separate consequences following the MTBI from consequences following more recent events in life, the so-called "black box". During 3 (and even more in 11) years, many things could have happened that affected the answers on the different questionnaires. Insecurity is inevitable when carrying out long-term follow-ups. Interviews are a good complement to questionnaires when opening the black box and seeing its contents. Interviews are also a way of listening to the patient's voices in clinical research.

Like other studies performed with interviews, the results are an interpretation of the research participants' statements. In turn, the statements in the current study are the patients' interpretations of their lived experiences. There may be more than one possible interpretation of the interview text. We argue, however, that due to thorough analysis of the text the present results are valid.

In conclusion, MTBI can result in long-term symptoms and disabling consequences. These are observed both 3 and 11 years after the injury event, as illustrated in this study by questionnaires and interviews. The long-term consequences of MTBI must be addressed by healthcare and society as real and

possible issues, and it is important that resources and adequate knowledge exist to enable the identification of symptoms and proper treatment of affected individuals.

REFERENCES

1. Holm L, Cassidy JD, Carroll LJ, Borg J, Centre NTFoMTBIotWC. Summary of the WHO Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2005; 37: 137–141.
2. Ponsford J, Willmott C, Rothwell A, Cameron P, Kelly AM, Nelms R, et al. Factors influencing outcome following mild traumatic brain injury in adults. J Int Neuropsychol Soc 2000; 6: 568–579.
3. Binder LM, Rohling ML, Larrabee GJ. A review of mild head trauma. Part I: Meta-analytic review of neuropsychological studies. J Clin Exp Neuropsychol 1997; 19: 421–431.
4. Kashluba S, Paniak C, Blake T, Reynolds S, Toller-Lobe G, Nagy J. A longitudinal, controlled study of patient complaints following treated mild traumatic brain injury. Arch Clin Neuropsychol 2004; 19: 805–816.
5. Binder LM. A review of mild head trauma. Part II: Clinical implications. J Clin Exp Neuropsychol 1997; 19: 432–457.
6. Stålnacke BM, Björnstig U, Karlsson K, Sojka P. One-year follow-up of mild traumatic brain injury: post-concussion symptoms, disabilities and life satisfaction in relation to serum levels of S-100B and neurone-specific enolase in acute phase. J Rehabil Med 2005; 37: 300–305.
7. King NS. Post-concussion syndrome: clarity amid the controversy? Br J Psychiatry 2003; 183: 276–278.
8. Bazarian JJ, Blyth B, Mookerjee S, He H, McDermott MP. Sex differences in outcome after mild traumatic brain injury. J Neurotrauma 2010; 27: 527–539.
9. Hall RC, Chapman MJ. Definition, diagnosis, and forensic implications of postconcussional syndrome. Psychosomatics 2005; 46: 195–202.
10. Ryan LM, Warden DL. Post concussion syndrome. Int Rev Psychiatry 2003; 15: 310–316.
11. Carroll LJ, Cassidy JD, Peloso PM, Borg J, von Holst H, Holm L, et al. Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004 Suppl 43: 84–105.
12. Fourtassi M, Hajjioui A, Ouahabi AE, Benmassaoud H, Hajjaj-Hassouni N, Khamlichi AE. Long term outcome following mild traumatic brain injury in Moroccan patients. Clin Neurol Neurosurg 2011; 113: 716–720.
13. Bryant RA, Harvey AG. Postconcussive symptoms and posttraumatic stress disorder after mild traumatic brain injury. J Nerv Ment Dis 1999; 187: 302–305.
14. Sojka P, Stålnacke BM, Björnstig U, Karlsson K. One-year follow-up of patients with mild traumatic brain injury: occurrence of post-traumatic stress-related symptoms at follow-up and serum levels of cortisol, S-100B and neuron-specific enolase in acute phase. Brain Inj 2006; 20: 613–620.
15. Ponsford J, Cameron P, Fitzgerald M, Grant M, Mikocka-Walus A. Long-term outcomes after uncomplicated mild traumatic brain injury: a comparison with trauma controls. J Neurotrauma 2011; 28: 937–946.
16. Lundin A, de Boussard C, Edman G, Borg J. Symptoms and disability until 3 months after mild TBI. Brain Inj 2006; 20: 799–806.
17. Lannsjö M, af Geijerstam JL, Johansson U, Bring J, Borg J. Prevalence and structure of symptoms at 3 months after mild traumatic brain injury in a national cohort. Brain Inj 2009; 23: 213–219.
18. Heitger MH, Jones RD, Frampton CM, Ardagh MW, Anderson TJ. Recovery in the first year after mild head injury: divergence of symptom status and self-perceived quality of life. J Rehabil Med 2007; 39: 612–621.
19. Hou R, Moss-Morris R, Peveler R, Mogg K, Bradley BP, Belli A. When a minor head injury results in enduring symptoms: a prospective investigation of risk factors for postconcussional syndrome after mild traumatic brain injury. J Neurol Neurosurg Psychiatry 2012; 83: 217–223.
20. Kraus J, Hsu P, Schaffer K, Vaca F, Ayers K, Kennedy F, et al. Preinjury factors and 3-month outcomes following emergency department diagnosis of mild traumatic brain injury. J Head Trauma Rehabil 2009; 24: 344–354.
21. Stålnacke BM. Community integration, social support and life satisfaction in relation to symptoms 3 years after mild traumatic brain injury. Brain Inj 2007; 21: 933–942.
22. Jakola AS, Müller K, Larsen M, Waterloo K, Romner B, Ingebrigtsen T. Five-year outcome after mild head injury: a prospective controlled study. Acta Neurol Scand. 2007; 115: 398–402.
23. Zumstein MA, Moser M, Mottini M, Ott SR, Sadowski-Cron C, Radanov BP, et al. Long-term outcome in patients with mild traumatic brain injury: a prospective observational study. J Trauma 2011; 71: 120–127.
24. Andersson EE, Bedics BK, Falkmer T. Mild traumatic brain injuries: a 10-year follow-up. J Rehabil Med. 2011; 43: 323–329.
25. Levack WM, Kayes NM, Fadyl JK. Experience of recovery and outcome following traumatic brain injury: a metasynthesis of qualitative research. Disabil Rehabil 2010; 32: 986–999.
26. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
27. Styrke J, Stålnacke BM, Sojka P, Björnstig U. Traumatic brain injuries in a well-defined population: epidemiological aspects and severity. J Neurotrauma 2007; 24: 1425–1436.
28. Sullivan M, Karlsson J. The Swedish SF-36 Health Survey III. Evaluation of criterion-based validity: results from normative population. J Clin Epidemiol 1998; 51: 1105–1113.
29. Sundin EC, Horowitz MJ. Impact of Event Scale: psychometric properties. Br J Psychiatry 2002; 180: 205–209.
30. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today 2004; 24: 105–112.
31. Sullivan M, Karlsson J, Ware JE. The Swedish SF-36 Health Survey – I. Evaluation of data quality, scaling assumptions, reliability and construct validity across general populations in Sweden. Soc Sci Med 1995; 41: 1349–1358.
32. Stulemeijer M, van der Werf S, Bleijenberg G, Biert J, Brauer J, Vos PE. Recovery from mild traumatic brain injury: a focus on fatigue. J Neurol 2006; 253: 1041–1047.
33. Sigurdardottir S, Andelic N, Roe C, Jerstad T, Schanke AK. Post-concussion symptoms after traumatic brain injury at 3 and 12 months post-injury: a prospective study. Brain Inj 2009; 23: 489–497.
34. Hoffman JM, Dikmen S, Temkin N, Bell KR. Development of posttraumatic stress disorder after mild traumatic brain injury. Arch Phys Med Rehabil 2012; 93: 287–292.
35. Emanuelson I, Andersson Holmkvist E, Björklund R, Stålhammar D. Quality of life and post-concussion symptoms in adults after mild traumatic brain injury: a population-based study in western Sweden. Acta Neurol Scand 2003; 108: 332–338.
36. Yeates GN, Gracey F, McGrath JC. A biopsychosocial deconstruction of "personality change" following acquired brain injury. Neuropsychol Rehabil 2008; 18: 566–589.
37. Strandberg T. Adults with acquired traumatic brain injury: experiences of a changeover process and consequences in everyday life. Soc Work Health Care. 2009; 48: 276–297.
38. Nochi M. Reconstructing self-narratives in coping with traumatic brain injury. Soc Sci Med 2000; 51: 1795–1804.
39. Nochi M. "Loss of self" in the narratives of people with traumatic brain injuries: a qualitative analysis. Soc Sci Med 1998; 46: 869–878.
40. Dean PJ, O'Neill D, Sterr A. Post-concussion syndrome: prevalence after mild traumatic brain injury in comparison with a sample without head injury. Brain Inj 2012; 26: 14–26.

J Rehabil Med 2013; 45: 765–770

ORIGINAL REPORT

FACTORS AFFECTING PARTICIPATION AFTER TRAUMATIC BRAIN INJURY

Jerry Larsson, MSc[1], Ann Björkdahl, PhD[1,2], Eva Esbjörnsson, PhD[1] and Katharina S. Sunnerhagen, MD, PhD[1,3]

From the [1]Rehabilitation Medicine, Institute of Neuroscience and Physiology, University of Gothenburg, [2]Ersta Sköndal University College, Gothenburg, Sweden and [3]Sunaas Rehabilitation Hospital, The Medical Faculty, Oslo University, Oslo, Norway

Objective: **The aim of this work was to explore the extent to which social, cognitive, emotional and physical aspects influence participation after a traumatic brain injury.**
Design/subjects: **An explorative study of the patient perspective of participation 4 years after traumatic brain injury. The cohort consisted of all patients (age range 18–65 years), presenting in 1999–2000, admitted to the hospital (n=129). Sixty-three patients responded; 46 males and 17 females, mean age 41 (range 19–60) years.**
Methods: **Four years after the injury, the European Brain Injury Questionnaire (EBIQ), EuroQol-5D, Swedish Stroke Register Questionnaire and Impact on Participation and Autonomy (IPA) questionnaire were sent to the sample. Data were analysed with logistic regression.**
Results: **On the EBIQ, 40% of the sample reported problems in most questions. According to IPA, between 20% and 40% did not perceive that they had a good participation. The analyses gave 5 predictors reflecting emotional and social aspects, which could explain up to 70% of the variation in participation.**
Conclusion: **It is not easy to find single predictors, as there seems to be a close interaction between several aspects. Motor deficits appear to have smaller significance for participation in this late state, while emotional and social factors play a major role.**

Key words: social participation; brain injury; depression; self-centring; cognitive.

J Rehabil Med 2013; 45: 765–770

Correspondence address: Jerry Larsson, Rehabilitation Medicine, Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden. E-mail: jerry.larsson@vgregion.se

Accepted April 29, 2013

INTRODUCTION

Traumatic brain injury (TBI) is a significant problem worldwide, which has an impact not only on the person, but on society as well. The incidence of TBI is approximately 400/100,000 inhabitants, and the number of disability cases as a result of TBI was estimated in 1996 at approximately 5.3 million in the USA and 6.2 million in Europe (1, 2).

Participation is a core in all models of disability according to the World Health Organization (WHO) and International Classification of Functioning, Disability and Health (ICF) (3). There is also a general consensus that the goal of rehabilitation after TBI is to achieve good participation in society. According to Cicerone, measuring participation as an outcome of rehabilitation is the most meaningful way to measure outcome, but it is probably also the most challenging method, since there are many things that contribute to a person's level of participation (4). "Participation" is defined in the ICF as "involvement in a life situation". The opposite of participation, "restrictions to participation", is defined as "problems an individual may experience in involvement in life situations" (3).

Persons with TBI often experience limitations in their participation. In a study of 160 persons, Wiese et al. showed that 81% with moderate and severe TBI had not returned to pre-injury levels of leisure participation 1 year after the injury (5). Their activity had changed from being engaged in partying, drug and alcohol use and sports to watching television. It appears that a large number of individuals with TBI will experience changed and reduced leisure participation over extended periods (6, 7). In a longitudinal study from Taiwan, it was reported that patients still had difficulties with social interactions and family relationships 6 years after TBI, even though they could live and work independently (8).

It is important to consider factors other than the direct consequences of the trauma that can also influence participation. For example, in another study in this group, it was noted that it is necessary to consider pre-morbid factors in the rehabilitation (9). Of those who were on sick leave on the day of occurrence of the trauma, 80% were still on sick leave 4 years after the trauma, compared with 40% of those who were not on sick leave on the day of the trauma.

Depression is common after all forms and severities of TBI (10). The prevalence of depression in the TBI group is thought to be more than 50% and, specifically, the patient with a pre-morbid poorer psychosocial functioning and greater psychiatric distress is more prone to secondary depression after TBI (11).

Much is still unknown about the factors involved in the ability to participate in society after TBI, and it is important to gain better knowledge about the influence of different factors, such as somatic, emotional, cognitive and environmental factors.

 doi: 10.2340/16501977-1184

 ISSN 1650-1977

The aim of this work was to explore the extent to which the social, cognitive, emotional and physical aspects influence participation after a TBI, according to the individual's subjective experience.

MATERIAL AND METHODS

Participants

The study was carried out at Sahlgrenska University Hospital, Gothenburg, Sweden, which has a catchment area of approximately 900,000 inhabitants. The cohort was made up of all patients with a TBI classified as S06.2 and S06.3 according to International Classification of Diseases – 10th revision (ICD-10) ($n = 129$) (excluding the mild injuries that are often diagnosed as commotio S06.0). The persons included in the study were between 18 and 65 years of age and admitted to the emergency room at the hospital during a two-year period (1999–2000). A survey was sent to the participants that could be reached ($n = 99$). A flow-chart for the study inclusion is shown in Fig. 1.

The ethics committee of the University of Gothenburg approved the study.

Procedure and instruments

Four years after the injury a letter was sent to each patient at home, asking them to complete 4 questionnaires: EuroQol-5D (EQ-5D), a self-report of health-related quality of life, consisting of 5 domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) (12), to which is added a visual analogue scale (VAS) for evaluation of perceived health-related quality of life, where 0 = worst imaginable health status and 100 = best imaginable health status; the European Brain Injury Questionnaire (EBIQ), a self-report measure for persons who are brain injured, that measures the subjective experience of cognitive, emotional and social difficulties (13); the Impact on Participation and Autonomy Questionnaire (IPA) (14), a questionnaire with 39 items measuring participation in accordance with the definition set out in the ICF; and a questionnaire from the Swedish Stroke Register (http://www.riks-stroke.org/index.php?content=form) concerning living conditions, activities of daily living and support (modified so that the questions started with "since your brain injury…"). Demographic data and severity of the trauma, according to the Reaction Level Scale (RLS) (15), were gathered from medical charts. The RLS score was converted to the Glasgow Coma Scale (GCS), which is presented here (16).

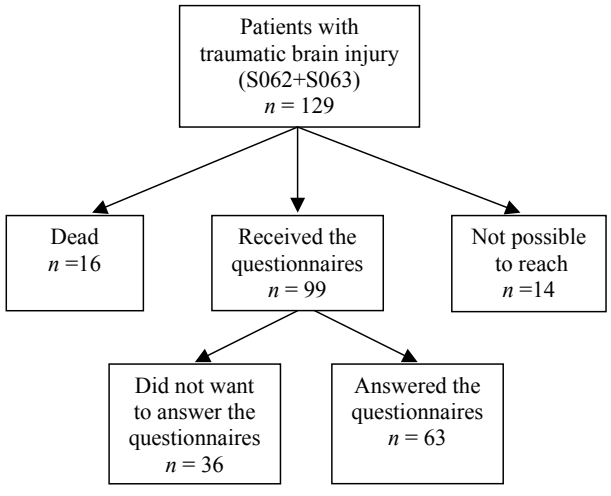


Fig. 1. Study recruitment.

Data analysis

As most data were ordinal, non-parametric statistics were used and the logistic regression was chosen as suitable for this kind of data. The level of significance was set to $p = 0.05$. Statistical analysis was carried out with the SPSS, Version 20 (SPSS Inc., Chicago, IL, USA).

Descriptive data are presented for gender, age, cause and severity of the trauma and GCS. The EQ-5D's 5 domains and the EBIQ were used to describe the sample and the experience of difficulties after the injury. The percentage of the sample indicating problems according to single items in EBIQ is presented.

The IPA was used to describe the experience of participation in society. The analysis included 4 domains from IPA (autonomy indoors, family role, autonomy outdoors and social life/relationship). The response options were 0 = very good, 1 = good, 2 = fair, 3 = poor and 4 = very poor. In the analyses, the data were dichotomized into good (0–1) and not so good participation (2–4). The activities and participation factors of the IPA are fundamental and important for life, and therefore the answer "fair" was also interpreted as not so good participation.

To identify what factors influence participation in society, items that were considered relevant for participation in the different IPA domains were chosen and logistic regressions were carried out between these items and each of the IPA domains. Items reflected social, cognitive and emotional aspects (EBIQ) as well as aspects of mobility (EQ-5D) and dependence in "Daily hygiene". Due to the correlations between the different EBIQ domains (risk for multicollinearity) being too high it was impossible to use the EBIQ domains for the regression analysis, and therefore single questions without a high inter-correlation were selected instead. This was examined by correlation analysis (Spearman's), where questions with correlations below 0.40 were selected. After this selection 15 items remained. However, there was no item representing communication, which was considered important, and therefore 3 items on communication were added, resulting in 18 items. Because of the sample size in the study a maximum of 5 factors in each logistic regression was considered feasible. To reduce the number of items for each regression with the different IPA domains, 5 relevant factors were selected according to clinical experience and relevance for the domain. For the selection of relevant factors to the regression model, we decided to rely on clinical experience and theoretical knowledge, rather than using mathematics. For the domain of social life we valued contact with others, dependence and initiative as important aspects and thereby chose these items for the model. For the domain "family role" we valued dependence, communication and cognitive aspects as important. Autonomy outdoors was expected to be related to dependence, social and cognitive aspects. For the domain "Autonomy indoors" we valued dependence and close relations with family and caregivers to influence the possibility of participation.

Finally, the items included in the different regressions were; "difficulty communicating what you want to say", "leaving others to take the initiative in conversations", "losing contact with your friends" (social aspects), "trouble concentrating", "feeling unable to get things done", "failing to notice other people's mood" (cognitive aspects), "others do not understand your problems", lack of interest in your surroundings", "thinking only of yourself" (emotional aspects), "mobility" (EQ-5D), "daily hygiene" (Swedish Stroke register). To explore whether gender, age and severity of injury would improve the models, these variables were added in the regression, but, as they did not have a positive effect, the original model was chosen to decrease the number of variables in the model. For the degree of variance explained in the logistic regression the Cox & Snell (17) and Nagelkerke (18) were used, and reported as an interval.

RESULTS

Sixty-three out of the 99 subjects who received the survey responded (Fig. 1) (46 males and 17 females). At the time of

the injury the mean age was 41 years (standard deviation (SD) 12, age range 19–60 years), and 21% were under 30 years, 33% between 31 and 40 years, 18% between 41 and 50 years, and 28% over the age of 50 years. According to the GCS, 16% were classified as mild, 54% as moderate, and 30% as severe brain injury. The drop-out from the original sample of 129 persons consisted of 16 subjects who were not longer alive, 14 who could not be reached, and 36 who did not respond or who declined to participate in the study. There were no significant differences between the group of responders and the drop-outs.

At the follow-up 4 years after trauma 52% of the sample was employed full- or part-time. Ninety-seven percent lived in their own homes, 3% lived in group homes, and 30% lived in one-person households. A large proportion of the sample reported that they had functional disabilities. On the EQ-5D, 25% of the group stated that they had problems (some or severe problems) with mobility. Fifteen percent had problems with self-care, 33% with usual activities, 58% with pain, and 58% with anxiety/depression. On the EQ-5D VAS scale, the group stated their health as a mean of 68 of a best possible 100, which, compared with a Swedish control group (mean = 82) this is under the 25th percentile.

The results of the EBIQ on single questions showed that 40% of the sample stated having problems in as much as 43 of the 62 questions, and 60% reported problems on 8 single questions of the EBIQ (Fig. 2).

The IPA questionnaire, impact for participation and autonomy, showed that 40% of subjects did not experience any good participation in the domain of "autonomy outdoors", and this was also the opinion of 36% in the domain of "social life and relationship". Dissatisfaction was also expressed in the other domains, such as 34% regarding "family role" and 21% in "autonomy indoors". The domain "work and education" was not relevant for the majority (81% did not work or study), and this domain was thus excluded from the analysis.

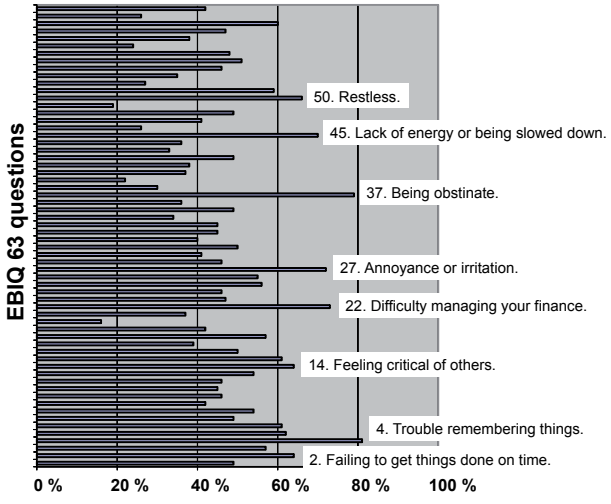


Fig. 2. Percentage of the sample that rated problems on each of the 63 European Brain Injury Questionnaire (EBIQ) items. Those items for which more than 60% of the sample indicated problems are highlighted.

Table I. *Logistic regression model for participation in the domain of "social life" (IPA), with single items of European Brain Injury Questionnaire (EBIQ) from the domains motivation and communication, the ability to perform daily hygiene (Swedish Stroke Register Questionnaire) and mobility (EuroQol (EQ-5D))*

	p-value	Odds ratio	95% CI for odds ratio
Feeling unable to get things done EBIQ 26	0.079	4.276	0.847–21.600
Lack of interest in your surroundings EBIQ 38	0.042*	10.431	1.090–99.839
Losing contact with your friends EBIQ 60	0.004**	16.215	2.449–107.360
Daily hygiene (Swedish Stroke Register Questionnaire)	0.256	7.833	0.224–273.360
Mobility (EQ-5D)	0.561	0.555	0.076–4.051

*$p \leq 0.05$; **$p \leq 0.01$.
CI: confidence interval.

Logistic regression analysis between selected items reflecting social, cognitive and emotional aspects, mobility and dependence and the different domains of the IPA was used to examine factors that had an influence on participation in society. The models for the different domains were retrieved by separate processes, as explained in the methods section, and the contents were found to differ between the domains (Tables I–IV). The goodness-of-fit for the models were good according to the Hosmer and Lemeshow Test (19). Poor fit in this test is indicated by a significance value less than 0.05 and the significance values in our models were 0.574 for social life, 0.533 for family role, 0.938 for outdoor, and 0.634 for indoors participation. From the logistic regressions 5 significant predictors were retrieved that reflected emotional and social aspects (Tables I–IV). In none of the regression analyses, were mobility or dependency in daily hygiene significantly predictive of the experience of participation.

Table II. *Logistic regression model for participation in the domain of "family role" (IPA), with single items of European Brain Injury Questionnaire (EBIQ) from the domains isolation, cognition and communication and mobility (EuroQol (EQ-5D))*

	p-value	Odds ratio	95% CI for odds ratio
Others do not understand my problems EBIQ 6	0.010**	23.591	2.130–261.327
Trouble with concentration EBIQ 22	0.065	31.257	0.804–1215.909
Mobility (EQ-5D)	0.571	1.860	0.218–15.908
Difficulty in communication EBIQ 35	0.247	2.740	0.451–16.662
Thinking only of myself EBIQ 39	0.048*	18.969	1.030–349.514

*$p \leq 0.05$; **$p \leq 0.01$.
IPA: Impact on Participation and Autonomy; CI: confidence interval.

Table III. *Logistic regression model for participation in the domain of "autonomy outdoors" (IPA), with single items of European Brain Injury Questionnaire (EBIQ) from the domains communication, isolation and cognition, the ability to perform daily hygiene (Swedish Stroke Register Questionnaire) and mobility (EuroQol (EQ-5D))*

	p-value	Odds ratio	95% CI for odds ratio
Mobility (EQ-5D)	0.592	1.804	0.209–15.607
Daily hygiene (Swedish Stroke Register Questionnaire)	0.156	20.614	0.315–1350.633
Losing contact with your friends EBIQ 60	0.022*	9.442	1.377–64.749
Others do not understand my problems EBIQ 6	0.024*	11.491	1.382–95.522
Failing to notice other people's mood EBIQ 23	0.030*	7.502	1.218–46.225

*$p \leq 0.05$.
IPA: Impact on Participation and Autonomy; CI: confidence interval.

DISCUSSION

The aim of this study was to explore what factors most affect the level of participation after a TBI in the individual's subjective experience.

The study sample showed a trauma background from mild to severe brain injury in accordance with a TBI population diagnosed S06.2 and S06.3. Many subjects reported a large number of problems 4 years after the TBI, as expected. In the EBIQ, 40% reported problems in 43 of 62 questions, and 20% stated problems in as many as 58 out of the 62 questions. The same tendency was seen in the EQ-5D, where 15–58% of the sample reported problems in different domains. It is worth noting that 25% of subject reported problems in mobility, 15% in self-care, and 33% in daily activities, and that the highest extent of problems, 58%, was related to anxiety/depression and, also as a high percentage (58%), pain 4 years after their TBI. The high percentage of problems with pain was, to some extent, unexpected, and therefore was not included in the regression models. However, in recent years, there has been a consensus in the research as to the importance of emotional problems, post-traumatic stress disorder and chronic pain for the impact on outcome after TBI (10, 20–24), and future studies should perhaps consider the impact of pain.

Table IV. *Logistic regression model for participation in the domain of "autonomy indoors" (IPA), with single items of European Brain Injury Questionnaire (EBIQ) from the domains isolation and communication, the ability to perform daily hygiene (Swedish Stroke Register Questionnaire) and mobility (EuroQol (EQ-5D))*

	p-value	Odds ratio	95% CI for odds ratio
Others do not understand my problems EBIQ 6	0.039*	37.003	1.207–1134.493
Thinking only of myself EBIQ 39	0.023*	16.956	1.484–193.736
Leaving it to others to start conversations EBIQ 55	0.108	9.424	0.612–145.136
Mobility (EQ-5D)	0.665	2.219	0.067–73.118
Daily hygiene (Swedish Stroke Register Questionnaire)	0.072	11.591	0.802–167.559

*$p \leq 0.05$.
CI: confidence interval.

The experienced level of participation reported in the IPA ranged from very good to very poor, and it is impossible to say what an acceptable level is. Is a "fair" participation good enough after a successful rehabilitation? What can be expected after a brain injury? In this study, between 20% and 40% of the sample did not perceive good participation according to the answers on the IPA items. On the other hand, that means that 60%–80% experienced that they had good participation, even though the answer "fair" participation was not included in this group. The participation was not dependent on gender or severity of the brain injury. However, the areas of participation that were rated in the IPA are fundamental in life, and the goal of rehabilitation is to try to help brain-injured persons to achieve a participation good enough to make them feel satisfied, rather than a level of participation that is "fair", or which only occurs in some aspects.

The results of the IPA showed that the largest proportion experienced good participation in the domain of "autonomy indoors", which can be explained by the fact that only 25% had problems with mobility. In the other domains as much as 35–40% of the sample did not experience good participation. The objective was to try to find explanations for which factors have a relation to the level of participation. One conclusion was that it is difficult to find single predictors because of the many interacting variables that form a very complex context and reality. In the present study, pain, anxiety and depression were found to be major problems in the sample (58%). Somatic, emotional and cognitive problems after TBI are often associated with post-traumatic stress disorder and chronic pain, a constellation of findings that has been called the polytrauma clinical triad (20). That several factors interact in this way probably explains why it is so difficult to find single robust predictors. Better knowledge of these interactions may be a way to improve rehabilitation in order to reach good participation in society.

A range of components has been associated with participation after stroke and TBI. However, the impact of contextual factors (personal and environmental) is not yet well understood or documented (25). The findings of this study could therefore contribute to this area of knowledge, highlighting the importance of a well-functioning interaction between the injured brain and the environment, as well as of the emotional aspects and subjective experience in terms of having an influence on participation.

In our search for predictors of participation, we used the EBIQ questionnaire. The EBIQ domains were closely cor-

related, thus it was not meaningful to make an analysis at the domain level, which was a limitation of the study. Instead, the regression models had to be based on single items from the EBIQ that did not correlate with each other. This meant that, as not all questions could be included, a selection was necessary, which may have implied a loss of information. On the other hand, the significant results seem to be relevant to clinical experience and in line with other research (26–28). Another limitation could be the rather large drop-out, but in the analysis of drop-out there were no significant difference between the groups in age, gender or severity of injury, and therefore we think the result is possible to generalize.

Taking the results of the 4 models together, there were 5 different items that were significant as predictors based on the EBIQ answers that reflected different kinds of problems experienced. There may be a variety of reasons why these problems originate from different areas. The 5 items were "lack of interest in your surroundings", "losing contact with your friends", "others do not understand my problems", "thinking only of myself" and "failing to notice other people's mood". Depression is common after a brain injury (21) and can be an explanation for all of the above items. That the focus of the injured persons is on themselves and their situation is also common and understandable, as the injured person often has quite enough to do in taking care of his own problems and is not able to pay great attention to others. Cognitive problems often accompany a brain injury, and problems with attention and working memory also come with a mild injury and may result in difficulties in observing and following what is going on around, and may appear to be a lack of interest. Taking note of signs and other people's feelings may also be a problem. Difficulties in getting things done, and losing friends, can both be consequences of executive inability, i.e. initiating and finalizing tasks. The last of the predictors, the experience that others do not understand their problems, can be explained as the difficulty for a person who has not experienced cognitive problems to really understand what cognitive problems mean. In addition, the injured person may have difficulty explaining the problems, or may have exaggerated demands. In this study, it seems that emotional and social factors have a great influence on the level of participation. In line with these results is the conclusion of Wise's study (5) that, after TBI, activities change from partying and sports to watching television.

In the domains of "autonomy outdoors" and "autonomy indoors" it was expected that mobility would be an important factor for participation, but this was not verified in this study. This should not be interpreted such that mobility is unimportant for outdoor or indoor autonomy, but could indicate that rehabilitation has good means to compensate for this kind of problem. It might have been expected that mobility and personal care would also have influenced the participation of the domains of "family role" and "social life", as this kind of dependency is often a pressure on the relation to family and friends. Perhaps like the above, the Swedish social healthcare system provides satisfying assistance and good assistive devices, which means that other factors have a greater impact

It was interesting to note that those who reported good participation in the IPA stated their health in the VAS scale of the EQ-5D to be at the same level as the Swedish norm group, while those who stated "not good participation" reported a low current health status in the EQ-5D. This could be understood such that a person with good participation also perceives having a good health status, in spite of the presence of deficits.

In conclusion, the study found that the sample of TBI reported a number of activity limitations, and approximately 40% also experienced restrictions in participation in the domains of social life, family role and autonomy outdoors. The analyses gave 5 predictors reflecting emotional and social aspects, which could explain up to 70% of the variation in participation. The study also tells us that a great deal of the explanation should also be seen as being connected to an interaction between several aspects. The findings will contribute to the body of knowledge, but further studies are needed to be able to improve participation for persons with disability after a TBI.

REFERENCES

1. Chua KS, Ng YS, Yap SG, Bok CW. A brief review of traumatic brain injury rehabilitation. Ann Acad Med Singapore 2007; 36: 31–42.
2. Truelle JL, Fayol P, Montreuil M, Chevignard M. Community integration after severe traumatic brain injury in adults. Curr Opin Neurol 2010; 23: 688–694.
3. World Health Organization. International Classification of Functioning, Disability and Health: ICF. Geneva: World Health Organization; 2001.
4. Cicerone KD. Participation as an outcome of traumatic brain injury rehabilitation. J Head Trauma Rehabil 2004; 19: 494–501.
5. Wise EK, Mathews-Dalton C, Dikmen S, Temkin N, Machamer J, Bell K, et al. Impact of traumatic brain injury on participation in leisure activities. Arch Phys Med Rehabil 2010; 91: 1357–1362.
6. Harrison-Felix C, Whiteneck G, DeVivo M, Hammond FM, Jha A. Mortality following rehabilitation in the traumatic brain injury model systems of care. NeuroRehabil 2004; 19: 45–54.
7. Dykeman BF. School-based interventions for treating social adjustment difficulties in children with traumatic brain injury. J Instruct Psychol 2003; 30: 225–230.
8. Huang SJ, Ho HL, Yang CC. Longitudinal outcomes of patients with traumatic brain injury: a preliminary study. Brain Inj 2010; 24: 1606–1615.
9. Larsson J, Esbjornsson E, Bjorkdahl A, Morberg I, Nilsson M, Sunnerhagen KS. Sick leave after traumatic brain injury. The person or the diagnosis – which has greater impact? Scand J Public Health 2010; 38: 541–547.
10. Guillamondegui OD, Montgomery SA, Phibbs FT, McPheeters ML, Alexander PT, Jerome RN, et al.Tramatic brain injury depression. Rockville, MD: Agency for Healthcare Research and Quality (US); 2011 Apr, Report no.: 11-EHC017-EF.
11. Moldover JE, Goldberg KB, Prout MF. Depression after traumatic brain injury: a review of evidence for clinical heterogeneity. Neuropsychol Rev 2004; 14: 143–154.
12. Brooks R. EuroQol: the current state of play. Health Policy 1996; 37: 53–72.
13. Teasdale TW, Christensen AL, Willmes K, Deloche G, Braga L, Stachowiak F, et al. Subjective experience in brain-injured patients and their close relatives: a European Brain Injury Questionnaire study. Brain Inj 1997; 11: 543–563.
14. Cardol M, de Haan RJ, van den Bos GA, de Jong BA, de Groot IJ. The development of a handicap assessment questionnaire: the

Impact on Participation and Autonomy (IPA). Clin Rehabil 1999; 13: 411–419.
15. Starmark JE, Stalhammar D, Holmgren E. The Reaction Level Scale (RLS85). Manual and guidelines. Acta Neurochir (Wien) 1988; 91: 12–20.
16. Starmark JE, Stalhammar D, Holmgren E, Rosander B. A comparison of the Glasgow Coma Scale and the Reaction Level Scale (RLS85). J Neurosurg 1988; 69: 699–706.
17. Cox DR, Snell EJ. Applied statistics: principles and examples. London: Chapman and Hall; 1981.
18. Nagelkerke NJD. Maximum likelihood estimation of functional relationships. Berlin; New York: Springer-Vlg; 1992.
19. Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. New York; Chichester: Wiley; 2000.
20. Risdall JE, Menon DK. Traumatic brain injury. Philos Trans R Soc Lond B Biol Sci 2011; 366: 241–250.
21. Hart T, Brenner L, Clark AN, Bogner JA, Novack TA, Chervoneva I, et al. Major and minor depression after traumatic brain injury. Arch Phys Med Rehabil 2011; 92: 1211–1219.
22. Fogelberg DJ, Hoffman JM, Dikmen S, Temkin NR, Bell KR. Association of sleep and co-occurring psychological conditions at 1 year after traumatic brain injury. Arch Phys Med Rehabil 2012; 93: 1313–1318.
23. Arango-Lasprilla JC, Krch D, Drew A, De Los Reyes Aragon CJ, Stevens LF. Health-related quality of life of individuals with traumatic brain injury in Barranquilla, Colombia. Brain Inj 2012; 26: 825–833.
24. Bedard M, Felteau M, Marshall S, Campbell S, Gibbons C, Klein R, et al. Mindfulness-based cognitive therapy: benefits in reducing depression following a traumatic brain injury. Adv Mind Body Med 2012; 26: 6.
25. Hoyle M, Gustafsson L, Meretith P, Ownsworth T. Participation after stroke: do we understand all the components and relationships as categorised in the ICF? Brain Impairment 2012; 13: 4–5–15.
26. Pierce CA, Hanks RA. Life satisfaction after traumatic brain injury and the World Health Organization model of disability. Am J Phys Med Rehabil 2006; 85: 889–898.
27. Hart T, Hoffman JM, Pretz C, Kennedy R, Clark AN, Brenner LA. A longitudinal study of major and minor depression following traumatic brain injury. Arch Phys Med Rehabil 2012; 93: 1343–1349.
28. Sveen U, Ostensjo S, Laxe S, Soberg HL. Problems in functioning after a mild traumatic brain injury within the ICF framework: the patient perspective using focus groups. Disabil Rehabil 2013; 35: 749–757.

J Rehabil Med 2013; 45: 771–777

ORIGINAL REPORT

FATIGUE, PSYCHOSOCIAL ADAPTATION AND QUALITY OF LIFE ONE YEAR AFTER TRAUMATIC BRAIN INJURY AND SUSPECTED TRAUMATIC AXONAL INJURY; EVALUATIONS OF PATIENTS AND RELATIVES: A PILOT STUDY

Eva Esbjörnsson, PhD[1], Thomas Skoglund, MD, PhD[1] and Katharina S. Sunnerhagen, MD, PhD[1,2]

From the [1]Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden and [2]Sunnaas Rehabilitation Hospital, Medical Faculty, Oslo University, Oslo, Norway

Objective: **To describe fatigue and its relationship to cognition, psychosocial adjustment, quality of life (QoL), work status and relative's experiences 12 months after suspected traumatic axonal injury.**

Methods: **Eighteen patients were assessed with the Daily Fatigue Impact Scale (D-FIS), the Barrow Neurological Institute Screen for Higher Cerebral Functions (BNIS), the European Questionnaire 5 Dimensions health-related quality of life, the Glasgow Coma Outcome Scale Extended, and the European Brain Injury Questionnaire (EBIQ) (patient and relative). Return to work was registered.**

Results: **At 1 year, fatigue still caused great problems in daily life. Although fatigue and cognition (BNIS) did not correlate, the more fatigued patients subjectively experienced significantly more cognitive dysfunction. Although D-FIS and QoL did not correlate, most patients reported that feelings of tiredness and dullness related to having lower QoL. However, lower QoL was associated with cognitive and attention disability (BNIS), subjective perception of executive dysfunction, lack of motivation, and mood disturbances (EBIQ). Neither fatigue nor cognition associated with return to work. The general consequences of traumatic axonal injury showed good agreement between patients' and relatives' experiences.**

Conclusion: **The patient's subjective experience of the impact of traumatic axonal injury seems to be most essential, as it is the objective reality that the patient responds to, and this should therefore be assessed and treated.**

Key words: head trauma; diffuse axonal injury; fatigue; cognition; quality of life; employment.

J Rehabil Med 2013; 45: 771–777

Correspondence address: Eva Esbjörnsson, Rehabilitation Medicine, Per Dubbsgatan 14, 3rd floor, Sahlgrenska University Hospital, SE-413 45 Göteborg, Sweden. E-mail: eva.esbjornsson@neuro.gu.se

Accepted April 23, 2013

INTRODUCTION

Axonal injury (AI) (traumatic axonal injury (TAI) diffuse axonal injury (DAI)), is common after traumatic brain injury (TBI) and may contribute to clinical manifestations (1). It is poorly defined as a clinical syndrome and is difficult to verify when non-invasive (1). Although axonal degeneration is suggested to continue even years after injury (2), a "pure" DAI/TAI rarely seems to be identified (3).

Fatigue is a complex and subjective phenomenon with multifactorial origins. Psychological fatigue is defined as decreased motivation, extended mental activity, or boredom, occurring in situations that require effort, cause concern, or involve chronic depression (4). According to the coping hypothesis (4), the mental fatigue reported by 43–73% of TBI patients (4) is related to the increased mental effort (4, 5) necessary to overcome attention deficit and slowed processing, in order to reach an adequate level of performance in everyday life. Various hypotheses regarding an association between fatigue and the organic damage referred to by Johansson et al. (6) have suggested that metabolic and structural lesions disrupt the usual activation process in pathways that interconnect different regions of the brain, resulting in fatigue. Impaired information-processing speed is also related to TAI (7). A patient's slower speed when exposed to interference tasks suggested significant factors related to subjectively mental fatigue in persons with TBI (4, 6), such as difficulty resisting distractions and maintaining focus (8).

No associations have been found between fatigue and injury severity or time since injury, age (4, 5, 9, 10), cognitive impairment, or gender (4, 10), although fatigue has been shown to be more severe among women (9). Fatigue seems to improve during the first year, but not change later on (11), even though it can last for several years (6, 10). Fatigue may interfere with return to work (6, 12), quality of life (QoL), well-being (6, 9) and social and recreational life (6), but no association with participation in major life activities was reported (9). Fatigue-related QoL was reported to be associated with somatic symptoms and chronic perceived situational stress (13). It has been suggested that fatigue might be an effect of the brain injury itself (6, 9) and not a result of pain, depression or sleep deprivation (6).

Cognitive impairment and executive dysfunctions are common after TBI and TAI (3, 7, 14–20), as is impaired self-awareness (15, 21–22). It has been suggested that the medial prefrontal and posterior cingulated cortex are important regions

for self-reflective thought and a sense of self-reflection (23). Patients may under-report cognitive and behavioural difficulties, which are the true residuals of their brain injury (22). However, patients who had a more appropriate and realistic perception of their deficits, were reported to have less psychopathological symptoms, better neuropsychological function and greater independence (24).

With regard to behaviour, mood disturbance and disorders of behavioural control and regulation are particularly common (25) for patients with TBI. In particular, irritability, anger and aggression are suggested to be more characteristic of depression than sadness and tearfulness. Having a depressive mood endorsed more injury-related difficulties, which showed a strong relationship between mood and experienced psychosocial functioning, and indicated that perceived changes in daily functioning continue to influence emotional well-being over time after the injury (26).

Brain dysfunction associated with neuropsychological disturbances has appeared to influence the relationship between the distress level of family members and their ratings of impaired awareness in patients with TBI (27). Relatives have been found to report more difficulties than patients on all subscales of the European Brain Injury Questionnaire (EBIQ), most frequently regarding somatic and cognitive problems (28).

Objectives

The objective of this study was to describe experienced fatigue and its relationship to cognition, psychosocial adjustment, health and QoL, and also related to work status 12 months after TBI and suspected TAI. A further objective was to describe the patient's self-reported problems, and compare these with their relatives' perceptions regarding the patient's cognitive function, behaviour and mental state.

METHODS

The study population was examined in the acute phase, at 6 and 12 months, when orientation was recovered (Glasgow Coma Scale (GCS) = 14) and the patients were testable, according to the pre-screen of the Barrow Neurological Institute Screen for Higher Cerebral Functions (BNIS). This study describes the situation of the patients 12 months after TBI. Results from the longitudinal study have been presented previously (16).

All patients < 65 years of age were referred to Sahlgrenska University Hospital during the period June 2006 to September 2009 and had sustained TBI. Patients were included in the study if they fulfilled the criteria for a suspected pure TAI: patients who experienced an affected consciousness and/or focal neurological symptoms without an explanation seen on the computerized tomography (CT) scan of the brain. Thus, patients with haemorrhages and/or oedema that could explain their affected neurology were excluded.

The catchment area included the western part of southern Sweden, in the region of Västra Götaland, which has approximately 1 million inhabitants between the ages of 16 and 65 years.

At 12 months, self-reported fatigue, cognitive and executive function, psychosocial adaptation and health-related QoL were assessed by the patient and compared with their relatives' perceptions.

The Regional Ethical Review Board of the University of Gothenburg approved the study, and informed consent was obtained from all participants or their next of kin.

Instruments

Demographics, Glasgow Coma Scale scores (GCS) and the cause of the trauma were obtained from each patient's chart upon arrival at the hospital. Level of consciousness was assessed using the Reaction Level Scale (RLS), which was translated to the GCS presented here (29).

The Daily Fatigue Impact Scale (D-FIS) was chosen to register subjectively perceived fatigue (30). For subjects who were followed longitudinally, the 8 items of D-FIS, selected from the original FIS items (31), were shown to reflect changes in patient's reports of fatigue (30). D-FIS measures the fatigue impact of physical tiredness and lack of energy. The response to each item is given on a 5-point scale, where 0 = no problems and 4 = extreme problems. The maximum score is 32 points.

The BNIS, which was used to measure cognitive function (32), was validated in Sweden (33, 34). The initial pre-screen assesses whether the patient is testable according to consciousness/alertness, basic communicative ability and participation. BNIS consists of 7 subscales, of which only attention/concentration is reported here. Scores are obtained for both the subscales and the total instrument. The maximum score is 50 points, where a score < 47 points indicates cognitive dysfunction.

The European Questionnaire 5 Dimensions health-related quality of life (EQ-5D) was established by the EuroQol Group in 1987 to describe and evaluate self-reported health outcomes and health-related QoL (35). The EQ-5D consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The patients describe their actual health state by marking on a 3-point scale, where A = no problems, B = some or moderate problems, and C = unable or extreme problems. Each dimension is treated separately. The health dimensions are complemented by a visual analogue scale (VAS) for marking experienced general health status and QoL, where 0 = worst imaginable health state and 100 = best imaginable health state.

The EBIQ is a self-reporting questionnaire of the subjectively perceived cognitive, emotional and social difficulties resulting from TBI (36). EBIQ consists of 63 questions in 9 domains: somatic, cognitive, motivation, irritability/impulsivity, depression, isolation, consequences, communication, and core problems (in general). The cognitive domain is composed of 2 subscales: memory and planning. The patient answers the statements according to perceived difficulty on a 3-point scale, where 1=not at all, 2 = a little, and 3 = a lot. Three questions are added toward the end regarding the patient's evaluation of the extent to which the consequences of the trauma have impacted the lives of their next of kin. A parallel version is constructed for the nearest relative to estimate the consequences of the trauma for the patient. Both the patient and the relative answered these questionnaires.

Glasgow Outcome Scale Extended (GOSE) was used to estimate TBI outcomes (37). Along with TBI symptoms, the scale assesses disability in participation and activity on an extended 8-point scale.

Work status, qualified as ≥ 25% employment was registered.

Statistics

Descriptive statistics are presented as frequencies and percentages, and as means with standard deviations and/or medians and ranges. Non-parametric statistics were used (Mann-Whitney *U* test, Wilcoxon signed-rank test, Kruskal-Wallis test and χ^2 test) for analysing the differences between groups, and Pearson correlation for analysing associations between variables. A significance level of $p \leq 0.01$ was accepted as indicating significance. For statistical calculations, the SPSS program package 15.0 was used.

RESULTS

Background

A total of 22 patients was included; however, the study sample comprised 18 patients, as 2 patients were still not testable 1 year after the TBI, 1 had died and 1 was missing.

The median age for males ($n=9$) was 25 years (range 19–48 years), and 42 years (range 20–62 years) for females ($n=9$). The age difference was not significant. The majority of patients had higher (≥12 years) education (males: $n=9$; females: $n=6$). The patient demographics are presented in Table I.

The median GCS for the study sample was 9.5 (range 3–15). Two patients did not have any affected consciousness. However, for these, MRI identified TAI subcortically in the white matter, in the hemispheres and in the brain stem, respectively.

Fatigue (Daily Fatigue Impact Scale)

After 1 year, the median value of D-FIS still indicated an experienced fatigue that resulted in great to extreme problems in daily life (median 15 (range 3–24)). No significant difference between the sexes or any association with age or GCS was found.

The D-FIS and the EBIQ scores correlated significantly ($p=0.004$), where fatigue was associated with subjectively perceived cognitive problems ($p<0.001$), especially difficulties in memory ($p=0.001$) and planning ($p<0.001$). Although patients who reported more fatigue also experienced worse cognitive dysfunction (Table II), no association was found between fatigue and cognition as measured by the BNIS.

Experiencing fatigue as a more comprehensive problem was associated with feeling generally more tired and dull (82.4%) ($p<0.001$), having difficulties making decisions ($p=0.004$), getting things done on time ($p<0.001$), and having to work slowly in order to get things right ($p<0.001$) (EBIQ). Fatigue also influenced reacting too quickly to things other people said and did ($p<0.001$). Fatigue did not correlate with any of the dimensions of the EQ-5D, and no association was found between fatigue and activity and participation, as assessed by the GOSE.

Cognition (Barrow Neurological Institute Screen for Higher Cerebral Functions)

One year after TBI, 17 patients, including the 2 not testable patients, ($n=20$; 85%) still had cognitive dysfunction (median 44 (range 18–49)). No significant cognitive difference was found between the sexes, and neither cognition (total BNIS score) nor the subscale of attention was associated with fatigue.

Patients with a less depressed mood functioned better cognitively ($p=0.005$) than the more easily irritated and depressed patients who perceived themselves to be more isolated ($p=0.009$) and considered TBI to have had a greater impact in general on their situation ($p=0.001$).

Table I. *Demographic data (*n*=18)*

M/F, *n*	9/9
Age, years, M/F, median	25/42
Education, <12 years/≥12 years, *n*	4/14
Cause, traffic accidents/falls/other, *n*	10/5/3
GCS, median (range)	9.5 (3–15)
Location of TAI, 0/1/2/3, *n*	4/1/7/6

GCS: Glasgow Coma Scale; TAI: traumatic axonal injury; M: male; F: female.
Location of TAI: 0=no; 1=subcortical; 2=corpus callosum; 3=brain stem.

Table II. *Pearson correlation coefficients 12 months after traumatic brain injury (TBI) and traumatic axonal injury (TAI): between D-FIS and EBIQ total score and subscales; between D-FIS and the dimensions of the EQ-5D; between D-FIS and GOSE; and between BNIS total score and the subscale of attention and EBIQ, EQ-5D and GOSE*

	D-FIS total score	*p*-value	BNIS total score	*p*-value	Attention	*p*-value
EBIQ						
Total score	0.660	0.004*	–0.631	0.009*	–0.630	0.009*
Somatic	0.576	0.015	–0.346	0.189	–0.433	0.094
Cognitive	0.837	0.000*	–0.518	0.040	–0.436	0.091
Memory	0.747	0.001*	–0.436	0.091	–0.282	0.290
Planning	0.809	0.000*	–0.514	0.042	–0.477	0.062
Motivation	0.273	0.289	–0.481	0.059	–0.390	0.135
Irritation	0.548	0.023	–0.509	0.044	–0.610	0.012
Depression	0.334	0.190	–0.665	0.005*	–0.608	0.013
Isolation	0.266	0.302	–0.633	0.009*	–0.776	0.000*
Consequences	0.557	0.020	–0.727	0.001*	–0.633	0.008*
Communication	0.577	0.015	–0.531	0.034	–0.492	0.053
"Core"	0.505	0.039	–0.344	0.192	–0.441	0.088
EQ-5D mobility	0.116	0.658	–0.693	0.003*	–0.813	0.000*
Hygiene	0.317	0.215	–0.602	0.014	0.501	0.048
Activity	0.262	0.309	–0.282	0.291	–0.392	0.133
Pain	0.411	0.101	–0.340	0.197	–0.252	0.347
Anxiety/ depression	0.170	0.513	–0.257	0.337	–0.400	0.125
Health status (QoL)	–0.544	0.029	0.885	0.000*	0.747	0.001*
GOSE	0.007	0.980	0.628	0.007*	0.672	0.003*

*$p\leq0.01$ (Sig. 2-tailed); **$p\leq0.001$ (Sig. 2-tailed).
D-FIS: Daily Fatigue Impact Scale; EBIQ: European Brain Injury Questionnaire; EQ-5D: European Questionnaire 5 dimensions of health-related quality of life; BNIS: Barrow Neurological Institute Screen of Higher Cerebral Functions; GOSE: Glasgow Outcome Scale Extended.

On the subscale of attention it was found that the more inattentive a patient was, the stronger the feeling of being isolated ($p<0.001$) and experiencing the consequences after the injury as more debilitating ($p=0.008$).

Perceived health and quality of life (EuroQol-5D)

No significant difference was found in QoL between the sexes; likewise, age or GCS did not correlated with QoL. Of 17 patients, 70.6% described a moderate level of pain unrelated to headache, which was reported by more than half the group (53%). According to the EQ-5D, no patients reported major problems with anxiety/depression. However, anxiety/depression (EQ-5D) and the EBIQ total score correlated significantly ($p=0.006$), wherein the more anxious persons reported more behavioural, psychosocial and mood problems (Table III).

Those who reported a moderate anxious/depressed mood (58.8%) were more easily irritated ($p=0.008$), depressed ($p=0.001$), socially isolated ($p=0.004$) and unmotivated ($p=0.004$) (EBIQ) than the less anxious/depressed. They also reported the injury as having more serious consequences on activity ($p=0.005$).

Feeling tired and dull (82.4%), having to do things slowly (76.5%), being restless (76.5%) or stubborn (76.4%) and

having problems with concentration (76.5%) had the greatest effect on patients' QoL.

Health-related QoL correlated with the perception of general consequences of the trauma ($p = 0.001$), the primary interferences being an inability to manage one's own hygiene ($p < 0.001$) and major activities ($p = 0.005$) (Table III). Patients who reported a better QoL were found to have better cognitive function ($p < 0.001$) and attention ($p = 0.001$) (BNIS) (Table II) and perceived themselves to be more motivated ($p = 0.005$), to have fewer problems in planning ($p = 0.008$), to be less depressed ($p = 0.004$) and socially isolated ($p = 0.006$) (EBIQ) compared with those who had a lower QoL (Table III).

No significant difference was found in QoL between the sick-listed patients and those who had returned to work ($p = 0.017$).

Comparison between the reports of patients and their next of kin (European Brain Injury Questionnaire)

Significant positive correlations were found between the perceptions of patients and their relatives regarding the general consequences after the TBI ($p < 0.001$), particularly in the domains of cognition ($p = 0.001$), memory ($p = 0.002$) and planning ($p = 0.001$). Patients who felt more unmotivated were also reported by the next of kin to be more isolated ($p = 0.002$). There was no significant correlation between the patient and the next of kin in estimating the motivation of the patient ($p = 0.064$). The majority of the relatives regarded the patient as being tired and dull (93.4%) or stubborn (93.4%), having to do things more slowly (80%) or unable to get things done (71.4%) and being impulsive or too quick to react to things other people said (66.6%). Patients were also described as having problems with headache (73.4%), mood swings (73.3%), irritability (71.4%), outbursts (66.6%) and concentration (66.6%). Furthermore, they appeared to find everything troublesome (66.7%) and were insensitive to other people's mood (71.4%). Patients also reported these problems, but often perceived them as being less serious.

Both groups also reported family problems after the TBI, the patients to a somewhat lesser extent (53.4%) compared with the next of kin (73.3%). Change in the next of kin's mood was experienced by 60% of the patients, compared with 66.6% of the relatives, who were also more likely to report the patient as having a decreased libido (66.6%) than the patients (47%) themselves.

EuroQol-5D

Patients who had to depend upon others to manage their personal hygiene ($p < 0.001$) and activity in daily life ($p = 0.005$) were more likely to report greater consequences caused by the trauma. (Table III). The more mobile patients had significantly better cognition ($p = 0.003$) and attention ($p < 0.001$) (BNIS) than the more disabled patients (Table II).

Glasgow Outcome Scale Extended

The GOSE assessment did not differ significantly between the sexes and was not associated with age. No association was found between fatigue and GOSE, but activity and participation correlated significantly with cognition (BNIS) ($p = 0.007$) and the subscale of attention ($p = 0.003$) (Table II). Patients with better cognitive function were rated as less disabled. Also, patients who expressed a better QoL received somewhat higher GOSE scores ($p = 0.010$).

Return to work

Five patients had returned to 75–100% paid employment 12 months after TBI. No significant differences were found regarding fatigue, as the working group scored their fatigue (range 5–22) almost equally to the non-working group (range 3–24). Neither did cognitive function (BNIS) differ between the groups.

However, those who had returned to work were significantly more attentive ($p = 0.004$) (BNIS) and assessed as more active and participating ($p = 0.002$) (GOSE). No significant difference was found in QoL between the working group (median 80.0

Table III. *Pearson correlation coefficients at 12 months between European Brain Injury Questionnaire (EBIQ) total score and subscales and European Questionnaire 5 Dimensions health-related quality of life (EQ-5D)*

	EQ-5D											
	Mobility	*p*-value	Hygiene	*p*-value	Activity	*p*-value	Pain	*p*-value	Anxiety/ depression	*p*-value	QoL	*p*-value
EBIQ												
Total score	0.386	0.126	0.576	0.016	0.534	0.027	0.327	0.200	0.633	0.006**	–0.716	0.002*
Somatic	0.117	0.654	0.277	0.282	0.386	0.126	0.346	0.174	0.421	0.093	–0.346	0.190
Cognitive	0.258	0.318	0.559	0.020	0.446	0.073	0.372	0.141	0.335	0.188	–0.625	0.010*
Memory	0.175	0.501	0.381	0.131	0.310	0.226	0.305	0.233	0.303	0.237	–0.520	0.039
Planning	0.280	0.276	0.607	0.010*	0.481	0.050	0.375	0.138	0.322	0.207	–0.635	0.008*
Motivation	0.225	0.385	0.399	0.112	0.398	0.114	–0.009	0.971	0.661	0.004*	–0.660	0.005*
Irritation	0.351	0.167	0.383	0.130	0.353	0.164	0.449	0.071	0.617	0.008*	–0.601	0.014
Depression	0.427	0.087	0.564	0.018	0.520	0.032	0.144	0.582	0.735	0.001*	–0.674	0.004*
Isolation	0.462	0.062	0.500	0.041	0.486	0.048	0.329	0.198	0.664	0.004*	–0.652	0.006*
Consequences	0.501	0.041	0.764	0.000*	0.643	0.005*	0.229	0.376	0.478	0.052	–0.738	0.001*
Communication	0.254	0.325	0.325	0.203	0.449	0.070	0.443	0.075	0.523	0.031	–0.573	0.020
"Core"	0.267	0.301	0.345	0.175	0.281	0.275	0.107	0.684	0.431	0.084	–0.480	0.117

*$p \leq 0.01$ (Sig. 2-tailed); **$p \leq 0.001$ (Sig. 2-tailed).

(range 51–100)) and the patients still on sick leave (median 55 (range 35–75)) ($p = 0.017$). This could be compared with the normal value in Sweden of mean 83.49 (35).

DISCUSSION

The objective of this study was to examine the experience of fatigue and its relationship with behavioural and psychosocial outcomes, cognitive function, and QoL, as well as with work status 12 months after TBI and suspected TAI. A further objective was to examine patients' self-reported problems, and to compare these with their relatives' experiences, regarding dysfunctions in the patient's behaviour, cognition and mood.

This study should be considered as a pilot study due to the small sample size, perhaps as a result of the inclusion criteria and the difficulty of identifying a "pure" TAI (3), which reduced the generalizability of the results.

Because fatigue is a complex and subjective phenomenon with multifactorial origins (4), it was important to cover various functions after TBI that could have impacted fatigue.

In choosing our instruments, we wanted to use short, reliable and validated instruments, that were easy to administer and easy for the patient to understand and respond to despite the cognitive impact and fatigue associated with TBI (38), especially during the acute phase. The instruments also needed to be sensitive enough to differentiate between the 3 assessments reported in the longitudinal follow-up study of the first year, which was previously reported (16).

Prolonged fatigue is a well-known consequence of TBI (4–6), and no recovery appears to occur after the first year post-injury (11). Supported by previous research, this study found no significant associations between fatigue and severity of injury (GCS), cause of trauma (4, 5, 9, 10), or age (5). In addition, no difference was shown between the sexes; a result supported by some research (4, 10) but contrary to others (9).

One year after TBI, 85% of the sample patients still had cognitive dysfunction (BNIS). Although no significant correlation was found between cognition (as measured by the BNIS) and fatigue (D-FIS), a similar finding to previously reported results (10), the subjective perception of general cognitive problems, especially memory and the executive function of planning, correlated significantly with fatigue (D-FIS); moreover, the majority of patients who reported that fatigue caused great to extreme problems in daily life also reported feeling tired and dull (82.4%).

In our study, the more fatigued patients (three-quarters of the sample) subjectively perceived concentration and memory problems; a need to do things slowly; difficulty in planning, making decisions, getting things done on time; more impulsive reactions; and a feeling of being dull and restless (EBIQ). The subjective perception of fatigue thus seems to include an interaction of cognitive dysfunctions, emotions and behavioural changes. It might also be that the cognitive dysfunctions, very common after TBI and TAI (3, 7, 14–20), were related to the mental effort necessary to sustain attention and compensate for slow processing (4–8), reported by 76.5% in our study, and cognitive deficits resulting in an experience of fatigue. Encountering problems can lead to psychological fatigue, which works to protect the person from further frustration and failure, while potentially causing boredom or a decrease in motivation (4). It was found that the more unmotivated patients also experienced more anxiety/depressive mood ($p = 0.004$) and a lower QoL ($p = 0.005$) (Table III), which also might cause the patient (13) and family (27) distress.

That perceived changes in daily functioning appears to influence emotional well-being over time after TBI was reported by Pagulayan et al. (26), who found that patients who reported more depressive symptoms endorsed more injury-related difficulties, showing a strong relationship between depression and perceived psychosocial functioning. This research supports our results, as we found that the more anxious/depressed patients (EQ-5D) generally experienced more behavioural, psychosocial and mood problems (Table III), as they were significantly more irritated, depressed, unmotivated, inactive, and isolated (EBIQ) than the less anxious/depressed patients. These changes are common after TBI and might be a result of the brain injury itself (4, 6, 9), but these changes may also serve psychologically as protective strategies to reduce confrontation with inability, further fatigue, anxiety and stress. Bay & de-Leon (13) reported that chronic situational stress was associated with fatigue-related QoL in TBI. Irritability, as an expression of stress and anxiety (13), was found to associate significantly with experiencing more anxiety and isolation (Table III). More than half the group also reported mood swings, increased stubbornness and quick reactions to what others said and did, which might also be expressions of over-loading and stress (13).

Although no significant association was found between fatigue (D-FIS) and QoL, most patients (82.4%) reported a strong link between feelings of tiredness and dullness and perceiving a lower QoL, as previously reported (9). Also, significant correlations showed that cognitive and attention disability (BNIS), subjective perception of executive dysfunction, lack of motivation and mood disturbances (EBIQ) all resulted in a lower QoL (Table II and III).

Fatigue can interfere with return to work (6, 12), as evidenced by only 5 people in this study returning to adjusted employment during the first year; however, no significant difference was found in fatigue between this group and those still on sick-leave, in accordance with previously reported results (6). It might be that return to work requires increased mental effort to compensate for cognitive deficits and slowed processing, in order to reach an adequate level of performance (4, 5), which consumes mental energy and therefore leads to continuous fatigue.

Cognitive ability did not differ between the working and the sick-listed groups; however, those who returned to work showed a significantly better attention (BNIS), as reported previously (16). They were also assessed as more active and participating, according to the GOSE. No significant differences were found in perception of the consequences of TBI, mood or QoL between the working-group and the sick-listed

group. Although working patients were still fatigued, their ability to return to work after TBI might have given a feeling of more independence, less stress and less disability, resulting in greater confidence.

Patients may under-report cognitive and behavioural difficulties (22), but a more realistic perception of deficits that also testified to a better self-awareness was reported to associate with fewer psychopathological symptoms, better neuropsychological functioning and independence (15). When patients' reports were compared with those of their next of kin, significant agreement was found in experiences regarding the patient's cognitive ability, executive function and the general consequences after the injury. Regarding motivational, emotional and psychosocial variables, compared with their relatives, the patients seemed to somewhat under-report the severity of their dysfunctions. This might indicate deficits in self-awareness (12, 14) or a conscious suppression of the perceived remaining dysfunctions that poses a threat, which might trigger anxiety and stress and have a stressful impact on the family (4, 27).

The results indicate that fatigue and the subjective perception of overall cognitive, behavioural and psychosocial difficulties after TBI and TAI correlated. Although no correlation was found between fatigue and cognition, as measured by the BNIS, the subjective experience of cognitive dysfunction, particularly in planning and memory, was significantly associated with fatigue. For some people, the subjective experience is most essential, and seems to become the patient's objective reality, upon which his/her reactions are based.

Neither fatigue nor cognition differed significantly between the working and sick-listed groups. The non-working group still reported a greater impact of their injury regarding fatigue, cognition, executive function, mood, behaviour and QoL. However, family members did not report any significant differences in cognitive, emotional and behavioural functions between patients in the working and the sick-listed groups. One explanation for these results could be differences in the personalities between the two groups, where persons in the non-working group might be more fragile and vulnerable and react more strongly to alterations affecting their lives in ways they feel they cannot control, as they had before.

The results of this study indicate the importance of taking TBI patients with acute affected consciousness seriously, even if the CT scan does not verify any brain damage. Attending to the patient's own perceptions of the impact of the TBI and complementing rehabilitation with neuropsychological examination, treatment and support might improve the patient's outcome, although further research is needed.

ACKNOWLEDGEMENTS

The study was supported in part by a grant from the Health and Medical Care Committee of Västra Götaland. Cathrine Ritzén-Eriksson, Caisa Hofgren and Jerry Larsson have all been involved in logistics and assessments of patients. Without their input this work would not have been possible.

REFERENCES

1. Smith DH, Meaney DF, Shull WH. Diffuse axonal injury in head trauma. J Head Trauma Rehabil 2003; 18: 307–316.
2. Johnson VE, Stewart W, Smith DH. Axonal pathology in traumatic brain injury. Exp Neurol 2012; 246: 35–43.
3. Scheid R, Walther K, Guthke T, Preul C, von Cramon DY. Cognitive sequelae of diffuse axonal injury. Arch Neurol 2006; 63: 418–424.
4. Belmont A, Agar N, Hugeron C, Gallais B, Azouvi P. Fatigue and traumatic brain injury. Ann Readapt Med Phys 2006; 49: 283–288, 370–374.
5. Ziino C, Ponsford J. Measurement and prediction of subjective fatigue following traumatic brain injury. J Int Neuropsychol Soc 2005; 11: 416–425.
6. Johansson B, Berglund P, Ronnback L. Mental fatigue and impaired information processing after mild and moderate traumatic brain injury. Brain Inj 2009; 23: 1027–1040.
7. Felmingham KL, Baguley IJ, Green AM. Effects of diffuse axonal injury on speed of information processing following severe traumatic brain injury. Neuropsychology 2004; 18: 564–571.
8. Goethals I, Audenaert K, Jacobs F, Lannoo E, Van de Wiele C, Ham H, et al. Cognitive neuroactivation using SPECT and the Stroop Colored Word Test in patients with diffuse brain injury. J Neurotrauma 2004; 21: 1059–1069.
9. Cantor JB, Ashman T, Gordon W, Ginsberg A, Engmann C, Egan M, et al. Fatigue after traumatic brain injury and its impact on participation and quality of life. J Head Trauma Rehabil 2008; 23: 41–51.
10. Borgaro SR, Baker J, Wethe JV, Prigatano GP, Kwasnica C. Subjective reports of fatigue during early recovery from traumatic brain injury. J Head Trauma Rehabil 2005; 20: 416–425.
11. Bushnik T, Englander J, Wright J. Patterns of fatigue and its correlates over the first 2 years after traumatic brain injury. J Head Trauma Rehabil 2008; 23: 25–32.
12. McCrimmon S, Oddy M. Return to work following moderate-to-severe traumatic brain injury. Brain Inj 2006; 20: 1037–1046.
13. Bay E, de-Leon MB. Chronic stress and fatigue-related quality of life after mild to moderate traumatic brain injury. J Head Trauma Rehabil 2011; 26: 355–363.
14. Kinnunen KM, Greenwood R, Powell JH, Leech R, Hawkins PC, Bonnelle V, et al. White matter damage and cognitive impairment after traumatic brain injury. Brain 2011; 134: 449–463.
15. Ghajar J, Ivry RB. The predictive brain state: timing deficiency in traumatic brain injury? Neurorehabil Neural Repair 2008; 22: 217–227.
16. Esbjornsson E, Skoglund T, Mitsis MK, Hofgren C, Larsson J, Sunnerhagen KS. Cognitive impact of traumatic axonal injury (TAI) and return to work. Brain Inj 2013; 27: 521–528.
17. Lipton ML, Gulko E, Zimmerman ME, Friedman BW, Kim M, Gellella E, et al. Diffusion-tensor imaging implicates prefrontal axonal injury in executive function impairment following very mild traumatic brain injury. Radiology 2009; 252: 816–824.
18. Kraus MF, Susmaras T, Caughlin BP, Walker CJ, Sweeney JA, Little DM. White matter integrity and cognition in chronic traumatic brain injury: a diffusion tensor imaging study. Brain 2007; 130: 2508–2519.
19. Azouvi P, Vallat-Azouvi C, Belmont A. Cognitive deficits after traumatic coma. Prog Brain Res 2009; 177: 89–110.
20. Fork M, Bartels C, Ebert AD, Grubich C, Synowitz H, Wallesch CW. Neuropsychological sequelae of diffuse traumatic brain injury. Brain Inj 2005; 19: 101–108.
21. Lux WE. A neuropsychiatric perspective on traumatic brain injury. J Rehabil Res Dev 2007; 44: 951–962.
22. Prigatano GP. Impaired self-awareness after moderately severe to severe traumatic brain injury. Acta Neurochir Suppl 2005; 93:

39−42.
23. Johnson SC, Baxter LC, Wilder LS, Pipe JG, Heiserman JE, Prigatano GP. Neural correlates of self-reflection. Brain 2002; 125: 1808−1814.
24. Noe E, Ferri J, Caballero MC, Villodre R, Sanchez A, Chirivella J. Self-awareness after acquired brain injury-predictors and rehabilitation. J Neurol 2005; 252: 168−175.
25. Seel RT, Macciocchi S, Kreutzer JS. Clinical considerations for the diagnosis of major depression after moderate to severe TBI. J Head Trauma Rehabil 2010; 25: 99−112.
26. Pagulayan KF, Hoffman JM, Temkin NR, Machamer JE, Dikmen SS. Functional limitations and depression after traumatic brain injury: examination of the temporal relationship. Arch Phys Med Rehabil 2008; 89: 1887−1892.
27. Prigatano GP, Borgaro S, Baker J, Wethe J. Awareness and distress after traumatic brain injury: a relative's perspective. J Head Trauma Rehabil 2005; 20: 359−367.
28. Holm S, Schonberger M, Poulsen I, Caetano C. Patients' and relatives' experience of difficulties following severe traumatic brain injury: the sub-acute stage. Neuropsychol Rehabil 2009; 19: 444−460.
29. Starmark JE, Stalhammar D, Holmgren E, Rosander B. A comparison of the Glasgow Coma Scale and the Reaction Level Scale (RLS85). J Neurosurg 1988; 69: 699−706.
30. Fisk JD, Doble SE. Construction and validation of a fatigue impact scale for daily administration (D-FIS). Qual Life Res 2002; 11: 263−272.
31. Fisk JD, Ritvo PG, Ross L, Haase DA, Marrie TJ, Schlech WF. Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. Clin Infect Dis 1994; 18 Suppl 1: S79−S83.
32. Prigatano GP AK, Rosenstein LD. Administration and scoring manual for the BNI screen for higher cerebral functions. Phoenix: Barrow Neurological Institute; 1995.
33. Hofgren C, Esbjornsson E, Aniansson H, Sunnerhagen KS. Application and validation of the barrow neurological institute screen for higher cerebral functions in a control population and in patient groups commonly seen in neurorehabilitation. J Rehabil Med 2007; 39: 547−553.
34. Prigatano GP AK, Rosenstein LD. BNI Screen [For higher cerebral functions. Manual swedish version.] Stockholm: Pearson Assessment and Information AB; 2008 (in Swedish).
35. Szende Agota WA. Measuring self-reported population health: an international perspective based on EQ-5D. EuroQol Group, editors. New York: Spring MED Publishing; 2004.
36. Teasdale TW, Christensen AL, Willmes K, Deloche G, Braga L, Stachowiak F, et al. Subjective experience in brain-injured patients and their close relatives: a European Brain Injury Questionnaire study. Brain Inj 1997; 11: 543−563.
37. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975; 1: 480−484.
38. Nichol AD, Higgins AM, Gabbe BJ, Murray LJ, Cooper DJ, Cameron PA. Measuring functional and quality of life outcomes following major head injury: common scales and checklists. Injury 2011; 42: 281−287.

J Rehabil Med 2013; 45: 778–784

ORIGINAL REPORT

COGNITIVE ACTIVITY LIMITATIONS ONE YEAR POST-TRAUMA IN PATIENTS ADMITTED TO SUB-ACUTE REHABILITATION AFTER SEVERE TRAUMATIC BRAIN INJURY

Jens Bak Sommer, MSc[1,2,3], Anne Norup, PhD[1], Ingrid Poulsen, PhD[1] and Jesper Mogensen, PhD[3]

From the [1]Research Unit on BRain Injury rehabilitation, Copenhagen (RUBRIC), Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen, University Hospital, Glostrup, [2]Department of Drug Design and Pharmacology and [3]The Unit for Cognitive Neuroscience, Department of Psychology, University of Copenhagen, Denmark

Objective: **To examine cognitive activity limitations and predictors of outcome 1 year post-trauma in patients admitted to sub-acute rehabilitation after severe traumatic brain injury.**

Subjects: **The study included 119 patients with severe traumatic brain injury admitted to centralized sub-acute rehabilitation in the Eastern part of Denmark during a 5-year period from 2005 to 2009.**

Methods: **Level of consciousness was assessed consecutively during rehabilitation and at 1 year post-trauma. Severity of traumatic brain injury was classified according to duration of post-traumatic amnesia. The cognitive subscale of Functional Independence Measure™ (Cog-FIM) was used to assess cognitive activity limitations. Multivariate logistic regression analyses were performed to identify predictors of an independent level of functioning.**

Results: **The majority of patients progressed to a post-confusional level of consciousness during the first year post-trauma. At follow-up 33–58% of patients had achieved functional independence within the cognitive domains on the Cog-FIM. Socio-economic status, duration of acute care and post-traumatic amnesia were significant predictors of outcome.**

Conclusion: **Substantial recovery was documented among patients with severe traumatic brain injury during the first year post-trauma. The results of the current study suggest that absence of consciousness at discharge from acute care should not preclude patients from being referred to specialized sub-acute rehabilitation.**

Key words: traumatic brain injury; TBI; acute brain injury; vegetative state; minimally conscious state; confusional state; consciousness disorders; rehabilitation outcome.

J Rehabil Med 2013; 45: 778–784

Correspondence address: Jens Bak Sommer, Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen, Universitetsparken 2, DK-2100 Copenhagen, Denmark. E-mail: jens.sommer@sund.ku.dk

Accepted June 13, 2013

INTRODUCTION

Advances in neurocritical care have led to a significant reduction in mortality after severe traumatic brain injury (TBI) (1), and despite national differences TBI mortality rates have declined substantially in the Nordic region (2). As a result, an increasing proportion of patients with the most severe injuries now survives TBI and is subsequently in need of specialized treatment and rehabilitation (3). From a Danish perspective, an epidemiological study has shown that the number of patients admitted to hospital for more than 3 months after TBI has increased by 64% from 1994 to 2002 (4).

Some of these patients remain in a state of severely disordered consciousness, such as coma, vegetative state (VS) (5), also known as unresponsive wakefulness syndrome (UWS) (6) and minimally conscious state (MCS) (7), for an indeterminate period of time post-injury.

Treatment and rehabilitation of patients with post-traumatic disorders of consciousness (DOC) have long been regarded with scepticism and nihilism concerning prognosis and outcome, which may be ascribed to the fact that loss of consciousness in these disorders has often been considered irreversible and similar to the end-stage of severe degenerative disorders (8). Furthermore, many patients with DOC have been deemed ineligible for rehabilitation as they have not been able to participate actively in standard rehabilitation interventions, and only a few specialized facilities have existed for this group of patients (9–11).

Despite significant progress in the understanding of pathophysiology and assessment (12, 13), knowledge of DOC among the general medical community still appears to be limited, even among professionals who are most likely to be responsible for the rehabilitation of patients with acquired brain injury. According to a Swedish survey from 2011, encompassing more than 1,000 physicians working within acute or rehabilitation care of patients with brain injury, only approximately half of the responding physicians knew the definition of VS/UWS, and nearly a quarter of respondents thought that patients in VS/UWS should never be admitted to rehabilitation or should be

given lower priority than other patients (14). This is, moreover, complicated by the fact that misdiagnosis of VS/UWS has been found to be common, with studies estimating that evidence of consciousness is missed in approximately 40% of these patients (15).

The exact epidemiology of VS/UWS is not known; however, the prevalence of the condition in hospital cases in Europe is estimated to be approximately 0.5–2 per 100,000 of the population per year (16). VS/UWS is thus a relatively rare condition, and limited knowledge of VS/UWS in the medical community may be ascribed to the fact that few physicians have had direct clinical experience with such patients (17). In addition, treatment of patients is often distributed over a broad range of institutions limiting specialization and accumulation of expertise among healthcare professionals (10, 14).

To improve the assessment and treatment of severe TBI and DOC in Denmark, early sub-acute rehabilitation of these patient groups was centralized to 2 specialized hospital units in the year 2000 (18). Thus, a continuous chain of care from accident site to trauma centre and to centralized specialized rehabilitation has been established for most of these patients in Denmark. Analogous centralized treatment programs for patients with severe TBI have subsequently been implemented or proposed in other Nordic countries (14, 19, 20).

Centralization of sub-acute rehabilitation has allowed for the prospective collection of data regarding demography, progress and outcome of patients with DOC and severe TBI in Denmark (18). The systematic registration of data during early rehabilitation may contribute to better prediction modelling, which may be of value in rehabilitation planning, counselling of relatives, and the identification of targets for intervention trials (3). As data now are available for larger cohorts of patients with DOC and severe TBI, and recent research suggests that further knowledge about the rehabilitation potential and long-term outcome of this patient population is strongly needed (14), the authors decided to undertake the current study.

The purpose of the study was to examine cognitive activity limitations 1 year post-trauma in patients with DOC and severe TBI admitted to sub-acute rehabilitation in the Eastern part of Denmark. Furthermore, demographic and clinical predictors of an independent level of functioning were investigated.

METHODS

Participants

Data were analyzed for patients consecutively admitted to the TBI Unit, Department of Neurorehabilitation, Copenhagen University Hospital, Glostrup, Denmark.

The TBI Unit is a highly specialized sub-acute rehabilitation unit that receives patients with severe TBI early after injury. The unit has an uptake area of approximately 2.5 million inhabitants covering the Eastern part of Denmark as well as the Faroe Islands and Greenland. At referral to the unit, highest priority is given to patients with a Glasgow Coma Scale score (GCS) (21) in the range 3–9 one day after cessation of sedation. Patients with a higher GCS score may also be admitted to the unit provided that severe focal neurological deficits, severe cognitive disorders and/or pronounced agitation are present. The rehabilitation regimen has been described elsewhere (18).

As a standard procedure, demographic and clinical data are prospectively registered for all patients admitted to the TBI Unit. The database of the unit is approved by the Danish Data Protection Agency. For the current study, we considered patients admitted during a 5-year period from 2005 to 2009. Inclusion criteria were: (*i*) TBI as cause of admission; (*ii*) a minimum age of 16 years; and (*iii*) participation in a follow-up assessment 1 year post-trauma. Patients with comorbidities that could interfere with the assessment of TBI-related cognitive disability were excluded, including patients with: (*i*) congenital or previously acquired brain injury; (*ii*) neurodegenerative disorders; and (*iii*) psychiatric disorder or substance abuse affecting daily functioning at time of injury. Individuals with no follow-up data and/or with missing data about comorbid disorders and cognitive disability prior to injury were also excluded.

Measures

Demographic variables. Age, sex and socio-economic status (SES) were registered at admission to the TBI Unit. SES was rated on a 5-level ordinal scale adopted from the Danish Head Trauma Database, a national clinical database for patients with head trauma. Level of SES was classified according to occupational achievement in combination with educational level and number of sub-ordinates in the workplace. In the statistical analyses, the 5-level scale was dichotomized into lower (level 4–5) and higher SES (level 1–3). Persons, who had never had a job or completed formal education, were assigned the lowest level of SES.

Duration of acute care. The duration of acute care was measured as the number of days from trauma to admission to the TBI Unit. During this period patients were primarily admitted to neurosurgical wards and intensive care units.

Post-traumatic amnesia (PTA). The duration of PTA was measured prospectively by neuropsychologists with Galveston Orientation and Amnesia Test (GOAT) (22). GOAT is a 10-item questionnaire that assesses orientation and memory after TBI. A score of ≥ 76 on 2 consecutive ratings marks the resolution of PTA. The duration of PTA was calculated as the number of days from trauma to the day criteria was met on GOAT. A minor proportion of the patients had not cleared PTA at discharge, and in these cases duration of PTA was estimated retrospectively at follow-up.

Level of consciousness (LOC). LOC was assessed prospectively by neuropsychologists from admission to discharge and at follow-up with the Rancho Los Amigos Levels of Cognitive Functioning Scale (RLA) (23). RLA is an ordinal scale comprising the following 8 levels: No response (RLA 1); Generalized response (RLA 2); Localized response (RLA 3); Confused – agitated (RLA 4); Confused – inappropriate (RLA 5); Confused – appropriate (RLA 6); Automatic – appropriate (RLA 7); Purposeful – appropriate (RLA 8). For descriptive purposes, the RLA was collapsed into 5 categories consisting of coma (RLA 1), VS/UWS (RLA 2), MCS (RLA 3), confusional state (RLA 4–6) and post-confusional state (RLA 7–8). These categories describe the stages of recovery typically seen following TBI in a more traditional neurological nomenclature (11, 24). MCS was assessed in accordance with the diagnostic criteria of the Aspen Workgroup (7), and patients fulfilling these criteria were categorized as RLA 3. LOC at admission was based on several neuropsychological assessments performed over the first days of admission and corroborated by behavioral observations from the interdisciplinary rehabilitation team. At follow-up a neuropsychological assessment of LOC was performed as part of an interdisciplinary examination. Family members or other care providers familiar with the patient were invited to participate in these examinations.

Cognitive activity limitations. The Cognition subscale of Functional Independence Measure (FIM™) (25) (Cog-FIM) was used to evaluate limitations in cognitive activities. Cog-FIM includes 5 items that as-

sess functional independence within the domains of comprehension, expression, social interaction, problem-solving and memory. Each item is rated on a 7-point scale from "total assistance" to "complete independence". The Cog-FIM total score ranges from 5 to 35, with higher scores indicating greater independence. In the analyses scores on each item were dichotomized into a dependent (scores 1–5) vs an independent cognitive activity level (scores 6–7). These are the 2 broad levels of functioning recognized by the scale defined by whether help from another person is required for performance of the task in question. The interdisciplinary team of each patient consisting of nurses, physio- and occupational therapists rated patients consecutively with Cog-FIM from admission to discharge and at follow-up. Nurses and therapists were trained in rating Cog-FIM, and the department is certified for using FIM™ by the Uniform Data Set for Medical Rehabilitation (UDSMR). Cog-FIM has been recommended as a core measure of cognitive activity limitations by the TBI Outcomes Workgroup (26).

Data analysis

Descriptive data are presented as 25th, 50th and 75th percentiles, ranges and percentages when appropriate. Kruskal-Wallis tests (H) and Mann-Whitney tests (U) were used to compare differences between subgroups of patients in scores on Cog-FIM and on continuous variables (age, duration of acute care and PTA) when parametric assumptions were not met. Bivariate correlations were calculated with Spearman's rho (r_s). Pearson's χ^2 and Fisher's exact test were used to evaluate differences in categorical variables.

Direct multiple logistic regression was conducted to identify predictors of an independent cognitive activity level within each domain on Cog-FIM at follow-up. Analyses were performed to ensure that the assumption of linearity of the logit was not violated. Multicollinearity was found to be insignificant, and the number of expected frequencies was adequate in all cells. Multivariate outliers in the regression solutions were identified by examining residuals and deviance statistics. Three patients with extreme values were identified, however analyses indicated that they neither had erroneous scores nor exerted an undue influence on regression coefficients, and consequently all of these patients were included in the final models.

A univariate attrition analysis was conducted to investigate systematic bias between patients with and without follow-up as well as between the total group of included and excluded patients.

All statistical tests were 2-sided and considered significant at $p < 0.05$. In case of multiple comparisons the significance level was adjusted with Bonferroni corrections. All analyses were conducted with the statistical software package PASW Statistics for Windows, version 18 (SPSS Inc., Chicago, IL, USA).

RESULTS

Study population

From 2005 to 2009 a total of 207 patients over the age of 16 years were admitted to the unit with a TBI diagnosis, and of these patients 157 (75.8%) participated in a 1 year follow-up examination. Reasons for patients being lost to follow-up were mortality ($n = 17$), refusal to participate ($n = 3$) and migration ($n = 6$). For the remainder of patients ($n = 24$) causes were unknown.

Due to previous brain injury and cognitive disability 35 (22.3%) patients with follow-up data were excluded from the study, and another 3 patients were excluded due to missing data on 1 or more predictor variables. Hence, a total of 119 patients (57.5%) fulfilled the inclusion criteria and were included in the statistical analyses.

Univariate analyses were conducted to investigate whether patients with follow-up differed systematically from patients without follow-up on study variables. Patients without follow-up were found to be significantly older (median 53.6 years) than patients with follow-up data (median 41.2 years, $U = 2703.00$, $p = 0.001$). Moreover, the former group had significantly lower scores on Cog-FIM at discharge from the TBI Unit (median = 7.0) compared with the latter (median = 23.0, $U = 1519.00$, $p < 0.001$). No differences were found concerning gender, SES, proportion of patients in VS/UWS at admission to rehabilitation or duration of acute care and PTA. The same differences were found when the total group of excluded patients was compared with included patients.

In the study group, Cog-FIM total scores at follow-up were significantly correlated with total scores at discharge from the TBI Unit ($r_s = 0.83$, $p < 0.001$) and patient age ($r_s = -0.26$, $p = 0.005$).

Table I provides demographic data and injury-related information for patients included in the study. Patients were primarily male (70.6%) and approximately one-quarter (26.8%) was 25 years old or younger. The vast majority of patients (89.9%) was admitted to the TBI Unit within 1 month post-trauma, and at admission to rehabilitation almost half of patients (48.7%) were still in VS/UWS or MCS (Fig. 1). Based on duration of PTA, 103 patients (86.6%) were classified as having extremely severe TBI (PTA > 4 weeks), whereas the remaining 16 patients (13.4%) had very severe TBI (PTA = 1–4 weeks) (27).

Level of consciousness and cognitive outcome 1 year post-trauma

The median time from trauma to follow-up was 13.1 months. LOC at follow-up is depicted in Fig. 1 for the 117 patients who were assessed with RLA. The vast majority of patients (84.6%) had progressed to a post-confusional state (PCS). Of the remainder, no patients were in VS/UWS, whereas 5 were in MCS (4.3%) and 13 (11.1%) in a confusional state (CS).

Table I. *Demographic and injury data (*n = *119)*

Characteristics	25th/50th/75th percentiles	Range
Age, years	24/39/54	16–78
Acute care stay, days	12/18/22	6–59
Rehabilitation stay, days	74/113/182	25–349
Cog-FIM at admission, total	5/5/6	5–34
RLA at admission	3/4/5	2–8
PTA, days	32/64/160	12–365
Trauma to follow-up, months	13/13/15	11–23
VS/UWS at admission, %	23.5	
Lower SES, %	72.3	
Sex, male, %	70.6	
Cause of injury, %		
Vehicular	72.3	
Fall	20.2	
Other	7.5	

RLA: score on Rancho Los Amigos Levels of Cognitive Functioning Scale; PTA: duration of post-traumatic amnesia; SES: socio-economic status; VS/UWS: vegetative state/unresponsive wakefulness syndrome; Cog-FIM: Cognitive subscale of Functional Independence Measure™.

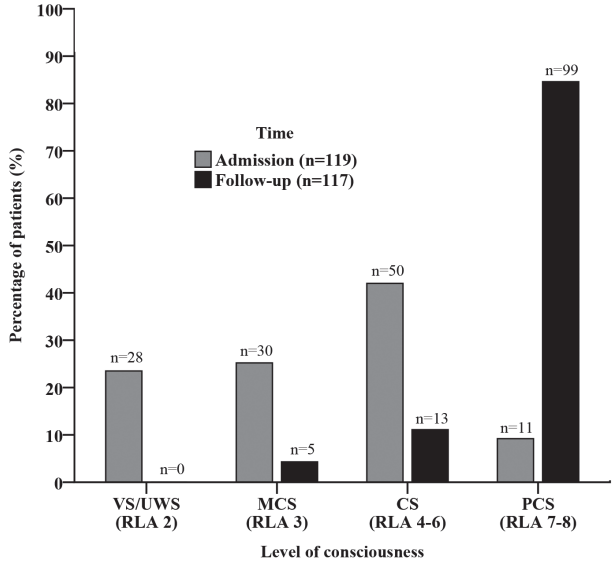


Fig. 1. Level of consciousness at admission to rehabilitation and at follow-up 1 year post-trauma. VS/UWS: vegetative state/unresponsive wakefulness syndrome; MCS: minimally conscious state; CS: confusional state; PCS: post-confusional state.

In the study group, median total scores on Cog-FIM improved from 5 at admission to 27 at follow-up (Fig. 2). Moreover, 6 patients (5%) had achieved the maximum score of 35 indicating complete independence within all of the assessed cognitive domains. A significant association was found between LOC at admission to rehabilitation and total scores on Cog-FIM 1 year post-trauma ($H(3) = 28.80$, $p < 0.001$). *Post-hoc* analyses with Bonferroni correction of the significance level to 0.017 indicated that patients admitted in VS/UWS had significantly lower scores than patients with MCS ($U = 203.50$, $p = 0.001$) or a higher LOC upon admission. However, outcomes for patients admitted in VS/UWS were extremely varied, with Cog-FIM total scores at follow-up ranging from 5 to 33.

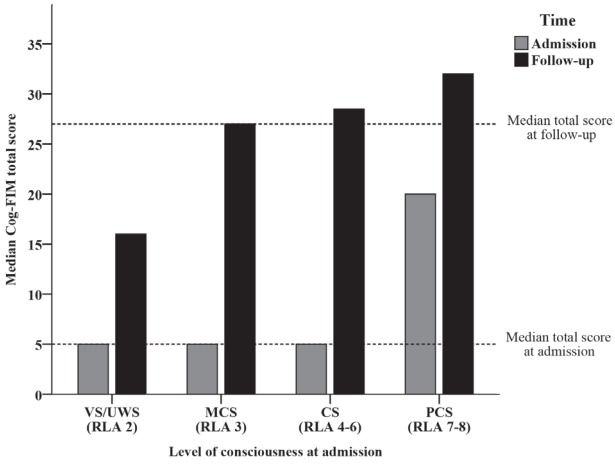


Fig. 2. Cognitive subscale of Functional Independence Measure™ (Cog-FIM) total scores at admission to rehabilitation and at follow-up 1 year post-trauma according to level of consciousness at admission ($n = 119$). VS/UWS: vegetative state/unresponsive wakefulness syndrome; MCS: minimally conscious state; CS: confusional state; PCS: post-confusional state.

Predictors of an independent cognitive activity level

The proportion of patients that achieved an independent cognitive activity level at follow-up varied from 32.8% to 58.0% between the 5 domains on Cog-FIM (Fig. 3).

Omnibus tests indicated that each of the 5 logistic regression models were statistically significant ($p < 0.001$ for all models), and outcome was in total predicted correctly for 76.5–81.5% of patients. Odds ratios (OR) for predictors within each domain on Cog-FIM are shown in Table II.

A longer duration of PTA was a significant negative predictor of an independent cognitive activity level within all domains on Cog-FIM (OR = 0.977–0.988, 95% confidence interval (95% CI) = 0.963–0.996). Lower SES was a significant negative predictor within the domains of problem-solving (OR = 0.287, 95% CI = 0.086–0.953) and memory (OR = 0.292, 95% CI = 0.087–0.982), while a longer duration of acute care was associated with a reduced probability of functional independence with regard to expression (OR = 0.913, 95% CI = 0.845–0.985).

DISCUSSION

A substantial proportion of patients with severe TBI and prolonged DOC was found to recover during the first year post-trauma. At admission, almost half of patients in the study group were in VS/UWS or MCS. However, at follow-up 1 year post-injury no patients were in VS/UWS and only 5 were in MCS. Moreover, 32.8% to 58.0% of the total number

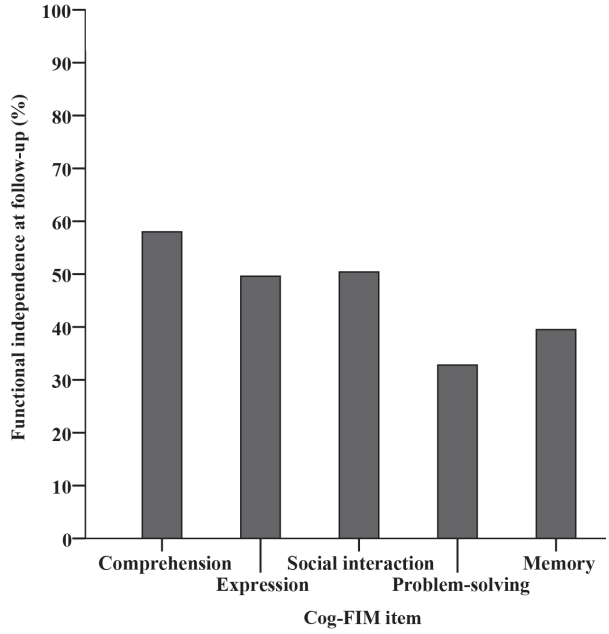


Fig. 3. Percentage of patients with an independent cognitive activity level within each Cognitive subscale of Functional Independence Measure™ (Cog-FIM) domain 1 year post-trauma ($n = 119$).

Table II. *Odds ratios (OR) for an independent cognitive activity level one year post-trauma. Significant odds ratios (OR) for each predictor and domain on Cognitive subscale of Functional Independence Measure™ (Cog-FIM) are depicted below in bold. An OR of less than 1 indicates a reduced probability of functional independence. Confidence intervals for significant predictors are presented in the text*

n=119	Comprehension	Expression	Social interaction	Problem-solving	Memory
Age	0.974	0.966	0.976	0.981	0.997
Sex (male)	0.593	0.499	0.546	0.723	0.392
Lower SES	0.590	0.937	0.607	**0.287***	**0.292***
Acute care	0.968	**0.913***	0.966	0.943	0.970
VS/UWS[a]	0.823	2.395	0.488	0.886	1.023
PTA	**0.982*****	**0.977*****	**0.988****	**0.979****	**0.977****

*$p<0.05$, **$p<0.01$, ***$p<0.001$.
[a]VS/UWS at admission to rehabilitation.
RLA: score on Rancho Los Amigos Levels of Cognitive Functioning Scale; PTA: duration of post-traumatic amnesia; SES: socio-economic status; VS/UWS: vegetative state/unresponsive wakefulness syndrome.

of patients had achieved functional independence within the 5 domains on Cog-FIM. SES, duration of PTA and acute care were significant predictors of cognitive activity limitations 1 year post-trauma with PTA being the only predictor that was significant across all domains.

Cognitive outcome 1 year post-trauma

As emergence from VS/UWS more than 1 year after TBI has been found to be infrequent and associated with severe residual disability (28, 29), a particularly encouraging finding in the current study was that no patients were in VS/UWS at follow-up. However, patients admitted in VS/UWS did have significantly lower scores on Cog-FIM at follow-up compared with patients in MCS or with a higher LOC upon admission to rehabilitation. Nevertheless, during the first year post-trauma median scores improved from 5 to 16 among patients admitted in VS/UWS, and outcomes at follow-up were extremely varied with scores on Cog-FIM ranging from total assistance to modified and complete independence.

Hence, the results of the present study indicate that VS/UWS at admission to rehabilitation is not uniformly associated with a poor cognitive outcome, and VS/UWS was, moreover, not a significant predictor of cognitive activity limitations 1 year post-trauma in any of the multivariate logistic regression models. In agreement with previous research (11, 30), the current study accordingly suggests that absence of consciousness at discharge from acute care should not preclude patients from being referred to specialized sub-acute rehabilitation. Furthermore, behavioral evidence of consciousness may be missed in the acute care setting due to a short duration of stay, sedation and limited access to specialized assessment methods (31), and referral to a specialized rehabilitation facility may thus be pivotal to a proper diagnosis and patient management.

At follow-up 5 patients were still in MCS in the study cohort; however, compared with recovery from VS/UWS recovery from MCS 1 year or longer after brain injury has been found to be more frequent. Luauté et al. (29) reported that approximately one-third of patients remaining in MCS 1 year after traumatic or non-traumatic brain injury exhibited functional improvement during the following 4 years. In this regard studies have shown some inconsistencies regarding the prognostic value of duration of MCS. Lammi et al. (32) did not find any significant associations between duration of MCS and most measures of functional and psychosocial outcome 2–5 years after TBI. However, as noted by the authors a small sample size may have attenuated statistical relationships, and in a larger cohort of patients Katz et al. (11) reported that duration of MCS and age were significant predictors of level of disability 1 year post-trauma. Interestingly, a relationship between duration of VS/UWS and the probability of emerging from MCS after traumatic and non-traumatic brain injury was found in the latter study. Out of a total of 23 patients with a follow-up period of at least 1 year, 5 failed to emerge from MCS, and all of these patients had been in VS/UWS for more than 8 weeks. Unfortunately, it was not possible to determine the duration of VS/UWS for the 5 patients in our sample who remained in MCS at follow-up. However, it seems reasonable to expect that at least some of these patients will improve over the months and years to come.

Previous research has suggested that Cog-FIM may be of limited value in the measurement of long-term outcome of patients with TBI due to a ceiling effect (33). In contrast, only 5% of patients had obtained the maximum score of 35 on Cog-FIM 1 year post-trauma in our study, which may be explained by the fact that only patients with the most severe TBI were included. In a similar manner, Hammond et al. (34) found that merely 16% of patients with moderate to severe TBI were at ceiling on Cog-FIM 1 year post-trauma. Altogether, this suggests that Cog-FIM may have utility as a measure of long-term cognitive activity limitations after more severe injuries, whereas ceiling effects may be a concern in studies primarily including patients with mild to moderate TBI.

The median Cog-FIM total score at follow-up in the present study is comparable to the results of a recent investigation of the longitudinal outcome of patients with DOC (30). In that study a median score of 25 was reported 1 year after TBI, and, interestingly, significant change in Cog-FIM total scores was seen from 1 to 5 years post-injury. During the same time interval Hammond et al. (34) also noted that scores only remained stable in 61% of patients with TBI, which was explained by improvement as well as decline in the functional level of patients. Thus considerable change is to be expected beyond 1 year post-trauma, and consequently the follow-up period in the present study may be too short to document long-term cognitive activity limitations.

An important question is to what extent the observed recovery may be ascribed to the administered rehabilitation intervention. Previous research indicates that the centralization of sub-acute rehabilitation of patients with severe TBI in Denmark has resulted in better rehabilitation outcomes (35). When data from an earlier cohort of patients admitted to the TBI Unit were compared with historical data from patients treated before centralization, significantly better outcomes were found at discharge in the former group for equal injury severity and length of stay. In addition, a recent prospective study from Norway indicates that an early comprehensive rehabilitation intervention does improve functional outcomes 1 year after severe TBI compared with a delayed and broken chain of treatment (19). Collectively, this suggests that centralized sub-acute rehabilitation may contribute to better outcomes after severe TBI. Nevertheless, the current study cannot make any conclusive claims concerning the effects of rehabilitation on recovery, as such analyses would require a different research design and a comparison with patients treated in alternative settings.

Predictors of cognitive activity limitations

A longer duration of PTA was consistently found to be associated with a reduced probability of an independent cognitive activity level, and across Cog-FIM domains odds of functional independence were reduced by approximately 1–2% with each additional day of PTA. This is not surprising considering that PTA has also been found to be a predictor of Cog-FIM total scores at discharge from acute care (36) and inpatient rehabilitation (37) after mild to severe TBI. Duration of PTA is positively correlated with the volume of grey and white matter lesions on MRI, and may thus reflect the extent of organic brain damage after TBI (38).

SES and duration of acute care were significant predictors of outcome within specific cognitive domains. Higher SES was associated with increased odds of functional independence concerning problem-solving, and memory. SES may be considered an indicator of pre-morbid cognitive reserve (39) and was tentatively included as a measure of such. However, a crude dichotomous variable was used in the present study, and as confidence intervals for the calculated odds ratios were very large, results are to be interpreted with caution.

Study limitations

Important limitations in the current study were the risk of systematic bias caused by patients lost to follow-up and the use of the RLA and qualitative neuropsychological assessments in the classification of LOC. As shown by Schnakers et al. (15) qualitative behavioral assessments may increase the likelihood of misdiagnosis in patients with DOC relative to when a standardized assessment tool such as the Coma Recovery Scale-Revised is applied. The total rate of diagnostic error in the current study is unknown. However, none of the included patients were assessed to be in VS/UWS at follow-up, and hence it is unlikely that signs of consciousness were missed in patients at this time-point. Moreover, as specialized assessment tools for VS/UWS and MCS are currently not used on a wide scale in acute care facilities (14), the main message of this and previous studies to professionals working within acute care is the considerable rehabilitation potential of patients with DOC (11, 30).

Attrition has been found to be substantial in previous longitudinal studies of TBI (40), and systematic bias may occur when a variable associated with attrition is also associated with the outcome of interest. In the current study, univariate analyses indicated that patients lost to follow-up were significantly older and had lower Cog-FIM total scores at discharge from the TBI Unit. The same differences applied, when the total group of excluded patients was compared with patients included in the study group. Since age was negatively correlated with Cog-FIM total scores at follow-up, and patients lost to follow-up had lower scores on Cog-FIM at discharge, patients with poor outcomes appeared to be missing systematically from the study. Accordingly, outcomes in the present study may have been positively biased with consequences for the external validity and generalizability of results.

Future research

The current study was mainly descriptive and exploratory rather than hypothesis testing and thus further investigation of the effects of sub-acute rehabilitation and prognostic factors in patients with severe TBI is warranted. Future studies should assess patients consecutively in the years post-trauma, since ongoing recovery is to be expected, and an effort should be made concerning the follow-up of patients of older age and with greater functional dependence at discharge from rehabilitation, as these patients may be particularly vulnerable to attrition. Moreover, the association between pre-morbid cognitive reserve and cognitive activity limitations post-trauma may be investigated using more specific and sensitive measures of cognitive reserve.

Conclusion

Overall, substantial recovery was documented 1 year post-trauma in patients with DOC and severe TBI admitted to sub-acute rehabilitation in the Eastern part of Denmark. SES, duration of acute care and PTA were significant predictors of functional independence within important cognitive domains 1 year after TBI. In accordance with previous research, the current study suggests that absence of consciousness at discharge from acute care should not preclude patients from being referred to sub-acute rehabilitation.

REFERENCES

1. Stein SC, Georgoff P, Meghan S, Mizra K, Sonnad SS. 150 years of treating severe traumatic brain injury: a systematic review of progress in mortality. J Neurotrauma 2010; 27: 1343–1353.
2. Sundstrøm T, Sollid S, Wentzel-Larsen T, Wester K. Head injury mortality in the Nordic countries. J Neurotrauma 2007; 24:

147–153.
3. Borg J, Röe C, Nordenbo A, Andelic N, de Boussard C, af Geijerstam J-L. Trends and challenges in the early rehabilitation of patients with traumatic brain injury: a Scandinavian perspective. Am J Phys Med Rehabil 2011; 90: 65–73.
4. Engberg AW, Teasdale TW. [Epidemiology and treatment of head injuries in Denmark 1994–2002, illustrated with hospital statistics.] Ugeskr Laeger 2007; 169: 199–203 (in Danish).
5. Jennett B, Plum F. Persistent vegetative state after brain damage. A syndrome in search of a name. Lancet 1972; 299: 734–737.
6. Laureys S, Celesia GG, Cohadon F, Lavrijsen J, León-Carrión J, Sannita WG, et al. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. BMC Med 2010; 8: 68.
7. Giacino JT, Ashwal S, Childs N, Cranford R, Jennett B, Katz DI, et al. The minimally conscious state: definition and diagnostic criteria. Neurology 2002; 58: 349–353.
8. Fins JJ. The ethics of measuring and modulating consciousness: the imperative of minding time. Prog Brain Res 2009; 177: 371–382.
9. Gray DS. Slow-to-recover severe traumatic brain injury: a review of outcomes and rehabilitation effectiveness. Brain Inj 2000; 14: 1003–1014.
10. Berube J, Fins J, Giacino J, Katz D, Langlois J, Whyte J, et al. The Mohonk Report. A report to Congress. Disorders of consciousness: assessment, treatment and research needs. New York: Mohonk; 2006.
11. Katz DI, Polyak M, Coughlan D, Nichols M, Roche A. Natural history of recovery from brain injury after prolonged disorders of consciousness: outcome of patients admitted to inpatient rehabilitation with 1 to 4 year follow-up. Prog Brain Res 2009; 177: 73–88.
12. Bruno M-A, Vanhaudenhuyse A, Thibaut A, Moonen G, Laureys S. From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: recent advances in our understanding of disorders of consciousness. J Neurol 2011; 258: 1373–1384.
13. Gosseries O, Bruno M-A, Chatelle C, Vanhaudenhuyse A, Schnakers C, Soddu A, et al. Disorders of consciousness: what's in a name? NeuroRehabilitation 2011; 28: 3–14.
14. Godbolt AK, Tengvar C, Johansson B, Stenson S, Borg J. Opportunity for inpatient brain injury rehabilitation for persons in a vegetative state: Survey of Swedish physicians. Am J Phys Med Rehabil 2011; 90: 482–489.
15. Schnakers C, Vanhaudenhuyse A, Giacino J, Ventura M, Boly M, Majerus S, et al. Diagnostic accuracy of the vegetative and minimally conscious state: Clinical consensus versus standardized neurobehavioral assessment. BMC Neurol 2009; 9: 35.
16. von Wild K, Gerstenbrand F, Dolce G, Binder H, Vos PE, Saltuari L, et al. Guidelines for quality management of apallic syndrome/vegetative state. Eur J Trauma Emerg Surg 2007; 3: 268–292.
17. Jennett B. Thirty years of the vegetative state: clinical, ethical and legal problems. Prog Brain Res 2005; 150: 537–543.
18. Engberg AW. A Danish national strategy for treatment and rehabilitation after acquired brain injury. J Head Trauma Rehabil 2007; 22: 221–228.
19. Andelic N, Bautz-Holter E, Ronning P, Olafsen K, Sigurdardottir S, Schanke AK, et al. Does an early onset and continuous chain of rehabilitation improve the long-term functional outcome of patients with severe traumatic brain injury? J Neurotrauma 2012; 29: 66–74.
20. Tengvar C, Krakau K, Molander C, Borg J. [Time for better organization of brain injury rehabilitation!] Lakartidningen 2006; 103: 3685–3686 (in Swedish).
21. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 304: 81–82.
22. Levin HS, O'Donnell VM, Grossmann RG. The Galveston Orientation and Amnesia Test. A practical scale to assess cognition after head injury. J Nerv Ment Dis 1979; 167: 675–684.
23. Hagen C, Malkmus D, Durham P. Levels of cognitive functioning. Downey, CA: Rancho Los Amigos Hospital; 1972.
24. Povlishock JT, Katz DI. Update of neuropathology and neurological recovery after traumatic brain injury. J Head Trauma Rehabil 2005; 20: 76–94.
25. Granger CV, Hamilton BB, Keith RA, Zielezny M, Sherwin FS. Advances in functional assessment for medical rehabilitation. Top Geriatr Rehabil 1986; 1: 59–74.
26. Wilde EA, Whiteneck GG, Bogner J, Bushnik T, Cifu DX, Dikmen S, et al. Recommendations for the use of common outcome measures in traumatic brain injury research. Arch Phys Med Rehabil 2010; 91: 1650–1660.
27. Jennett B, Teasdale G. Management of head injuries. Philadelphia, PA: Davis; 1981.
28. Estraneo A, Moretta P, Loreto V, Lanzillo B, Santoro L, Trojano L. Late recovery after traumatic, anoxic or hemorrhagic long-lasting vegetative state. Neurology 2010; 75: 239–245.
29. Luauté J, Maucort-Boulch D, Tell L, Quelard F, Sarraf T, Iwaz J, et al. Long-term outcomes of chronic minimally conscious and vegetative states. Neurology 2010; 75: 246–252.
30. Nakase-Richardson R, Whyte J, Giacino JT, Pavawalla S, Barnett SD, Yablon SA, et al. Longitudinal outcome of patients with disordered consciousness in the NIDRR TBI Model Systems Programs. J Neurotrauma 2012; 29: 59–65.
31. Majerus S, Gill-Thwaites H, Andrews K, Laureys S. Behavioral evaluation of consciousness in severe brain injury. Prog Brain Res 2005; 150: 397–413.
32. Lammi MH, Smith VH, Tate RL, Taylor CM. The minimally conscious state and recovery potential: A follow-up study 2 to 5 years after traumatic brain injury. Arch Phys Med Rehabil 2005; 86: 746–754.
33. Hall KM, Mann N, High WM Jr, Wright J, Kreutzer JS, Wood D. Functional measures after traumatic brain injury: ceiling effects of FIM, FIM+FAM, DRS, and CIQ. J Head Trauma Rehabil 1996; 11: 27–39.
34. Hammond FM, Hart T, Bushnik T, Corrigan JD, Sasser H. Change and predictors of change in communication, cognition and social function between 1 and 5 years after traumatic brain injury. J Head Trauma Rehabil 2004; 19: 314–328.
35. Engberg A, Liebach A, Nordenbo A. Centralized rehabilitation after severe traumatic brain injury – a population-based study. Acta Neurol Scand 2006; 113: 178–184.
36. de Guise E, LeBlanc J, Feyz M, Lamoureux J. Prediction of the level of cognitive functional independence in acute care following traumatic brain injury. Brain Inj 2005; 19: 1087–1093.
37. Kosch Y, Browne S, King C, Fitzgerald J, Cameron I. Post-traumatic amnesia and its relationship to the functional outcome of people with severe traumatic brain injury. Brain Inj 2010; 24: 479–485.
38. Schönberger M, Ponsford J, Reutens D, Beare R, O'Sullivan R. The relationship between age, injury severity and MRI findings after traumatic brain injury. J Neurotrauma 2009; 26: 2157–2167.
39. Stern Y. Cognitive reserve. Neuropsychologia 2009; 47: 2015–2028.
40. Corrigan JD, Harrison-Felix C, Bogner J, Dijkers M, Terrill MS, Whiteneck G. Systematic bias in traumatic brain injury outcome studies because of loss to follow-up. Arch Phys Med Rehabil 2003; 84: 153–160.

J Rehabil Med 2013; 45: 785–791

ORIGINAL REPORT

HEALTH-RELATED QUALITY OF LIFE 12 MONTHS AFTER SEVERE TRAUMATIC BRAIN INJURY: A PROSPECTIVE NATIONWIDE COHORT STUDY

Helene L. Soberg, PhD[1], Cecilie Røe, MD, PhD[1,2], Audny Anke, MD, PhD[3,4], Juan Carlos Arango-Lasprilla, PhD[5],Toril Skandsen, MD, PhD[6,7], Unni Sveen, PhD[1,8], Nicole von Steinbüchel, PhD[9] and Nada Andelic, MD, PhD[1]

From the [1]Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval, [2]Faculty of Medicine, University of Oslo, Oslo, [3]Department of Rehabilitation, University Hospital of North Norway, [4]Faculty of Health Sciences, Institute of Clinical Medicine, University of Tromso, Tromso, Norway, [5]IKERBASQUE, Basque Foundation for Science, University of Deusto Bilbao, Bilbao, Spain, [6]Department of Neuroscience, Faculty of Medicine, Norwegian University of Science and Technology (NTNU), [7]Department of Physical Medicine and Rehabilitation, St Olavs Hospital, Trondheim University Hospital, Trondheim, [8]Oslo and Akershus University College of Applied Sciences, Oslo, Norway and [9]Department of Medical Psychology and Medical Sociology, Georg-August-University, Goettingen, Germany

Objective: **To assess health-related quality of life in individuals with severe traumatic brain injury at 12 months post-injury, applying the Quality of Life after Brain Injury (QOLIBRI) instrument, and to study the relationship between injury-related factors, post-injury functioning and health-related quality of life.**

Design/subjects: **The study is part of a prospective, Norwegian multicentre study of adults (≥16 years old) with severe traumatic brain injury, as defined by a Glasgow Coma Scale score of 3–8 during the first 24 h post-injury. A total of 126 patients were included.**

Methods: **Socio-demographic data and injury severity variables were collected. Functioning at 3 and 12 months was assessed with the Glasgow Outcome Scale Extended (GOSE), the Functional Independence Measure (FIM), the Rivermead Post-concussion Questionnaire (RPQ), and the Hospital Anxiety and Depression Scale (HADS). Hierarchical regression analysis was applied.**

Results: **Mean QOLIBRI score was 68.5 (standard deviation = 18.8). Predictors of the QOLIBRI in the final regression model were: employment status ($p = 0.05$), GOSE ($p = 0.05$), RPQ ($p < 0.001$) and HADS ($p < 0.001$). The adjusted R^2 showed that the model explained 64.0% of the variance in the QOLIBRI score.**

Conclusion: **Symptom pressure and global functioning in the sub-acute phase of traumatic brain injury and psychological distress in the post-acute phase are important for health-related quality of life at 12 months post-injury. These domains should be the focus in rehabilitation aiming to improve health-related quality of life in patients with severe traumatic brain injury.**

Key words: traumatic brain injury; quality of life; depression; rehabilitation; outcome assessment.

J Rehabil Med 2013; 45: 785–791

Correspondence address: Helene Soberg, Department of Physical Medicine and Rehabilitation, Ulleval University Hospital, NO-0407 Oslo, Norway. E-mail: h.l.soberg@medisin.uio.no, helene.soberg@ulleval.no

Accepted March 12, 2013

INTRODUCTION

Traumatic brain injury (TBI) is a leading cause of death and disability around the world (1). Approximately 10 million people experience TBI every year. TBI is the most common cause of disability in people under 40 years of age. Those who survive TBI often face lifelong challenges and reduced health-related quality of life (HRQL) (2).

Individuals who have sustained a TBI often experience cognitive deficits (2), physical problems (3) and emotional issues (4). The cognitive changes include deficits in executive functioning (5), attention and information processing (6), memory and learning (7) and communication (8). Physical sequelae may include spasticity, mobility problems and chronic pain (9, 10). In addition, patients report long-term emotional problems, such as anxiety and depression (4). Many survivors find themselves unable to return to their pre-injury lives, causing feelings of loss of "self" (11) and reduced quality of life (12).

HRQL is considered an important outcome when describing problems in health and functioning in individuals with severe TBI (13, 14). The concept comprises a person's sense of well-being and satisfaction with life in terms of physical, psychological and social functioning; perceptions of self-efficacy; independence; social support; and self-concept (13, 15). In rehabilitation, the restoration of HRQL represents a complex challenge, both for individuals with TBI and for rehabilitation professionals.

Reduced HRQL has been identified in individuals with TBI compared with healthy controls or reference populations (12, 15, 16). Several factors associated with poorer HRQL in TBI populations have been reported, such as racial/ethnic minority status (17), female gender (18) or TBI symptomatology (12, 19). The literature has shown diverging results concerning the relationship between injury severity and HRQL. Some studies have reported lower HRQL for individuals with more severe TBI; other studies have reported lower HRQL for individuals

with mild TBI; in other studies, no difference with respect to injury severity was found (3, 12, 15).

The assessment of HRQL after TBI is performed primarily by global measures of well-being and generic measures of health and functioning, such as the Medical Outcome Study's Short Form-36 (SF-36) and EuroQol-5D (20). However, generic measures may not capture the particular problems of TBI, and the need for condition-specific HRQL instruments in TBI is emphasized (13, 21). Recently, the Quality of Life after Brain Injury (QOLIBRI), a condition-specific instrument for measuring HRQL after TBI, was developed in an international collaborative process (22–24). The QOLIBRI captures the individuals' well-being and satisfaction with their functioning and self, and provides a more precise measure of the individual's experience of living with a TBI than generic measures. The development process of QOLIBRI has been thorough, and it has been validated in 2,000 people after TBI of different severities (23, 24). To our knowledge, the QOLIBRI has not yet been applied to a population consisting of individuals with severe TBI 1 year after injury. The aim of this study was to assess HRQL in individuals with severe TBI at 12 months post-injury by applying the QOLIBRI. We also aimed to study the relationship between injury-related factors, post-injury functioning and symptoms at 3 and 12 months, and HRQL at 12 months. Based on previous research, we hypothesized that symptom pressure would be negatively associated with HRQL, but that there would not be a distinct association between TBI severity and HRQL over time.

METHODS

Study design

The present study is part of a larger prospective, population-based Norwegian multicentre study of adults with severe TBI who were admitted to neurosurgical departments between 2009 and 2011. Patients were included from the trauma centres in the 4 health regions in Norway: University Hospital of North Norway, representing the northern region; St Olavs Hospital, representing the central region; Haukeland University Hospital, representing the western region; and Oslo University Hospital, representing the southeastern region of Norway.

Inclusion criteria and procedure

The enrolment of patients and the collection of data in the acute phase were performed separately at the 4 university hospitals. The electronic patient register was searched weekly to identify all patients who had been admitted to the trauma referral centres for acute severe TBI.

Inclusion criteria stated that patients must be adults (age 16 years or older) and admitted within 72 h post-injury. The participants were required to meet the definition of severe TBI by displaying an unsedated Glasgow Coma Scale (GCS) score of 3–8 during the first 24 h. Exclusion criteria were: chronic subdural haematomas; pre-injury cognitive disability interfering with the assessments; severe psychiatric diseases; and drug abuse.

Participants

Between 2009 and 2011, 278 patients meeting the inclusion criteria were admitted to the 4 regional trauma hospitals. Of this initial cohort, 80 patients (28.8%) died during their stay in intensive care, and 20 patients (7%) died before the 12-month follow-up. For the present study, 162 patients were available for the 12-month follow-up, and QOLIBRI data were collected for 126 patients (77.8%). Data at 3 and 12 months were collected when the patients were admitted to the rehabilitation departments, or by telephone interview if they were discharged home. Because of time restrictions, we did not collect QOLIBRI data when we interviewed patients by telephone. The patient flow is detailed in Fig. 1. Seventy-eight percent of the 126 participants were men, and the mean age was 38.8 years (SD 17.8). There were no statistical differences in demographics and injury severity characteristics between the QOLIBRI responders and the other surviving participants who were non-responders on the QOLIBRI at 12 months. Descriptive statistics for the participants are shown in Table I.

Data collection

During the acute phase, data were drawn from medical records from the patients' stay in the neurointensive care units/neurosurgical departments. Data collected included demographic information, cause of injury (transport accidents, falls, assaults, others/sport injuries), GCS score, Abbreviated Injury Scale (AIS) score of the TBI (AIS head), Injury Severity Score (ISS), length of post-traumatic amnesia (PTA), and Rotterdam CT score.

Demographic variables collected included sex, age, and marital status, which was categorized into married or living with a partner; single, divorced or cohabiting. Level of education was dichotomized

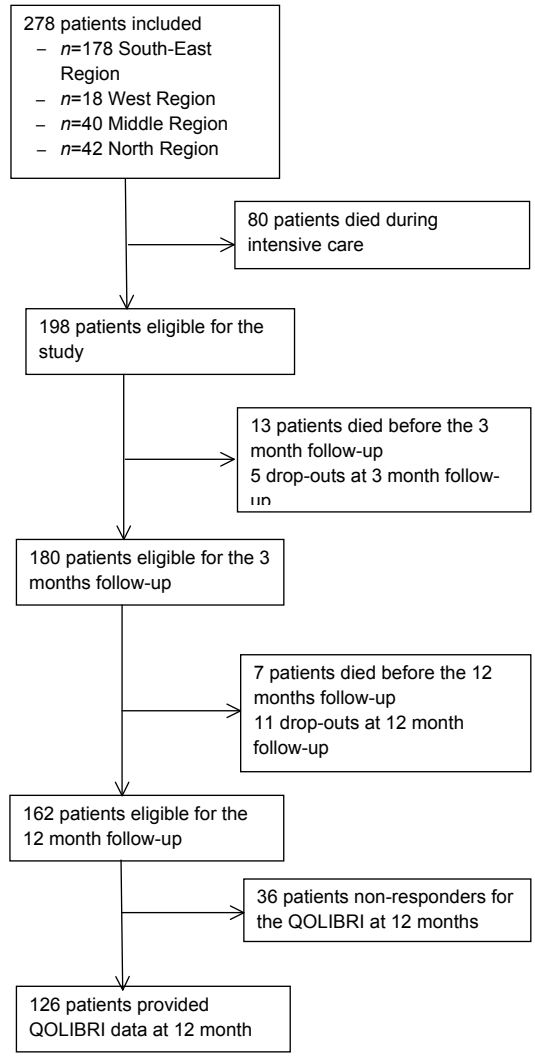


Fig. 1. Patient inclusion. QOLIBRI: Quality of Life after Brain Injury.

Table I. *Demographics at the time of injury of the participants (*n=*126)*

Demographic information	
Age, years, mean (SD)	38.9 (17.8)
Gender, men, *n* (%)	98 (77.8)
Marital status, *n* (%)	
Married/living with a partner	56 (44.4)
Single/divorced/cohabitating	69 (54.8)
Unknown	1 (0.8)
Education, *n* (%)	
Low	82 (65.1)
High	44 (34.9)
Pre-injury employment status, *n* (%)	
Employed/student	90 (71.5)
Sick-leave/vocational or medical rehabilitation/social security support/disability pension	16 (12.8)
Unemployed	7 (5.6)
Retired/homemaker	12 (9.5)
Unknown	1 (0.8)

SD: standard deviation.

as low or high: fewer than 13 years of education was considered low, and a university education was considered high. Pre-injury employment status was categorized into the following 4 categories: being employed or a student; receiving sick leave, vocational or medical rehabilitation, social security support or a disability pension; being unemployed; and being retired or a homemaker. The employment variable was further dichotomized as being employed or a student vs the other 3 categories. When possible and highly probable, missing data for education were imputed based on type of work. For example, a participant whose occupation was listed as "fisherman" was categorized as having a low education. Comorbidity was coded as: having no comorbidity, having a TBI prior to the present injury, or having another disease at time of injury (heart condition, neurological disorder, multiple comorbidities).

The GCS was used for estimating TBI severity (25). The lowest GCS score within the first 24 h post-injury, or at the site of injury in cases of pre-hospital intubation, was registered. Other injury severity scores were provided by the regional trauma registries at the hospitals. In the AIS scoring system, injury severity is graded as 1 (minor), 2 (moderate), 3 (serious), 4 (severe), 5 (critical) or 6 (maximum; lethal injury with no known cure) (26). For each participant, the score of their most severe brain injury, AIS-head, was registered.

The ISS is the sum of the 3 highest squared AIS scores in 3 different body regions (27). A score above 15 is considered a severe injury.

The Rotterdam CT score is a CT classification with a range from 1 (least severe) to 6 (most severe). This score describes the status of basal cisterns, midline shift, epidural mass lesion and intraventricular blood or traumatic subarachnoid haemorrhage (SAH). The score predicts mortality at 6 months post-injury (28). The Rotterdam CT scoring was performed by neuroradiologist in 3 of the 4 hospital regions, and by a neurosurgeon in the remaining region. Scoring was based upon CTs from the acute hospital stay, and the worst score registered was used for analysis.

The Functional Independence Measure (FIM) assesses activities of daily living (ADLs). It has 18 items: self-care, sphincter control, mobility, communication, cognition and social adjustment (29). It consists of a summary score and 2 sub-scales, the FIM Motor (FIM-M) and FIM Cognitive (FIM-COG). FIM-M ranges from 13 to 91 points, and FIM-COG ranges from 5 to 35 points. Total FIM scores were dichotomized at the lowest quartile for the regression analysis. The FIM-M score was dichotomized as low/high at 90 points, but otherwise a FIM-M score ≤77 is set as a cut-off for being limited in activities; assistance from another person is needed. The FIM-COG score was also dichotomized as low or high; at 30 points, which also is the cut-off for being limited in ADLs for this subscale; assistance from another person is needed. The FIM was scored at 12 months.

The Glasgow Outcome Scale Extended (GOSE) (30) is an outcome scale that assesses global functioning by a structured interview in which the patients are divided into the following categories: 1 (dead), 2 (vegetative state), 3 (lower severe disability and complete dependence on others), 4 (upper severe disability and some dependence on others), 5 (lower moderate disability and unable to work or only able to work at a lower level of performance), 6 (upper moderate disability and able to return to previous work with some adjustments), 7 (lower good recovery with minor physical or mental deficits), and 8 (upper good recovery). The GOSE scores were categorized as Severe Disability (GOSE 3–4), Moderate Disability (GOSE 5–6), and Good Recovery (GOSE 7–8). The GOSE was administered at 3 and 12 months post-injury.

The Rivermead Post-concussion Questionnaire (RPQ) is a self-report questionnaire originally designed to measure severity of post-concussion symptoms following mild TBI (31). It has 16 items on the following 3 subscales: somatic (headache, dizziness, nausea, noise sensitivity, sleep disturbance, fatigue, blurred vision, light sensitivity, double vision), emotional (irritability, depression, frustration, restlessness) and cognitive (memory, concentration, speed of thought). The RPQ has shown satisfactory psychometric properties. It is scored with a 5-point scale, ranging from 0 (no problems) to 4 (severe problems), and the sum score range is 0 to 64, with higher scores indicating more problems. The RPQ scores are the sum of symptoms scores, excluding the ratings of one because this score signifies a level that is the same as pre-injury.

The Hospital Anxiety and Depression Scale (HADS), a 14-item measure that has been validated for persons with TBI, was administered at 12 months post-injury (32, 33). The items are measured on a scale from 0 (not at all) to 3 (yes definitely), and the scores range is from 0 to 42, with higher scores indicating more problems. Scores above 8 points on each subscale are considered indicative of clinically significant depression and anxiety (32). The total score, a combination of the depression and anxiety subscale, was analysed in the current study as an indicator of psychological distress. Scores between 15 and 18 were considered possible cases, whereas scores of 19 or above were considered indicative of clinically significant psychological distress requiring treatment (32).

The QOLIBRI was the main outcome measure in the present study. It is a self-report measure of HRQL after a TBI, which has 37 items (23, 24). The first part taps on the responders' satisfaction with their HRQL in 4 domains (subscales) comprising cognition, self, daily life and autonomy, and social relationships. The second part relates to how bothered the responders rate themselves after TBI in 2 domains (subscales) concerning emotions and physical problems. Each item is scored on a 5-point scale, from 1 (not-at-all satisfied) to 5 (very satisfied), with reverse scoring on the bothered subscales (21, 23). The QOLIBRI was scored according to an algorithm published by von Steinbüchel et al. (23). Missing item scores on each subscale were imputed by the scale mean if less than one-third of the responses were missing. Raw scores were transformed into a score range of 0 (lowest) to 100 (highest) (22). Individual subscale scores and a total score were calculated. The QOLIBRI has shown satisfactory psychometric properties (21, 23). The internal consistency of the subscales and total score in the present study were measured with Cronbach's α: cognition ($\alpha = 0.92$), self ($\alpha = 0.92$), daily life and autonomy ($\alpha = 0.90$), social relationships ($\alpha = 0.84$), emotions ($\alpha = 0.89$), physical problems ($\alpha = 0.78$) and total score ($\alpha = 0.90$). The QOLIBRI was administered at 12 months. The QOLIBRI was most often not administered to patients who had a GOSE of 3 at 3 months. However, for 7 patients with a GOSE of 3, QOLIBRI was completed by family or a personal assistant (22).

Data analysis and statistics

Descriptive data are displayed as the mean, SD and range, or as the median and interquartile range (IQR). Cross-tabulations with χ^2-tests were performed for nominal data. Correlations were analysed with Spearman's ρ or Pearson's *r*. *t*-tests or analysis of variance (ANOVAs) were used to compare groups. Non-parametric statistical analyses were used for data that were not normally distributed.

Table II. *Injury-related data of the participants*

Injury characteristics	
GCS ($n=126$), mean (SD)	5.9 (1.8)
AIS-head ($n=124$), mean (SD)	4.2 (0.9)
ISS ($n=124$), mean (SD)	27.2 (11.8)
Length of PTA, ($n=124$), *n* (%)	
<1 weeks	29 (23.4)
1–2 weeks	17 (13.7)
2–3weeks	12 (9.7)
3–4 weeks	12 (9.7)
>4 weeks	54 (43.5)
Rotterdam score ($n=124$), mean (SD)	3.5 (0.9)
Injury mechanism ($n=126$), *n* (%)	
Traffic	61 (48.4)
Fall	49 (38.8)
Violence	7 (5.6)
Other	9 (7.1)
Injury type ($n=126$) *n* (%)	
Isolated TBI	55 (43.7)
TBI with multiple trauma	71 (56.4)

GCS: Glasgow Coma Scale; ISS: Injury Severity Score; PTA: post-traumatic amnesia; SD: standard deviation; TBI: traumatic brain injury; AIS: Abbreviated Injury Scale.

Hierarchical multiple linear regression analysis was performed to assess factors that were associated with the QOLIBRI outcome at 12 months post-injury. Variables with p-values ≤0.1 from the univariate regression analyses were included in the multivariate model. The model comprised 99 people, and using 8 people per predictor variable, the model allowed 12 variables. In the univariate linear regression analyses, sex, age and education did not fulfil the criteria, but these factors and work status at time of injury were included in the regression analyses to adjust for heterogeneity among socio-demographic data. Several of the associations between QOLIBRI outcome and injury severity, such as ISS, GCS, Rotterdam score, PTA and comorbidity, were not sufficiently strong to be applied in this study and, as such, these statistical tests will not be described further here.

The first step of the hierarchal regression analysis examined the following demographic variables: age, sex (male/female), education (low vs high), pre-injury employment status (employed/student vs others). The second step examined injury severity (AIS-head). The third and fourth steps examined post-injury functioning at 3 months (GOSE and RPQ) and 12 months (GOSE, dichotomized FIM-M and FIM-COG, RPQ and HADS), respectively. The RPQ and HADS were log10 transformed to improve the distribution. The results are presented as R^2, R^2 change, F change and standardized beta values.

p-values ≤0.05 were considered statistically significant. All variables in the analyses had ≤10% missing cases. Analyses were performed using IBM SPSS Statistics 19.

Table III. *Quality of Life after Brain Injury (QOLIBRI) scores at 12 months post-injury*

QOLIBRI scale	Mean (SD)
Cognition	68.3 (21.8)
Self	64.6 (22.9)
Daily life and autonomy	65.7 (24.1)
Social Relations	70.8 (21.4)
Emotions	75.1 (24.6)
Physical problems	68.6 (22.0)
Total score	68.5 (18.8)

SD: standard deviation.

Table IV. *Disability and functioning at 3 and 12 months post-injury. The results are shown as mean (SD) or median (IQR)*

	3 months	12 months
GOSE, mean (SD)	5.2 (1.3)	6.1 (1.4)
RPQ, median (IQR)	10.0 (4.0–18.0)	12.5 (4.0–23.0)
FIM-M, median (IQR)	n.a.	90.0 (90.0–91.0)
FIM-COG, median (IQR)	n.a.	34.0 (30.0–35.0)
FIM – Sum, median (IQR)	n.a.	125.0 (120.0–126.0)
HADS, median (IQR)	n.a.	8.0 (3.0–12.0)

n.a.: not applicable; SD: standard deviation; IQR: interquartile range; GOSE: Glasgow Outcome Scale Extended; RPQ: Rivermead Post-concussion Questionnaire; FIM; Functional Independence Measure: FIM-M: FIM Motor; FIM-COG: FIM Cognitive; HADS: Hospital Anxiety and Depression Scale.

RESULTS

The injury characteristics of the participants are shown in Table II. The majority of respondents were injured in road traffic accidents ($n=61$, 48.0%). The participants had severe injuries, with a mean GCS score of 5.9 (SD 1.9) and a mean AIS-head score of 4.2 (SD 0.9). Fifty-nine people (43.0%) had an AIS-head of 5, which is indicative of critical injuries.

Approximately 5.0% ($n=6$) of the patients reported a history of TBI prior to the present injury, and 39.0% ($n=49$) reported having one or more other comorbid diseases.

Mean QOLIBRI total score was 68.5 (SD 18.8). The subscale and total scores are displayed in Table III.

Table IV displays the post-injury disability and functioning scores. There was a significant reduction in disability of 0.9 points on the GOSE from 3 to 12 months ($p<0.001$). The distribution of GOSE disability categories at 3 and 12 months is shown in Table V. The ANOVA showed that there were significant differences in QOLIBRI scores between participants with good recovery on the GOSE at 12 months, who scored 81.1 points (SD 14.5), and those with moderate (61.1 points (SD 17.1), $p<0.001$) and severe disability (62.0 points (SD 17.5), $p=0.001$). According to the HADS, 17.9% of the participants had symptoms of psychological distress at 12 months post-injury. Six patients (5.0%) had mild-moderate symptom pressure, whereas 16 (13.0%) patients had symptoms of anxiety and depression that required treatment. According to the dichotomized FIM-M and FIM-COG scales, a small percentage of patients (6.7%) were limited in motor function such that they needed another person for assistance, whereas 20.0% were limited in cognitive tasks and needed another person for assistance.

Table V. *Distribution of patient frequency (%) in the Glasgow Outcome Scale Extended (GOSE) disability categories at 3 and 12 months for the 126 patients*

	3 months *n* (%)	12 months *n* (%)
GOSE 3–4, severe disability	25 (19.8)	12 (9.6)
GOSE 5–6, moderate disability	85 (67.4)	68 (53.9)
GOSE 7–8, good recovery	16 (12.7)	46 (36.5)

Table VI. *Results from the multiple hierarchical regression models of the Quality of Life after Brain Injury score (*n=*99)*

	Step 1	Step 2	Step 3	Step 4
Age at injury	0.13	0.12	0.12	0.08
Sex (men/women)	–0.05	–0.04	0.03	0.08
Education (low/high)	0.02	0.03	0.04	–0.01
Pre-injury employment (working or studying/other)	0.28**	0.28**	0.22*	0.15*
AIS-head		0.20*	0.25**	0.05
GOSE 3 months			0.26**	0.17*
RPQlg 3 months			–0.41***	–0.04
GOSE 12 months				0.17*
RPQlg 12 months				–0.30**
FIM-M low/high				0.05
FIM-C low/high				0.05
HADSlg				–0.40***
R^2	0.07	0.11	0.40	0.68
Adjusted R^2	0.03	0.06	0.36	0.64
R^2 Change	0.07	0.04	0.29	0.28
F Change	1.80	4.16*	22.44***	15.35***

*$p=0.05$; **$p=0.01$; ***$p<0.001$.
Standardized beta coefficients are presented.
AIS: Abbreviated Injury Scale; FIM; Functional Independence Measure: FIM-M: FIM Motor; FIM-COG: FIM Cognitive; GOSE: Glasgow Outcome Scale Extended; HADSlg; Hospital Anxiety and Depression Scale log10 transformed: RPQlg: Rivermead Post-concussion Questionnaire log10 transformed.

The results of the multiple regression analysis are presented in Table VI. The analysis showed that employment status before the injury was the only demographic factor that predicted HRQL on the QOLIBRI. AIS-head was a significant predictor when the model controlled for demographic factors (step 2) and functioning at 3 months (step 3). GOSE ($p=0.004$) and RPQ at 3 months ($p<0.001$) were significant predictors of the QOLIBRI. The adjusted R^2 showed that the regression model explained 64.0% of the variance in the QOLIBRI score. The R^2 change showed that demographic variables explained 7.0% of the variance; AIS-head added 4.0% to the explained variance, and functioning on the GOSE and RPQ at 3 months added another 29.0% of the variance. The last step added another 28.0% to the explained variance. The HADS was the strongest individual predictor in the final model ($p<0.001$).

DISCUSSION

This study is the first to describe HRQL in a population of patients with severe TBI using the QOLIBRI. The findings are consistent with other studies where the SF-36, a generic measure of HRQL commonly used in TBI outcome research, was applied (3, 16, 34). The current study supplements the larger multi-centre project by enforcing the patient perspective on subjective health, well-being and functioning after severe TBI (35).

Responses on the QOLIBRI subscales showed that there was no single aspect that was particularly more reduced than the others. Nonetheless, the patient's satisfaction with self, comprising items related to motivation, self-esteem, energy and self-perception, had the lowest subscale score. Fatigue is a well-known condition following TBI of all severities, which is linked to the change in cognitive capacity, sleep disturbance, pain and depression (19, 36). Concerning post-TBI feelings and perceptions of self, a recent review of a qualitative study performed by Levack et al. (11) describes several inter-related themes, including a mind/body disconnect, a disconnect with pre-injury identity, and the reconstruction of self-identity and of personhood.

Emotional well-being was the least reduced of the QOLIBRI subscales. This result is consistent with results on the HADS, which revealed that fewer than 20% of participants reported psychological distress at 12 months. However, participants reported more psychological distress on the HADS compared with the general population, in which the lifetime prevalence of depression is estimated to be 9% (37).

Compared with Truelle et al.'s study (22), in which 58% of patients were characterized as having a severe TBI, patients in the current study reported significantly higher HRQL (total score of 68.5 points vs 64.6 points). Comparatively higher scores were identified on all QOLIBRI subscales, except daily life, autonomy and physical function. The largest differences were in the areas of cognition, emotions and social relations. Comparing the differences between these two studies might shed some light on individuals' adaptation in the rehabilitation process. Recognition of the impact of the TBI on solving cognitive tasks and general tasks and demands may evolve over time; social relations may suffer, and the experienced emotional distress may increase.

Patients in the current study had sustained their TBI 12 months prior to evaluation, whereas the time since injury was considerably longer in the study by Truelle et al. (22). As such, participants were still in a rehabilitation and recovery phase and had been exposed to the requirements and expectations of everyday life (e.g. work participation, social demands) to a lesser extent than the previous sample. Therefore, the differences in scores might be caused by less exposure to socially and cognitively challenging situations. Moreover, recent recommendations made by the Norwegian Health Authorities (http://www.helsedirektoratet.no/IS-1279) resulted in the improvements to rehabilitation protocols available to these patients, as well as in more seamless chains of treatment. Improved care and rehabilitation efforts might contribute to less uncertainty with respect to the current and future situation and contribute to the HRQL (38).

Linear regression analysis was used to determine the factors that contribute to the HRQL at 12 months post-injury. Of demographic variables, only pre-injury work status was a predictor of HRQL on the QOLIBRI in all steps of the regression analysis, reflecting the importance of a pre-injury productive lifestyle to HRQL (12).The relationship between pre-injury work and HRQL has been well established in previous literature. Pre-injury employment status in this study may have served as a proxy for personal resources that might strengthen or impair perceived health status and HRQL post-TBI. However, this study was not designed to assess personal resources and their influence on HRQL.

In line with our hypothesis, injury severity variables, such as GCS, intra-cranial injury assessed by the Rotterdam CT Score

and the ISS, were not associated with HRQL. However, AIS head contributed significantly to the QOLIBRI score at the third step of the regression analysis, with predictors at 3 months indicating that a more severe head injury was associated with higher HRQL. This result is consistent with previous studies and suggests the link between severity of injury, reduced awareness and self-reported HRQL (39). However, AIS head was not a significant predictor in the final step of the regression with concurrent functional status and psychological distress added to the model. The association between injury severity and HRQL may dissolve over time, and other variables, such as psychological and social components, may become more important for HRQL at the later stages of injury (2, 14).

Global functioning, as evaluated by GOSE scores at 3 months and 12 months, was a significant predictor of HRQL in the current study. In addition, significant improvements in GOSE scores from 3 to 12 months post-injury were found, suggesting that disability following TBI is not static (38). Significant associations between recovery and QOLIBRI scores have been shown in other studies on TBI populations of all severities (21, 24). The analysis showed that patients with severe and moderate disability demonstrated the greatest reductions in HRQL; this result is consistent with Truelle's study (22). However, no significant differences in QOLIBRI mean scores were found between these two disability groups, suggesting that patients with the worst outcomes may adjust well to TBI consequences (24). Other possible explanations may include reduced awareness (39), impaired memory of problems within QOLIBRI domains or better support provided to severely disabled people compared those with moderate disability (22). Furthermore, in 7 cases, relatives assisted the patients in completing the QOLIBRI, which may have led to over- or under-estimation of the HRQL in the most severe patient group. However, patients with a good recovery also reported reduced HRQL compared with the highest scale scores. These findings highlight the importance of including the subjective patient experience in TBI outcome evaluations.

Participants' scores on the RPQ showed that the self-reported symptom pressure of the TBI reflecting somatic, cognitive and emotional impairments was lower at 3 months than at 12 months. One possible explanation for the increase in symptoms is that individuals with severe TBI may be less aware of their deficits for organic reasons, and thus these individuals may under-report symptoms during the first months post-injury (40). When the RPQ was added into the regression analysis, it was a significant predictor of HRQL. This finding suggests that a relationship exists between self-reported complaints and HRQL, supporting previous research (19). Our hypothesis that symptom pressure would be negatively associated with HRQL is similarly supported. However, no previous studies have reported RPQ as a predictor of HRQL in individuals with severe TBI.

In the current study, cognitive function was measured as self-reported symptoms on the RPQ, and cognitive functional ability was assessed via the FIM-COG by health personnel. FIM-COG scores were not associated with HRQL, even though satisfaction with cognitive functioning is a subscale of the QOLIBRI. More specifically, although the FIM-COG is widely used for evaluating cognitive sequelae in TBI, it is of limited sensitivity to cognitive disability after patient discharge from sub-acute rehabilitation and in TBI patients with high functional levels (3). Therefore, cognitive dysfunction may be underestimated in this study and may account for the non-significant relationship between FIM-COG and HRQL. In contrast, psychological distress at 12 months on the HADS was a significantly associated with HRQL, supporting our study hypothesis as well as other studies reporting that emotional status influences HRQL (4). Of course, depression and psychological distress are common problems after sustaining severe TBI, and significant correlations between the mental health subscales on the SF-36 and depression and between the QOLIBRI and depression have been identified in the TBI population (24).

Ahmadi et al. (41) found that, although patients in their study demonstrated reduced functioning on neuropsychological tests 12 months post-injury, and although depression was significantly more prevalent in patients than in healthy controls, the patients reported only moderately reduced HRQL on the SF-36. They emphasized that rehabilitation should be better targeted for both cognitive and psychological outcomes. In addition, Diaz (34) et al. reported a significant increase in the prevalence of major depressive disorder and generalized anxiety disorder after severe TBI. Depression was related to personality changes and had a negative impact on the HRQL on the SF-36.

The results of this study might serve to guide the rehabilitation processes for people with severe TBI. The strength of this multicentre study is that it used a representative cohort of Norwegian adults who were admitted to the trauma referral centres for severe TBI, who received rehabilitation care in the course of injury and who survived the first year after the injury. Nevertheless, a multicentre study will always be flawed by differences among study centres that are not documented, and by biases in registration procedures. Population norms are usually used to provide reference values for post-injury HRQL; however, such data do not exist for QOLIBRI scores.

In conclusion, our study indicates that somatic, emotional and cognitive symptom pressure and global functioning in the sub-acute phase of TBI, as well as psychological distress in the post-acute phase, are important for the self-perceived HRQL 12 months after injury. These domains are modifiable and should be the focus of rehabilitation interventions aiming to improve HRQL in patients with severe TBI.

ACKNOWLEDGEMENTS

We thank the Trauma Registry at Oslo University Hospital and Haukeland University Hospital for providing data regarding injury severity. We also thank Tone Jerstad, neuroradiologist for her effort in analysing the majority of CT scans and providing the Rotterdam scores. This multicentre study was funded by the Norwegian Research Council.

REFERENCES

1. De Silva MJ, Roberts I, Perel P, Edwards P, Kenward MG, Fernandes J, et al. Patient outcome after traumatic brain injury in

high-, middle- and low-income countries: analysis of data on 8927 patients in 46 countries. Int J Epidemiol 2009; 38: 452–458.
2. Dikmen SS, Machamer JE, Powell JM, Temkin NR. Outcome 3 to 5 years after moderate to severe traumatic brain injury. Arch Phys Med Rehabil 2003; 84: 1449–1457.
3. Andelic N, Sigurdardottir S, Schanke AK, Sandvik L, Sveen U, Roe C. Disability, physical health and mental health 1 year after traumatic brain injury. Disabil Rehabil 2010; 32: 1122–1131.
4. Draper K, Ponsford J, Schonberger M. Psychosocial and emotional outcomes 10 years following traumatic brain injury. J Head Trauma Rehabil 2007; 22: 278–287.
5. Lehtonen S, Stringer AY, Millis S, Boake C, Englander J, Hart T, et al. Neuropsychological outcome and community re-integration following traumatic brain injury: the impact of frontal and non-frontal lesions. Brain Inj 2005; 19: 239–256.
6. Mathias JL, Alvaro PK. Prevalence of sleep disturbances, disorders, and problems following traumatic brain injury: a meta-analysis. Sleep Med 2012; 13: 898–905.
7. Vakil E. The effect of moderate to severe traumatic brain injury (TBI) on different aspects of memory: a selective review. J Clin Exp Neuropsychol 2005; 27: 977–1021.
8. Ewing-Cobbs L, Barnes M. Linguistic outcomes following traumatic brain injury in children. Semin Pediatr Neurol 2002; 9: 209–217.
9. Safaz I, Alaca R, Yasar E, Tok F, Yilmaz B. Medical complications, physical function and communication skills in patients with traumatic brain injury: a single centre 5-year experience. Brain Inj 2008; 22: 733–739.
10. Nampiaparampil DE. Prevalence of chronic pain after traumatic brain injury: a systematic review. JAMA 2008; 300: 711–719.
11. Levack WM, Kayes NM, Fadyl JK. Experience of recovery and outcome following traumatic brain injury: a metasynthesis of qualitative research. Disabil Rehabil 2010; 32: 986–999.
12. Jacobsson LJ, Westerberg M, Lexell J. Health-related quality-of-life and life satisfaction 6–15 years after traumatic brain injuries in northern Sweden. Brain Inj 2010; 24: 1075–1086.
13. Bullinger M, Azouvi P, Brooks N, Basso A, Christensen AL, Gobiet W, et al. Quality of life in patients with traumatic brain injury-basic issues, assessment and recommendations. Restor Neurol Neurosci 2002; 20: 111–124.
14. Koskinen S, Hokkinen EM, Wilson L, Sarajuuri J, Von Steinbuchel N, Truelle JL. Comparison of subjective and objective assessments of outcome after traumatic brain injury using the International Classification of Functioning, Disability and Health (ICF). Disabil Rehabil 2011; 33 : 2464–2478.
15. Dijkers MP. Quality of life after traumatic brain injury: a review of research approaches and findings. Arch Phys Med Rehabil 2004; 85: S21–S35.
16. Andelic N, Hammergren N, Bautz-Holter E, Sveen U, Brunborg C, Roe C. Functional outcome and health-related quality of life 10 years after moderate-to-severe traumatic brain injury. Acta Neurol Scand 2009; 120: 16–23.
17. Arango-Lasprilla JC, Ketchum JM, Gary K, Hart T, Corrigan J, Forster L, et al. Race/ethnicity differences in satisfaction with life among persons with traumatic brain injury. Neurorehabilitation 2009; 24: 5–14.
18. Steel J, Youssef M, Pfeifer R, Ramirez JM, Probst C, Sellei R, et al. Health-related quality of life in patients with multiple injuries and traumatic brain injury 10+ years postinjury. J Trauma 2010; 69: 523–530.
19. Cantor JB, Ashman T, Gordon W, Ginsberg A, Engmann C, Egan M, et al. Fatigue after traumatic brain injury and its impact on participation and quality of life. J Head Trauma Rehabil 2008; 23: 41–51.
20. Nichol AD, Higgins AM, Gabbe BJ, Murray LJ, Cooper DJ, Cameron PA. Measuring functional and quality of life outcomes following major head injury: common scales and checklists. Injury 2011; 42: 281–287.
21. Hawthorne G, Kaye AH, Gruen R, Houseman D, Bauer I. Traumatic brain injury and quality of life: initial Australian validation of the QOLIBRI. J Clin Neurosci 2011; 18: 197–202.
22. Truelle JL, Koskinen S, Hawthorne G, Sarajuuri J, Formisano R, Von Wild K, et al. Quality of life after traumatic brain injury: the clinical use of the QOLIBRI, a novel disease-specific instrument. Brain Inj 2010; 24: 1272–1291.
23. Von Steinbuchel N, Wilson L, Gibbons H, Hawthorne G, Hofer S, Schmidt S, et al. Quality of Life after Brain Injury (QOLIBRI): scale development and metric properties. J Neurotrauma 2010; 27: 1167–1185.
24. Von Steinbuchel N, Wilson L, Gibbons H, Hawthorne G, Hofer S, Schmidt S, et al. Quality of Life after Brain Injury (QOLIBRI): scale validity and correlates of quality of life. J Neurotrauma 2010; 27: 1157–1165.
25. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
26. Association for the Advancement of Automotive medicine [homepage on the Internet]. 2008. The Abbreviated Injury Scale (AIS) 2005 – Update 2008. Available from: www.AAAM.org.
27. Baker SP, O'Neill B, Haddon W Jr., Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 1974; 14: 187–196.
28. Maas AI, Hukkelhoven CW, Marshall LF, Steyerberg EW. Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors. Neurosurgery 2005; 57: 1173–1182.
29. Uniform Data System for Medical Rehabilitation. Guide for the uniform data set for medical rehabilitation (Including the FIM instrument). New York: State University of New York at Buffalo; 1996.
30. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. J Neurotrauma 1998; 15: 573–585.
31. King NS, Crawford S, Wenden FJ, Moss NE, Wade DT. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. J Neurol 1995; 242: 587–592.
32. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67: 361–670.
33. Schonberger M, Ponsford J. The factor structure of the Hospital Anxiety and Depression Scale in individuals with traumatic brain injury. Psychiatry Res 2010; 179: 342–349.
34. Diaz AP, Schwarzbold ML, Thais ME, Hohl A, Bertotti MM, Schmoeller R, et al. Psychiatric disorders and health-related quality of life after severe traumatic brain injury: a prospective study. J Neurotrauma 2012; 29: 1029–1037.
35. Andelic N, Anke A, Skandsen T, Sigurdardottir S, Sandhaug M, Ader T, et al. Incidence of hospital-admitted severe traumatic brain injury and in-hospital fatality in Norway: a national cohort study. Neuroepidemiology 2012; 38: 259–267.
36. Englander J, Bushnik T, Oggins J, Katznelson L. Fatigue after traumatic brain injury: Association with neuroendocrine, sleep, depression and other factors. Brain Inj 2010; 24: 1379–1388.
37. Ayuso-Mateos JL, Vazquez-Barquero JL, Dowrick C, Lehtinen V, Dalgard OS, Casey P, et al. Depressive disorders in Europe: prevalence figures from the ODIN study. Br J Psychiatry 2001; 179: 308–316.
38. Seeley HM, Kirker S, Harkin C, Dias C, Richards H, Pickard JD, et al. Head injury rehabilitation: the role of a neurotrauma clinic. Br J Neurosurg 2009; 23: 530–537.
39. Sasse N, Gibbons H, Wilson L, Martinez-Olivera R, Schmidt H, Hasselhorn M, et al. Self-awareness and health-related quality of life after traumatic brain injury. J Head Trauma Rehabil 2012 Aug 29 [Epub ahead of print].
40. Sigurdardottir S, Andelic N, Roe C, Jerstad T, Schanke AK. Post-concussion symptoms after traumatic brain injury at 3 and 12 months post-injury: a prospective study. Brain Inj 2009; 23: 489–497.
41. Ahmadi SA, Meier U, Lemcke J. Detailed long-term outcome analysis after decompressive craniectomy for severe traumatic brain injury. Brain Inj 2010; 24: 1539–1549.

J Rehabil Med 2013; 45: 792–800

ORIGINAL REPORT

SEVERE TRAUMATIC BRAIN INJURIES IN NORTHERN SWEDEN: A PROSPECTIVE 2-YEAR STUDY

Maud Stenberg, MD[1], Lars-Owe Koskinen, MD, PhD[2], Richard Levi, MD, PhD[1] and Britt-Marie Stålnacke, MD, PhD[1]

From the [1]Department of Community Medicine and Rehabilitation, Rehabilitation Medicine and [2]Department of Pharmacology and Clinical Neuroscience, Division of Neurosurgery, Umeå University, Umeå, Sweden

Objective: **To assess: (*i*) the clinical characteristics and injury descriptors of patients with severe traumatic brain injury in Northern Sweden admitted to the single Neurotrauma Center (NC) serving this region; (*ii*) the care pathway of patients from injury to 3 months after discharge from the NC; and (*iii*) the outcomes at 3 months post-injury.**

Design: **Population-based prospective 2-year cohort study.**

Patients: **Patients age 17–65 years with acute severe traumatic brain injury, lowest non-sedated Glasgow Coma Scale (GCS) score of 3–8 within 24 h post-trauma.**

Methods: **Patients were treated according to an intracranial pressure-oriented protocol based on the Lund concept at the NC. They were assessed at 3 weeks after injury with Rancho Los Amigos Cognitive Scale Revised (RLAS-R), Levels of Cognitive functioning, and at 3 months with RLAS-R and Glasgow Outcome Scale Extended (GOSE).**

Results: **A total of 37 patients were included. Hospital deaths within 3 months post-injury occurred in 5 patients. After 3 months the RLAS-R scores were significantly improved ($p < 0.001$). Eight patients had both "superior cognitive functioning" on the RLAS-R and "favourable outcome" on the GOSE. Thirty-four patients (92%) were directly admitted to the NC. By contrast, after discharge patients were transferred back to one of several county hospitals or to one of several local hospitals, and some had multiple transfers between different hospitals and departments.**

Conclusion: **Overall outcomes were surprisingly good in this group of severely injured patients. The routines for transferring patients with severe traumatic brain injury from a geographically large, sparsely populated region to a regional NC to receive well-monitored neurosurgical care seem to work very well. The post-acute clinical pathways are less clearly reflecting an optimized medical and rehabilitative strategy.**

Key words: traumatic brain injury; outcome; demographics; critical pathways.

J Rehabil Med 2013; 45: 792–800

Correspondence address: Maud Stenberg, Department of Community Medicine and Rehabilitation, Rehabilitation Medicine, Bldg 9A, Umeå University Hospital, Umeå University, SE-901 85 Umeå, Sweden. E-mail: maud.stenberg@vll.se

Accepted April 25, 2013

INTRODUCTION

Traumatic brain injury (TBI) constitutes a major health problem globally, and is a leading cause of death and long-term disability (1). TBI is common in young adults and has a male predominance due, primarily, to high-risk behaviours most prevalent in this demographic subset of the general population (2). The specific epidemiology of TBI makes it particularly important both to prevent and optimally treat the condition, as the stakes from a lifetime perspective are unusually high. The most widely used severity classification of TBI is based on level of consciousness (LOC) at admission, e.g. as reflected in the Glasgow Coma Scale (GCS) (3). The annual incidence of all (i.e. mild to severe) instances of TBI in Sweden is estimated at 250–350/100,000 (2, 4). The subset of severe TBI (sTBI), as defined by GCS 3–8, is, however, much rarer, with incidence estimates of 4–8/100,000/year (2). However, despite its relative rarity, sTBI constitutes a major health problem, due to the major and often permanent functional impact of the injuries, and the individual suffering of patients and their families, as well as the very high societal costs. Today, in Sweden state-of-the-art medical treatment of patients with sTBI is typically conducted at specifically designated Neurotrauma Centers (NC), operating according to one or another of several proposed, standardized protocol-driven therapies, such as the Lund concept utilized in our region (5–7). This particular protocol has been evaluated in a number of outcome studies that have shown favourable results (8–10). As a benefit of improved neurosurgical care, survival rates have improved substantially; something that, at the same time, has created an increased need for rehabilitation (10). Early rehabilitation after sTBI includes assessment and treatment to improve the patient's level of functioning (11), as well as the prevention and treatment of secondary complications. However, the available evidence has demonstrated that formalized rehabilitation interventions have beneficial effects, both early and late after sTBI. Borg et al. (12) recently reported that continued access to rehabilitation competencies from acute management after sTBI is not the standard in Sweden.

Patients with sTBI comprise a heterogeneous group with varying complexity and prognosis. It is therefore of paramount importance in each individual case to assess key clinical descriptors, pertinent circumstances related to the injury,

and, perhaps most important of all, to define early prognostic indicators that could be used to triage individual need for rehabilitation and rehabilitation planning. Various scales have been developed for assessment of disability after TBI. The most commonly used outcome measure for sTBI is the Glasgow Outcome Scale (GOS) (13). This is a global and, admittedly crude, instrument that only roughly discriminates different levels of disability. A more sophisticated version of the GOS, the Glasgow Outcome Scale Extended (GOSE), has thus been developed, allowing for a more fine-tuned categorization of post-traumatic disability (14). Moreover, the so-called Rancho Los Amigos Scale Revised Levels of Cognitive Functioning (RLAS) (15) is yet another useful instrument that has been implemented in several studies to assess recovery after sTBI, and to create a knowledge base relevant to the design of novel and appropriate rehabilitation programmes.

This study was conducted in the North Health Region (NHR) in Sweden. The study is part of a larger prospective multicentre cohort study, the ProBrain study, which focuses on adults with sTBI admitted to neurosurgical departments across the country. Most research into outcome after sTBI has focused on injury severity, and few studies have considered the effect of geographical factors (16). As the NHR comprises mainly rural districts with geographically large, scarcely populated areas, with long distances between hospitals, the clinical setting in this part of the country differs substantially from the more urbanized, southern half of the country. The NHR setting is, however, representative of many other regions globally, thus motivating separate analysis. The questions are: Is it possible to obtain good or excellent outcomes in a scarcely populated, vast area? Will the logistics of transfers of patients allow for rapid admission to a single NC serving a very large region? The focus of this article is therefore on the analysis of sTBI management referred to Umeå University Hospital, being the single NC serving the northern half of the country, and thus displaying this particular logistic challenge.

The first aim of the study was to assess clinical characteristics (age, gender, education, marital status, occupation) and injury descriptors (aetiology, previous TBI, additional injuries, intoxication) of patients with sTBI in the NHR. The second aim was to track the clinical care pathways of patients from the scene of injury and up to 3 months after discharge. The third aim was to assess outcomes at 3 months post-injury.

METHODS

The study is a prospective, total population, cohort study conducted from January 2010 to December 2011. Eligible patients were consecutively included in the study, which comprised a structured initial assessment at 3 weeks and a subsequent follow-up 3 months post-injury.

The geographical area of NHR comprises almost half of the total area of the country (136,373 km^2). It is divided into 4 counties and has approximately 900,000 inhabitants, comprising only 10% of the total national population. Patients sustaining sTBI in the NHR typically will first be admitted to a county hospital or a local hospital in proximity to the venue of injury for initial assessment and stabilization prior to further transportation. In accordance with the clinical protocol during the study period, all subjects with sTBI, regardless of severity, complicating illness or concomitant injuries, were admitted to the NHR NC.

Patients

Inclusion criteria for this study were: patients aged 17–64 years; with acute sTBI with lowest non-sedated GCS score of 3–8 within 24 h post-trauma. Consecutive inclusion commenced in January 2010 and ceased after December 2011. Exclusion criterion for this study was death within 3 weeks of injury.

Treatment

Patients were treated according to an intracranial pressure (ICP)-oriented protocol based on the so-called Lund concept (5–7). This modified Lund protocol has been outlined elsewhere (8, 9). In summary, an aggressive neurosurgical approach is adopted, including prompt removal of intracranial haematomas. Patients are sedated, receive continuous analgesia, are mechanically ventilated and initially nursed in a supine position with no head elevation. Midazolam is used for sedation and fentanyl for analgesia. Patients are normo-ventilated (P_aCO_2 4.5–5.5 kPa) and P_aO_2 kept $\geq$ 12 kPa. Normovolaemia is maintained with preferably albumin infusion and packed red blood cells. Serum albumin ($\geq$ 40 g/l) and haemoglobin ($\geq$ 110 g/l) levels are maintained, and a neutral to slightly negative fluid balance is achieved by using furosemide as needed. Serum levels of sodium ($\geq$ 135 mmol/l) and blood glucose are kept within normal limits. Infusions of metoprolol and clonidine are used as needed after establishment of normovolaemia. The rationale behind this protocol is to normalize mean arterial blood pressure (MAP), to minimize fluid leakage through the capillary membrane, and to reduce stress mediated by the sympathetic nervous system. A minimum cerebral perfusion pressure (CPP) of 50 mmHg is accepted. Additional possible interventions to reduce an elevated/rising ICP (> 20 mmHg) are: low-dose barbiturates, ventriculostomy with intermittent drainage, and/or decompressive craniectomy.

Procedure

The primary hospital performed an initial computed tomography (CT) scan of the brain. (This investigation was often repeated upon arrival to the NC). Pictures were transferred electronically to the NC, where a neuroradiologist assessed the images, for this study particularly presence or absence of epidural and subdural haematomas, traumatic subarachnoidal haemorrhage, diffuse axonal injury, brain contusion(s), and impression fracture(s). The CT scans were also classified according to the Marshall classification (17). All clinical outcome data gathering was performed by one of the authors (MS) by patient assessment at 3 weeks and 3 months post-injury. Socio-demographic data and data regarding pre-morbid health were gathered by interviews of patients and/or significant others, also performed by MS. Data regarding injury characteristics and length of stay at the NC was retrieved from the medical records.

Outcomes

Outcome variables were survival/death, Glasgow Outcome Scale Extended (GOSE) (14) and Rancho Los Amigos Cognitive Scale Revised (RLAS-R) (15). The RLAS-R was used at both 3 weeks and 3 months, whereas the GOSE was used only at 3 months.

Instruments

Glasgow Coma Scale. The GCS (13) rates loss of consciousness (LOC) by assessment of the patient's verbal, eye opening, and motor responses on a scale of 3 to 15, with higher scores indicating better responses. In the NHR the 8-point Reaction Level Scale (RLS) (18) is widely used; the inclusion criterion was RLS 8–4. Comparison of these scales has been carried out (19). Lowest level of consciousness is presented as GCS.

Rivermead Post-traumatic Amnesia Protocol (RPAP). The RPAP comprises 5 questions. It documents the time-interval from brain injury to the return of continuous memory, including periods of unconsciousness and confusion. The interviewer asks questions so that the patient will relate their first memories after the accident in a coherent chronological order. Post-traumatic amnesia (PTA) classification is divided into 4

categories: Mild < 1 h, Moderate 1–24 h, Severe 1–7 days, and Very severe > 7 days (20).

Rancho Los Amigos Cognitive Scale Revised, Levels of Cognitive functioning. The RLAS-R Levels of Cognitive functioning (15) is a medical scale with scores from 1 to 10, representing 10 states of cognitive and behavioural functioning through which patients with TBI typically progress. Higher scores indicate improved functioning. The bottom level is "No Response, Total Assistance", and the top level is "Purposeful, Appropriate: Modified Independent". The RLAS-R levels were dichotomized into 2 categories: inferior functioning (RLAS I–VIII) and superior functioning (RLAS-R IX–X). The scale is used for assessment of cognitive and behavioural recovery after TBI with coma. Patients are thus assessed by reaction to stimuli, ability to follow instructions, presence of confusion, behaviour with and without meaning, cooperation, attention, ability to maintain attention to the environment, verbal ability, memory, orientation and higher cognitive ability.

Glasgow Outcome Scale Extended. The GOSE (14) extends the 5 categories of the previously developed GOS (21) to 8, thereby increasing its sensitivity. The 8 categories span from "Dead" (score 1) to "Upper Good Recovery" (score 8). Results were dichotomized into "Unfavourable outcome" (GOSE 1–6), and "Favourable outcome" (GOSE 7–8).

Table I. *Demographic characteristics of patients with severe traumatic brain injury in Northern Sweden 2010–2011 with lowest (non-sedated) Glasgow Coma Scale score 8–3, age 17–65 years*

Demographic characteristics	
Patients *n* (%)	37 (100.0)
Gender *n* (%)	
Male	26 (70.3)
Female	11 (29.7)
Age, years, mean (SD) [range]	41.3 (15.2) [17–64]
Male	40.1 (15.3) [17–64]
Female	44.0 (14.9) [22–63]
Education, *n* (%)	
< 12 years	23 (62.2)
= 12 years	11 (29.7)
> 12 years	3 (8.1)
Employment and livelihood when the accident occurred, *n* (%)	
Working (50–100%) or student (50–100%)	24 (64.9)
Unemployed (50%)	1 (2.7)
Sick-leave, full or part time (25–100%)	9 (24.3)
Social care	4 (10.8)
Other	3 (8.1)
Marital status *n* (%)	
Single person without children	13 (35.1)
One parent with children	2 (5.4)
Married, cohabitating without children	15 (40.5)
Married, cohabitating with children	5 (13.5)
Living with other	2 (5.4)
Known drug or alcohol misuse at time of injury, *n* (%)	
Yes	11 (29.7)
No	26 (70.3)
Previous brain injury requiring hospitalization, *n* (%)	
Yes	12 (32.4)
No	24 (64.9)
Missing	1 (2.7)
Previous brain injury (*n* = 14), *n* (%)	
Male	9 (24.3)
Female	5 (13.5)

SD: standard deviation.

Statistical analysis

Data were analysed with SPSS, version 19.0 for Windows. Data are reported as means. Non-parametric tests were used as the samples were small and/or not normally distributed. Thus, the Mann-Whitney *U* test was used for the comparison of continuous variables, and Wilcoxon's signed-rank test for the study of paired observation variables. A χ^2 test was used for the comparison of proportions.

Table II. *Injury characteristics of patients with severe traumatic brain injury (sTBI) in Northern Sweden 2010–2011 with lowest (non-sedated) Glasgow Coma Scale (GCS) score 8–3, age 17–65 years*

Injury characteristics	
Causes of sTBI, *n* (%)	
Road traffic accident, snowmobile, ATV, as a cyclist or pedestrians hit by car	11 (29.7)
Fall > 2 m	10 (27.0)
Fall, same level or unspecified	10 (27.0)
Bicycle accident	2 (5.4)
Horse accident	2 (5.4)
Skiing accident	1 (2.7)
Unknown	1 (2.7)
Lowest unsedated GCS first 24 h, *n* (%)	
3	9 (24.3)
4–5	13 (35.2)
6–8	15 (40.5)
Lowest unsedated GCS first 24 h, median (range)	5 (3–8)
Length of stay-intensive care, median (*n* = 34) (range)	16.9 (2–54)
Signs of influence of alcohol and/or drugs at time of injury, *n* (%)	
Yes	18 (48.6)
No	19 (51.4)
Additional injury, *n* (%)	
Yes	13 (35.1)
No	24 (64.9)
Post-traumatic amnesia, *n* (%)	
Severe 1–7 days	1 (2.7)
Very severe > 7 days	36 (97.3)
Marshall CT classification, *n* (%)	
I	1 (2.7)
II	15 (40.5)
III	6 (16.2)
IV	8 (21.6)
V	0 (0.0)
VI	7 (18.9)
Main diagnosis included patients, *n* (%)	
S062 Diffuse brain injury	9 (24.3)
S063 Focal brain injury	2 (5.4)
S064 Epidural haemorrhage	5 (13.5)
S065 Traumatic subdural haemorrhage	17 (45.9)
S066 Traumatic subarachnoidal haemorrhage	2 (5.4)
S068 Other specified intracranial injury	2 (5.4)
Total	37 (100.0)
Retrospective review, additional patients found, age 18–65 years	
Male/female, *n* (%)	6/0 (100/0)
Age, years, mean (range)	49.8 (31–56)
Death within 3 months, *n* (%)	2 (33.3)
Main diagnosis: S062 Diffuse brain injury, *n* (%)	1 (16.7)
Main diagnosis: S064 Epidural haemorrhage, *n* (%)	1 (16.7)
Main diagnosis: S065 Traumatic subdural haemorrhage, *n* (%)	4 (66.7)
Total	6 (100.0)
Included patient and retrospective review additional patients found 2010 and 2011, *n* (%)	43

ATV: all-terrain vehicle; CT: computed tomography.

Ethics

This study is a part of a multicentre study that was approved by the Regional Ethics Committee of Stockholm, Sweden (number 2009/1644/31/3).

RESULTS

A total of 37 patients with acute sTBI fulfilling the inclusion criteria were identified during the study period and included in the analyses. Thorough subsequent audits within the NHR to identify possible missed patients revealed an additional 6 persons, all males, who had sustained sTBI during the study period. As they were not identified within 3 weeks post-injury (as stipulated in the study protocol), they were not included in the study.

Clinical patient descriptors

Clinical patient descriptors are presented in Tables I and II. The majority were males. Mean age at injury was 41.3 years (men 40.1, females 44.0 years). Males had less education than the females. Most patients had sustained acute traumatic subdural hematomas. The lowest unsedated GCS in the first 24 h varied widely, with GCS 3 in 9 patients (24%), GCS 4–5 in 13 patients (35%) and GCS 6–8 in 15 patients (40%). Most cases were due to falls. All injury causes, except falls on the same level and "unknown", were classified as high-energy trauma. Thirteen patients (35.1%) had additional injuries: traumatic spinal cord injury ($n=2$), vertebral fracture, pelvic fracture, long-bone fracture, rib fracture ± pneumothorax, clavicular fracture, and/or intra-abdominal injuries. Two patients were pregnant. Thirty-six out of 37 patients (97%) had a post-traumatic amnesia > 7 days, thus qualifying as "very severe brain injury" according to the Rivermead PTA protocol. Mean length of stay in NC ($n=34$) was 16.9 days. Although there was a trend towards longer LOS in those with additional injuries, this difference did not reach statistical significance.

The age and gender distribution of the first CT scan, causes of sTBI, worst GCS within the first 24 h, previous brain injury in need of medical contact, additional injury, and TBI with signs of influence of alcohol or drugs, are shown in Table III.

Alcohol

Eighteen patients, 15 males and 3 females, (48.6%) were under the influence of alcohol and/or drugs (as demonstrated by clinical assessment, anamnestic information and/or blood test) at the time of injury (Tables II and III). Known current drug and/or alcohol abuse was present in 11 patients (29.7%).

Table III. *Comparison causes of severe traumatic brain injury (sTBI), Worst Glasgow Coma Scale (GCS) in the first 24 h, Previous Brain Injury In need of medical contact, Additional injury, Traumatic Brain Injury with signs of influence of alcohol and/or drugs with age group and gender*

	Age			Gender		
	≤25 years *n* (%)	26–49 years *n* (%)	≥50 years *n* (%)	Male *n* (%)	Female *n* (%)	Total *n* (%)
Causes of sTBI						
Road traffic accident, snowmobile, ATV, as a cyclist or pedestrians hit by car	6 (55)	5 (45)	0 (00)	7 (64)	4 (36)	11 (100)
Fall > 2 m	2 (20)	3 (30)	5 (50)	8 (80)	2 (20)	10 (100)
Fall, same level or unspecified fall	2 (20)	1 (10)	7 (70)	8 (80)	2 (20)	10 (100)
Bicycle accident	0 (00)	1 (50)	1 (50)	1 (50)	1 (50)	2 (100)
Skiing accident	0 (00)	1 (100)	0 (00)	1 (00)	0 (00)	1 (100)
Horse accident	0 (00)	2 (100)	0 (00)	0 (00)	2 (100)	2 (100)
Unknown	1 (100)	0 (00)	0 (00)	1 (100)	0 (00)	1 (100)
Total; group of age or gender	11 (30)	13 (35)	13 (35)	26 (70)	11 (30)	37 (100)
Worst GCS in the first 24 h						
3	1 (11)	3 (33)	5 (56)	6 (67)	3 (33)	9 (100)
4	3 (50)	1 (17)	2 (33)	4 (67)	2 (33)	6 (100)
5	2 (29)	4 (57)	1 (14)	5 (71)	2 (29)	7 (100)
6	2 (22)	3 (33)	4 (44)	6 (67)	3 (33)	9 (100)
7	3 (75)	0 (00)	1 (25)	4 (100)	0 (00)	4 (100)
8	0 (00)	2 (100)	0 (00)	1 (50)	1 (50)	2 (100)
Total; group of age or gender	11 (30)	13 (35)	13 (35)	26 (70)	11 (30)	37 (100)
Previous brain injury in need of medical contact						
Yes	4 (29)	3 (21)	7 (50)	9 (64)	5 (36)	14 (100)
No	7 (30)	10 (44)	6 (26)	17 (74)	6 (26)	23 (100)
Total; group of age or gender	11 (30)	13 (35)	13 (35)	26 (70)	11 (30)	37 (100)
Additional injury						
Yes	6 (46)	4 (31)	3 (23)	8 (61)	5 (39)	13 (100)
No	5 (21)	9 (38)	10 (42)	18 (75)	6 (25)	24 (100)
Total; group of age or gender	11 (30)	13 (35)	13 (35)	26 (70)	11 (30)	37 (100)
Traumatic brain injury with signs of influence of alcohol and/or drugs						
Yes	6 (33)	5 (28)	7 (39)	15 (83)	3 (17)	18 (100)
No	5 (26)	8 (42)	6 (32)	11 (58)	8 (42)	1 (100)
Total; group of age or gender	11 (30)	13 (35)	13 (35)	26 (70)	11 (30)	37 (100)

ATV: all-terrain vehicle.

Significantly more intoxicated patients ($n=10$) had experienced previous TBI in comparison with the non-intoxicated patients ($n=4$) ($p=0.040$). sTBI due to current high-energy trauma was more common among intoxicated ($n=11$) than among non-intoxicated patients ($p=0.041$).

Computed tomography scan

Time to first CT scan was less than 1 h for 4 patients, less than 3 h for 20 patients (55%) and less than 4 h for 30 patients (82%). The exact time elapsed from injury to CT scan was missing for 7 patients, all of whom, however, were within time limits for inclusion in the study (Table IV).

The first CT scan obtained post-injury showed that 27 patients (73%) had sustained traumatic subdural hematoma. Brain contusion(s) was found in 28 patients (76%), and 29 patients (78%) had traumatic subarachnoidal haemorrhage. Detailed results are shown in Fig 1. and Fig. 3.

Intracranial pressure

Mean ICP (mmHg) was calculated for each patient for the hour with highest ICP during the first 5 days post-trauma. Mean ICP for 31 of these patients ranged between 15 and 20 mmHg (Fig. 2). For 3 of the patients ICP was not measured, and 3 were, at that initial stage, treated abroad.

Table IV. *Time to first computed tomography (CT) scan of the brain from accident to first hospital*

Time from accident	*n* (%)
0–60 min	4 (11)
61–120 min	11 (30)
121–180 min	5 (14)
181–240 min	10 (27)
241–1,320 min	5 (14)
Total	35 (95)
Time not available	2 (5)
Total	37 (100)

Clinical outcomes

Death within 3 months. Hospital deaths within 3 months post-injury occurred in 5 patients (Table V). The primary diagnosis was traumatic subdural haematoma in 4 patients. They received intensive care for 21.6 days (range 19–31 days). Only one of the patients who died had significant additional injuries. Two of the patients who died were intoxicated at the time of injury. Causes of death were, respectively: post-traumatic inoperable arteriovenous fistula and aspiration pneumonia, acute and recurring tracheal bleedings, meningitis and aspiration pneumonia, pneumonia stagnation of secreation in the airways and intracranial rebleeding (after discharge to local hospital).

GOSE and RLAS-R. Table VI shows the distribution of GOSE and RLAS-R scores at 3 months post-injury. The RLAS-R scores were significantly improved from 3 weeks (5.26 ± 3.07) to 3 months (8.0 ± 2.45) ($p<0.001$), and 19 patients had "superior functioning" on the RLAS-R IX–X. Eight patients had both a "superior functioning" on the RLAS-R and a "favourable outcome" on the GOSE 7–8. There were no significant differences in outcomes between patients intoxicated or not intoxicated at injury on the GOSE (4.5 ± 2.3 vs 3.9 ± 2.3, $p=0.196$) and the RLAS-R (8.7 ± 1.9 vs 7.3 ± 2.7, $p=0.151$).

Clinical care pathways. Most patients (92%) were admitted directly to the regional NC. After discharge, patients were typically transferred back to 1 of several county or local hospitals (Fig. 4). They were also found to commonly be transferred between different departments within a given hospital.

CT classification	Age, years			Gender		
	<25 *n* (%)	26–49 *n* (%)	>50 *n* (%)	Male *n*=26 *n* (%)	Female *n*=11 *n* (%)	Total=37 *n* (%)
 Traumatic subdural haemorrhage	6 (22)	9 (33)	12 (44)	21 (78)	6 (22)	27 (73)
 Epidural haemorrhage	2 (40)	3 (60)	0 (00)	2 (40)	3 (60)	5 (14)
 Diffuse axonal injury	4 (80)	1 (20)	0 (00)	3 (60)	2 (40)	5 (14)
 Impressions fracture	2 (33)	3 (50)	1 (17)	4 (67)	2 (33)	6 (16)
 Brain contusion	10 (36)	9 (32)	9 (32)	20 (71)	8 (29)	28 (76)
 Traumatic subarachnoidal haemorrhage	8 (28)	10 (35)	11 (38)	22 (76)	7 (24)	29 (78)

Fig. 1. First computerized tomography (CT) scan of the brain compared with age and gender.

DISCUSSION

This study shows the clinical pathways in the NHR in Sweden. In this rural area, which covers almost half of the country, most patients nevertheless are shown to be swiftly transported directly to the regional

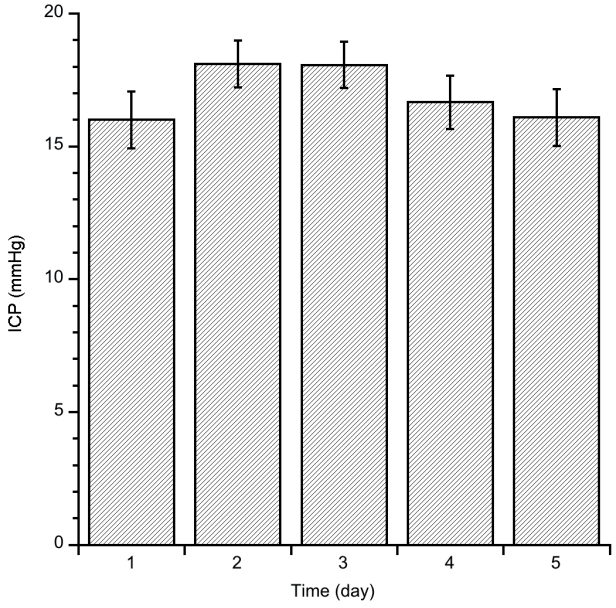


Fig. 2. Mean intracranial pressure (ICP) during the first 5 days post-trauma ($n=31$).

NC. Thus, routines for pre-acute care seem to be well-established, not only in theory, but also in practice. By contrast, post-acute care after discharge from NC seemingly lacks the structured rigour of the referral and neurointensive processes. Patients are often transferred back to local hospitals at a fairly early stage. Furthermore, in many instances transfers additionally occur across departments. The medical rationale of this dispersion is not clear. There are probably several reasons behind the marked differences between acute and post-acute logistics. Although centralized and standardized treatment and rehabilitation are also likely to be needed in the post-acute stage, the individual patient's differences and needs are factors that tend to grow in importance as the patient gradually becomes medically stabilized (22), and such aspects may have played a role in the choice of diverging pathways of the patients in the present study. Costs may be another operative factor, as each county has its own budget and has to cover the costs for patient care outside its jurisdiction. In addition, the severity of residual disability and projected prognosis is also likely to be a factor that determines the choice of post-acute clinical pathway.

Well-organized pre-hospital transportation systems for patients with sTBI have also been reported from rural regions of Norway (11). In these areas, rehabilitation in the early phases is based on close collaboration between the neurosurgical departments and rehabilitation units, but capacity problems may delay inpatient rehabilitation (12). Since similar difficulties with insufficient management routines in Sweden and Norway have been observed, researchers recently proposed a Scandinavian organization model that integrates neurointensive care and qualified rehabilitation, and ensures an effective chain of rehabilitation activities after sTBI (12). Differences in post-acute pathways after sTBI have also been demonstrated from other countries. A study from Colorado, USA (23) found that different paths reflected the outcome, and almost 25% of patients with sTBI received no rehabilitation at all. In studies that have evaluated patients with sTBI from rural and urban areas, poorer outcomes for rural residents have often been reported (16). However, with an integrated acute and post-acute network of services, similar results have been shown for rural and urban groups in Australia (24). These findings underline the importance of structured interventions in the early rehabilitation process.

In accordance with previous studies, most patients in the present study were males (4, 11, 25). Falls have commonly been reported as an injury cause typical in TBI affecting children and old persons (4, 11,

		GCS						
		3	4	5	6	7	8	
		$n=9$	$n=6$	$n=7$	$n=9$	$n=4$	$n=2$	Total=37
	CT classification	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
	Traumatic subdural haemorrhage	7 (26)	3 (11)	5 (18)	8 (30)	3 (11)	1 (4)	27 (100)
	Epidural haemorrhage	1(20)	0 (0)	1 (20)	1 (20)	1 (20)	1 (20)	5 (100)
	Diffuse axonal injury	1 (20)	2 (40)	0 (0)	1 (20)	0 (0)	1 (20)	5 (100)
	Impressions fracture	1 (17)	1 (17)	1 (17)	2 (33)	0 (0)	1 (17)	6 (100)
	Brain contusion	4 (14)	6 (21)	5 (18)	7 (25)	4 (14)	2 (7)	28 (100)
	Traumatic subarachnoidal haemorrhage	8 (28)	4 (14)	5 (17)	7 (24)	4 (14)	1 (3)	29 (100)

Fig. 3. First computed tomography (CT) scan of the brain compared with Glasgow Coma Scale (GCS).

Table V. *Hospital deaths within 3 months after injury*

	Median (range)	*n* (%)
Total		5 (100)
Gender		
Male		4 (80)
Female		1 (20)
Main diagnosis		
S062 Diffuse brain injury		1 (20)
S065 Subdural haemorrhage		4 (80)
Age, years	50.8 (19–64)	5 (100)
Lowest unsedated GCS first 24 h		
3		3 (60)
5		1 (20)
6		1 (20)
Length of stay in intensive care, days	21.6 (9–31)	5 (100)
Length, need of sedation, days	11 (5–20)	4 (80)
Additional injury		
No		4 (80)
Yes		1 (20)
Intraventricular blood or subarachnoid haemorrhage		5 (100)

GCS: Glasgow Coma Scale.

25), but were also the most frequent cause in our middle-aged patient population. Nevertheless, motor vehicle accidents are often the cause of injuries in younger persons (11, 25), especially males (4), and contributed to one-third of injuries in the present study. The findings of falls as the leading cause of injury were consistent with a previous study from our hospital (4) of all severity grades of TBI and with a recent Norwegian study of sTBI (25). In contrast, studies from the USA (23) and Australia report motor vehicle injuries as more common than falls both in rural and urban areas (24). This difference may be explained by differences in the infrastructure, traffic intensity, and transport systems in these countries in comparison with Scandinavia.

The male patients in our study had a lower education level in comparison with females, and more males than females were intoxicated at time of injury. Alcohol use at the time of injury has been shown to be a risk factor for TBI (26, 27). Although most studies have shown a relationship between alcohol and poorer outcome after TBI (27, 28), some studies have found no correlation between blood alcohol concentration and TBI outcome (29, 30). In the present study, significantly more patients who were under the influence of alcohol at time of injury had a history of previous TBI and were more often injured by high-energy trauma in comparison with the non-intoxicated patients. However, there was no significant difference between these groups on GOSE and RLAS 3 months post-injury. Based on some laboratory studies it has been argued that alcohol might have a neuroprotective effect (31, 32). To complicate an assessment of the influence of alcohol on prognosis in TBI, it is obvious that a substantial alcohol intake in itself may depress the LOC. Thus, patients intoxicated by alcohol at the time of injury may have lowered GCS scores partially or totally due to alcohol ingestion, rather than due to the severity of brain trauma, and may then be initially classified as having more severe TBI than they actually have.

For assessment of outcomes, the GOSE and RLAS scales were used. All patients improved significantly on the RLAS from 3 weeks to 3 months. At 3 months, of the 19 patients in the 2 highest RLAS categories and the 8 patients on the highest GOSE levels, 3 and 2 patients, respectively, had the lowest GCS score of 3 during the first 24 h in the acute stage. Thus,

Table VI. *Lowest unsedated Glasgow Coma Scale (GCS) first 24 h, signs of alcohol and/or drugs at time of injury and Rancho Los Amigos Cognitive Scale Revised (RLAS-R) and GOSE after 3 months. RLAS-R inferior functioning (RLAS I-VIII) and superior functioning (RLAS-R IX–X), Glasgow Outcome Scale Extended (GOSE) Unfavourable outcome (GOSE 1–6), and Favourable outcome (GOSE 7–8)*

Lowest unsedated GCS first 24 h	*n* (%)	Traumatic brain injury with signs of influence of alcohol and/or drugs *n* (%)	Hospital deaths *n* (%)	GOSE 1–8 after 3 months *n* (%)	RLAS-R after 3 months *n* (%)
GCS 3	9 (24)	4 (22)	3 (33)	GOSE 1–6 = 7 (78) GOSE 7–8 = 2 (22)	Deaths = 3 (33) RLAS II–VII = 3 (33) RLAS IX–X = 3 (33)
GCS 4	6 (16)	3 (17)	0 (0)	GOSE 3–6 = 4 (67) GOSE 7–8 = 2 (33)	RLAS III–VII = 4 (67) RLAS IX–X = 2 (33)
GCS 5	7 (19)	4 (22)	1 (14)	GOSE 1–5 = 3 (43) GOSE 7–8 = 4 (57)	Deaths = 1 (14) RLAS V = 1 (14) RLASIX–X = 5 (71)
GCS 6	9 (24)	4 (22)	1 (11)	GOSE 1–6 = 7 (78) GOSE 8 = 2 (22)	Deaths = 1 (11) RLAS V–VIII = 4 (44) RLAS IX–X = 4 (44)
GCS 7	4 (11)	2 (11)	0 (0)	GOSE 4–6 = 2 (50) GOSE 8 = 1 (25) Missing = 1 (25)	RLAS IX–X = 3 (75) Missing = 1(25)
GSC8	2 (5)	1(6)	0 (0)	GOSE 3–5 = 2 (100)	RLAS X = 2(100)
Total	37 (100)	18 (100)	5 (14)	GOSE 1–6 = 28 (76) GOSE 7–8 = 8 (22) Missing = 1 (3)	Deaths = 5 (14) RLAS II–VIII = 12 (32) RLAS IX–X = 19 (51) Missing = 1 (3)

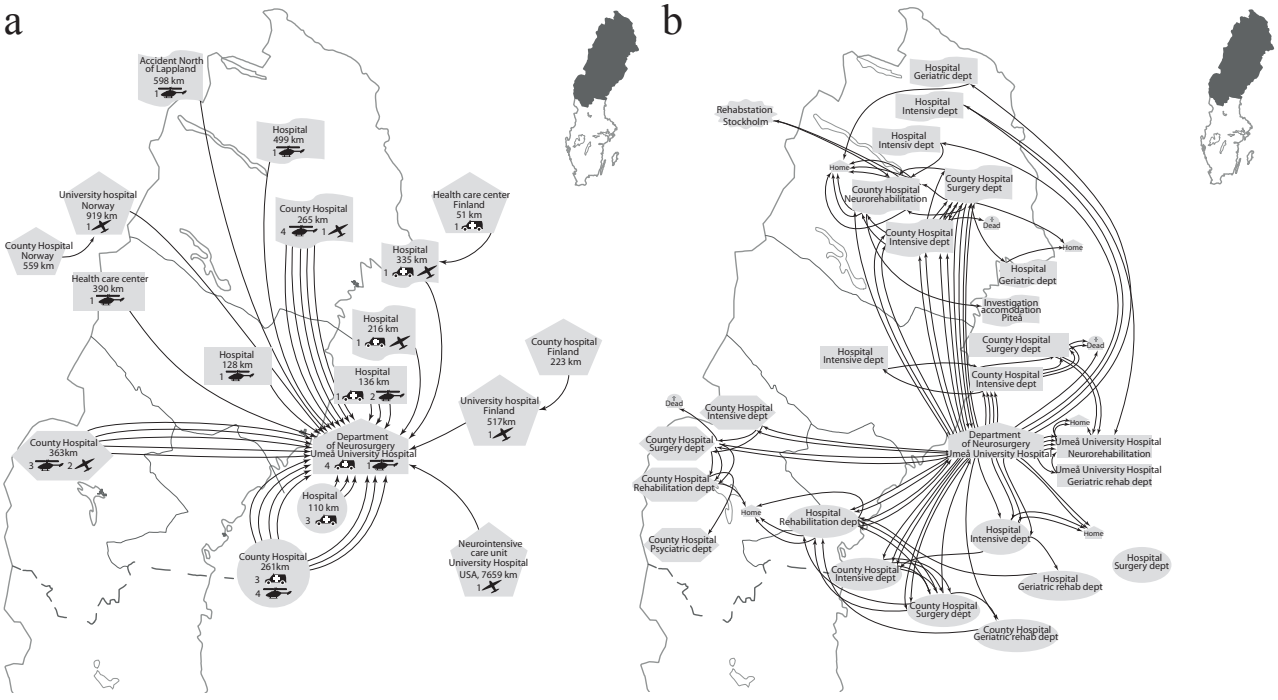


Fig. 4. (a) Clinical care pathway to the Department of Neurosurgery, Umeå University Hospital in northern Sweden (*left:* map of northern Sweden). (b) Clinical care pathway during 3 months after discharge (*right:* map of northern Sweden). Rehabilitation NHR: Rehabilitation North Health Region.

the majority of the assessed patients experienced good recovery as regards cognitive and behavioural functioning, and around one-quarter was considered as having both "superior cognitive functioning" (15) and a "favourable outcome" (14). However, it is worth noticing that even if positive results on the GOSE and the RLAS were measured, patients may still not be fully recovered at 3 months after the injury and may experience subtle deficits not covered by these instruments. Therefore, it seems reasonable to assume that some of the patients were in need of further rehabilitation interventions and follow-up.

This study has several strengths, such as a prospective design and a close collaboration as regards case identification, which resulted in most patients being included. Even the 6 patients missed for inclusion were subsequently identified, making it possible to account for this small group too. The study design and the well-established acute clinical pathways make it extremely unlikely that study results could be flawed by skewed inclusion. In addition, the extant protocols allow for referral even of those patients with seemingly very poor prognoses. Furthermore, one of the authors (MS) examined all patients, both at 3 weeks and 3 months, and ensured that data were precisely and completely documented. The number of patients in the study was rather small, but comprises the total or near-total regional population of sTBI patients injured during 2 years, and is in accordance with a recent study from northern Norway that also included older patients (25). One limitation of the study is that blood alcohol concentration (BAC) was not measured in all patients, thus decreasing the accuracy in determining the contribution of alcohol to the early clinical picture and the putative effects of alcohol on outcomes. Even with the best intentions, not all trauma patients have BAC measured at the time of admission (33).

In conclusion, the results of this study show that the routines for swiftly transferring all patients with sTBI from a geographically large, sparsely populated, rural area to a single regional NC to receive strict and well-monitored neurosurgical and neurointensive care according to a well-validated protocol seem to work well; something that is also reflected in outcome measurements, in which a high proportion of patients was found to be recovered at 3 months despite very liberal clinical inclusion criteria. In contrast, the post-acute clinical pathways are less clearly reflecting an optimized medical and rehabilitative strategy. The dispersion of patients and frequent transfers between and within a fairly large number of hospitals suggests that non-medical factors are influencing decisions, and raises doubts as to whether it is possible to maintain top-level neurorehabilitation in so many locations. Further research will examine the causes and effects of this state of affairs.

ACKNOWLEDGEMENTS

The authors would like to thank the patients and their relatives, the clinical staff of our unit, especially psychologist Anna-Lisa Nilsson. The authors also thank neuroradiologist, senior consultant Per Jonasson for assessing the CT scans and colleagues at the NC for helping us to recruit patients, colleagues in the intensive care unit and colleagues in rehabilitation department in the NHR. This study was supported by grants from Västerbotten County Council.

REFERENCES

1. Tagliaferri F, Compagnone C, Korsic M, Servadei F, Kraus JA. Systematic review of brain injury epidemiology in Europe. Acta Neurchir 2006; 148: 255–268.
2. Kleiven S, Peloso PM, von Holst H. The epidemiology of head injures in Sweden from 1987 to 2000. Inj Control Saf Promot 2003; 10: 173–180.
3. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
4. Styrke J, Stålnacke BM, Sojka P, Björnstig U. Traumatic brain injures in a well- defined population: epidemiological aspects and severity. J Neurotrauma 2007; 24: 1425–1436.
5. Asgeirsson B, Grande PO, Nordstrom CH. A new therapy of post-trauma brain oedema based on haemodynamic principles for brain volume regulation. Intensive Care Med 1994; 20: 260–267.
6. Grande PO, Asgeirsson B, Nordstrom CH. Physiologic principles for volume regulation of a tissue enclosed in a rigid shell with application to the injured brain. J Trauma 1997; 42: S23–S31.
7. Grande PO, Asgeirsson B, Nordstrom CH. Volume-targeted therapy of increased intracranial pressure: the Lund concept unifies surgical and non-surgical treatments. Acta Anaesthesiol Scand 2002; 46: 929–941.
8. Olivecrona M, Rodling-Wahlstrom M, Naredi S, Koskinen LO. Effective ICP reduction by decompressive craniectomy in patients with severe traumatic brain injury treated by an ICP-targeted therapy. J Neurotrauma 2007; 24: 927–935.
9. Olivecrona M, Rodling-Wahlstrom M, Naredi S, Koskinen LO. Prostacylin treatment in severe traumatic brain injury – a microdialysis and outcome study. J Neurotrauma 2009; 26: 1251–1262.
10. Eker C, Schalen W, Asgeirsson B, Grande PO, Ranstam J, Nordstrom CH. Reduced mortality will increase demands for rehabilitation services. Brain Inj 2000; 14: 605–619.
11. Andelic N, Bautz-Holter E, Ronning P, Olafsen K, Sigurdardottir S, Schanke AK, Sveen U, Tornas S, Sandhaug M, Roe C. Does an early onset and continuous chain of rehabilitation improve the long-term functional outcome of patients with severe traumatic injury? J Neurotrauma 2012; 29: 66–74.
12. Borg J, Roe C, Nordenbo A, Andelic N, de Boussard C, af Geijerstam JL. Trends and challenges in the early rehabilitation of patients with traumatic brain injury. A Scandinavian perspective. Am J Phys Med Rehabil 2011; 90: 65–73.
13. Jennet B, Bond M. Assessment of outcome after severe brain damage – a practical scale. Lancet 1975; 1: 480–484.
14. Lindsay Wilson JT, Laura EL, Pettigrew, Graham, Teasdale M. Structured Interviews for Glasgow Outcome scale and the Extended Glasgow Outcome Scale: Guidelines for their use. J Neurotrauma 1998; 15:5 73–585.
15. Hagen C, Malkmus D, Durham P. Levels of cognitive functioning. In: Professional Staff Association of Rancho Los Amigos Hospital, editors. Rehabilitation of the head injured adult: comprehensive physical management. Downey, CA: Rancho Los Amigos Hospital Inc.; 1987.
16. Schootman M, Fuortes L. Functional status following traumatic brain injuries: population – based rural-urban differences. Brain Inj 1999; 13: 995–1004.
17. Marshall LF, Bowers Marshall S, Klauber MR, van Berkum Clark M, Eisenberg H M, Jane JA, et al. A new classification of head injury based on computerized tomography. J Neurosurg 1991; 75: S14–S20.
18. Starmark JE, Stålhammar D, Holmgren E. The Reaction Level Scale (RLS85). Manual and guidelines. Acta Neurochir 1988; 91: 12–20.
19. Starmark JE, Stålhammar D, Holmgren E, Rosander B. A comparisation of the Glasgow Coma Scale and the Reaction Level Scale (RLS85). J Neurosurg 1988; 69: 699–706.
20. King NS, Crawford S, Wenden FJ, Moss NEG, Wade DT, Caldwell FE. Measurement of post traumatic amnesia: how reliable is it? J Neurol Neurosurg Psychiatry 1997; 62: 38–42.
21. Jennet B, Bond M. Assessment of outcome after severe brain damage a practical scale. Lancet 1975; 1: 480–484.
22. Chesnut RM, Carney N, Maynard H, Mann NC, Patterson P, Helfand M. Summary report: evidence for the effectiveness of rehabilitation for persons with traumatic brain injury. J Head Trauma Rehabil 1999; 14: 176–188.
23. Mellick D, Gerhart KA, Whiteneck GG. Understanding outcomes based on the post-acute hospilization pathways followed by persons with traumatic brain injury. Brain Inj 2003; 17: 55–71.
24. Harradine PG, Winstanley JB, Tate R, Cameron ID, Baguley IJ, Harris RD. Severe traumatic brain injury in New South Wales: comparable outcomes for rural and urban residents. Med J Aust 2004; 181: 130–134.
25. Andelic N, Anke A, Skandsen T, Sigurdadottir S, Sandhaug M, Ader T, et al. Incidence of hospital-admitted severe traumatic brain injury and in-hospital fatality in Norway: a national cohort study. Neuroepidemiology 2012; 38: 259–267.
26. Opreanu RC, Kuhn D, Basson MD. Influence of alcohol on mortality in traumatic brain injury. J Am Coll Surg 2010; 210: 997–1007.
27. Chen CM, Yi HY, Yoon YH, Dong C. Alcohol use at time of injury and survival following traumatic brain injury: results from National Trauma Data Bank. J Stud Alcohol Drugs 2012; 73: 531–541.
28. Rootman DB, Mustard R, Kalia V, Ahmed N. Perceptions and realities of testing for alcohol and other drugs in trauma patients. J Trauma 2007; 63: 1370–1373.
29. Brickley MR, Shepered JP. The relationship between alcohol intoxication, injury severity and Glasgow Coma Score in assault patients. Injury 1995; 26: 311–314.
30. Alexander S, Kerr ME, Yonas H, Marion DW. The effects of admission alcohol level on cerebral blood flow and outcomes after severe traumatic injury. J Neurotrauma 2004; 21: 575–583.
31. Kelly DF, Lee SM, Pinanong PA, Hovda DA. Paradoxical effects of acute ethanolism in experimental brain injury. J Neurosurg 1997; 86: 876–882.
32. Tureci E, Dashti R, Tanriverdi T, Sanus GZ, Oz B, Uzan M. Acute ethanol intoxication in a model of traumatic brain injury: the protective role of moderate doses demonstrated by immunoreactivity of synaptophysin in hippocampal neurons. Neurol Res 2004; 26: 108–112.
33. Golan JD, Marcoux J, Golan E, Schapiro R, Johnston KM, Maleki M, et al. Traumatic brain injury in intoxicated patients. J Trauma 2007; 63: 365–369.

J Rehabil Med 2013; 45: 801–807

ORIGINAL REPORT

IMPACT OF PERSONAL AND ENVIRONMENTAL FACTORS ON EMPLOYMENT OUTCOME TWO YEARS AFTER MODERATE-TO-SEVERE TRAUMATIC BRAIN INJURY

Marit V. Forslund, MS[1,2], Cecilie Røe, PhD[1,2], Juan C. Arango-Lasprilla, PhD[4], Solrun Sigurdardottir, PhD[3,5] and Nada Andelic, PhD[1,3]

From the [1]Department of Physical Medicine and Rehabilitation, Oslo University Hospital, [2]Faculty of Medicine, University of Oslo, [3]CHARM (Research Centre for Habilitation and Rehabilitation Models and Services), Faculty of Medicine, University of Oslo, Oslo, Norway, [4]IKERBASQUE (Basque Foundation for Science), University of Deusto, Bilbao, Spain and [5]Sunnaas Rehabilitation Hospital Trust, Akershus, Norway

Objectives: **To describe employment outcomes and assess the impact of personal and environmental factors on employment outcomes 2 years after moderate-to-severe traumatic brain injury.**

Design/subjects: **A prospective cohort of 100 patients with moderate-to-severe traumatic brain injury, aged 16–55 years, hospitalized in a Trauma Referral Centre during the period 2005–2007 and followed up at 1 and 2 years post-injury.**

Methods: **Variables of interest were divided into personal and environmental factors. Personal factors include socio-demographics (age, gender, education, work demands, marital status and child-care). Environmental factors included social (support by friends), institutional (number of rehabilitation services, need for well-coordinated healthcare services), and physical (access to own transportation) factors. A multivariate logistic regression analysis was conducted with employment (working part-/full-time or studying) at 2-year follow-up as the dependent variable, and including independent variables based on significance from a univariate analysis, adjusting for injury severity.**

Results: **At the 2-year follow-up, 44% of patients were employed. Patients with less severe injuries (odds ratio (OR) = 1.2, $p = 0.03$), those supported by friends (OR = 3.5, $p = 0.07$), those not in need of well-coordinated health services (OR = 4.1, $p = 0.04$), and patients driving a vehicle at the 1-year follow-up (OR = 8.4, $p < 0.001$) were more likely to be employed at the 2-year follow-up.**

Conclusion: **Rehabilitation professionals should be aware of the role of environmental factors when planning vocational rehabilitation services after traumatic brain injury.**

Key words: traumatic brain injury; environmental factors; employment; prospective study.

J Rehabil Med 2013; 45: 801–807

Correspondence address: Marit Vindal Forslund, Olav M. Troviks vei 28 (H505), NO-0864 Oslo, Norway. E-mail: mvforslund@gmail.com

Accepted April 11, 2013

INTRODUCTION

Traumatic brain injury (TBI) is a leading cause of death and disability in young adults (1). A large proportion of patients with moderate-to-severe TBI experience long-term physical and cognitive impairment as well as emotional and psychosocial problems, which often have negative effects on patients' independence and productivity (1–6). Employment is an essential area of participation for the entire working age population and is a particular challenge in TBI (7, 8).

Employment rates after TBI vary widely between studies. A review by Shames et al. (7) found that 13–70% of TBI patients returned to work (RTW) between 6 weeks and 7 years post-injury. A systematic review by van Velzen et al. (9) found that approximately 40% had returned to work 2 years after TBI. The discrepancy between studies may partly be due to variations in the data collected and a lack of consistency in methodologies. Different definitions of employment and employment systems may further increase the variance in reported rates. Some longitudinal studies have noted that employment rates increase over time after TBI (10, 11), whereas others have suggested increased unemployment among individuals with TBI (12).

Kreutzer et al. (11) investigated employment stability by following previously employed patients over a period of 4 years after injury. The study found that only 34% of patients were stably employed (employed at all 3 follow-up times). Twenty-seven percent were unstably employed (employed at 1 or 2 follow-up times), and 39% were stably unemployed. Fleming et al. (13) investigated whether the patients' work situation changed from before the injury to the follow-up an average of 3.5 years after TBI. A total of 46.5% patients had returned to work at follow-up. Of these patients, 74.5% were working in the same or a similar job as they had held before the injury.

Over the last decade, researchers have become increasingly concerned about the influence of personal and environmental factors on health and functioning after TBI (5, 7, 14). According to the International Classification of Functioning, Disability and Health (ICF) (15), personal factors are "the particular back-

ground of an individual's life and living, and comprise features of the individual that are not part of a health condition", such as gender, race, age, social background, education, profession, etc. Environmental factors are defined as "the physical, social and attitudinal environment in which people live and conduct their lives", such as products and technology, support and relationship, services, systems and policies.

Personal factors associated with lower employment rates after TBI include male gender, older age, less education, unemployment prior to injury, single status and affiliation with ethnic minority groups (5, 7, 11, 16–19). Among the environmental factors, Whiteneck et al. (20) reported that transportation barriers, surroundings, government policies, attitudes and the natural environment were related to less productivity 1 year post-injury. Vogenthaler et al. (21) found that the informal social support system was positively associated with employment outcomes at 4–7 years post-injury.

Less is known about the factors related to employment outcomes after TBI in Scandinavia (18, 22). There is reason to believe that the most important factors influencing employment in these countries differ from those reported in prior research with US samples. The Scandinavian countries are welfare states that provide healthcare, insurance against disability, sickness and unemployment, and old-age pensions for all citizens. There is a long tradition of organization and resource allocation within the Scandinavian healthcare systems for the comprehensive rehabilitation of patients with long-term disabilities (23). Such organization may lead to variation in the environmental factors that are important for employment outcomes in these countries compared with countries with other state systems.

The aims of this study were: (*i*) to describe employment outcomes 2 years after moderate-to-severe TBI; and (*ii*) to assess the role of pre-injury and 1-year post-injury personal and environmental factors in predicting employment outcomes 2 years after moderate-to-severe TBI in a Norwegian patient population. Because personal factors are generally not modifiable, we recorded environmental factors at the 1-year follow-up, to identify factors for which facilitation or intervention may be needed to improve outcomes in the later stages of injury.

MATERIAL AND METHODS

Design and study sample

A prospective cohort study was conducted with clinical follow-up evaluations at 1 and 2 years after injury. Patients with acute TBI were admitted to Oslo University Hospital, Ulleval, from May 2005 to May 2007. This hospital is the Trauma Referral Centre for the Southeast region of Norway, with a population of nearly 2.6 million people.

Inclusion criteria included: (*i*) age 16–55 years; (*ii*) residence in eastern Norway; (*iii*) admitted with International Classification of Diseases 10th edition (ICD-10) diagnosis S06.0–S06.9 within 24 h of injury; and (*iv*) considered to have moderate-to-severe TBI with a Glasgow Coma Scale (GCS) (24) score of 3–12 before intubation. Exclusion criteria included: (*i*) previous neurological disorders/injuries; (*ii*) associated spinal cord injuries; (*iii*) previously diagnosed severe psychiatric or substance abuse disorders; and (*iv*) unknown address or incarceration.

A total of 160 patients met the inclusion criteria. Twenty-seven patients (17%) refused to participate, and 23 (14%) died in acute or post-acute care. Ten (6%) patients had incomplete data and were later excluded, leaving 100 (63%) patients for analysis.

Assessments

Independent variables. According to the ICF classification system (15) and a study by Devitt et al. (14), the variables of interest were divided into personal and environmental factors. Personal factors include sociodemographic factors, such as age, gender, education, work demands, marital status and child-care. Environmental factors include social (support by friends), institutional (number of rehabilitation services used, use of long-term and well-coordinated healthcare services in the form of an individual plan), and physical (access to own transportation, i.e. driving a vehicle) factors.

Acute phase. Information on age (divided at the mean, ≤ 31 vs > 31 years), gender (male vs female), education (≤ 12 years vs > 12 years), marital status (living together with spouse/partner/family vs living alone), pre-injury employment status (employed vs unemployed) and work demands (physical or non-physical, blue or white collar, respectively) were collected in the acute phase. The Glasgow Coma Scale (GCS) score assessed initial injury severity and divided patients into moderate (score 9–12) and severe (score 3–8) TBI (24).

1-year follow-up. Employment status, marital status and child-care (yes vs no), support by friends (yes vs no), the spectrum of rehabilitation services used (i.e. access to community-based rehabilitation services: day care (nurse and/or personal assistant), physiotherapy, occupational therapy, speech therapy, psychologist, social worker and others) dichotomized into none vs 1 or more, having an individual plan (yes vs no), and driving a vehicle (yes (permitted to resume driving after accident) vs no (not permitted to resume driving or without driver's licence)) were registered at 1-year follow-up. Responsibility for child-care and support by friends were explored through the Community Integration Questionnaire (CIQ) and the questions "Who usually cares for the children in your home?" and "Do you have a best friend in whom you confide?", respectively (25, 26). In the present study, the internal consistency of the CIQ scale was measured with Cronbach's alpha and found satisfied ($\alpha = 0.827$). Child-care was dichotomized into yes ("yourself"/"yourself and someone else") and no ("someone else"/"not applicable").

Dependent variable. The outcome measure was employment status 2 years after TBI. Employment was dichotomized into employed and unemployed, where employment was defined as working part-/full-time or studying. An inclusive definition of employment was used including other productive activities, such as studying, as described in our previous studies (18, 6). The students denoted persons who are studying at a high school, college or university in order to enter particular professions. Working or studying full-time is equal to 37.5 productive hours per week (i.e. 100%) and part-time employment was defined as working less than 37.5 h per week. The unemployed group consisted of individuals with TBI who were unemployed or on sick leave/disability pension.

Procedure

Pre-injury and injury-related data were extracted from medical records in the acute phase. At 1- and 2-year follow-ups, an assessment was performed, and patients were interviewed by the physiatrist in the outpatient department. Due to patients' requests, 6 assessments and interviews were conducted in patients' homes.

The study was approved by the Regional Committee for Medical Research Ethics, East Norway, and the Norwegian Data Inspectorate. Written informed consent was obtained from all participants.

Statistical analysis

All analyses were performed using PASW (formerly SPSS) version 18.0. We used two-sided statistical analysis and a 5% significance level. Descriptive statistics, *t*-tests and Mann-Whitney *U* tests were used for continuous variables, and χ^2 were used for categorical variables.

Table I. *Personal and environmental factors at time of injury and 1-year follow-up in relation to employment 2 years after moderate-to-severe TBI* (n=*100)*

	Unemployed (*n*=56)	Employed (*n*=44)	*p*-value	Total (*n*=100)
Personal factors				
Age, years, mean (SD)	30.9 (11.6)	30.8 (11.2)	>0.30	30.9 (11.4)
Gender, *n* (%)			0.054	
Male	39 (70)	38 (86)		77
Female	17 (30)	6 (14)		23
GCS scores, mean (SD)	6.1 (3.0)	8.5 (2.8)	<0.001*	7.1 (3.2)
3–8	46 (82)	22 (50)		68
9–12	10 (18)	22 (50)		32
Education, *n* (%)			>0.30	
≤12 years	34 (61)	23 (52)		57
>12 years	22 (39)	21 (48)		43
Employment pre-injury, *n* (%)			0.007*	
Employed	40 (71)	43 (98)		83
Unemployed	16 (29)	1 (2)		17
Work demands, *n* (%)			>0.30	
Blue-collar	29 (52)	19 (43)		48
White-collar	27 (48)	25 (57)		52
Marital status pre-injury, *n* (%)			0.14	
Living alone	26 (46)	14 (32)		40
Living with spouse/partner/family	30 (54)	30 (68)		60
Marital status at 1-year, *n* (%)			>0.30	
Living alone	29 (52)	26 (59)		45
Living with spouse/partner/family	27 (48)	18 (41)		55
Care of children at 1-year, *n* (%)			0.067	
Yes	9 (16)	14 (32)		23
No	47 (84)	30 (68)		77
Environmental factors				
Cause of injury, *n* (%)			>0.30	
Traffic accidents	34 (61)	25 (57)		59
Other	22 (39)	19 (43)		41
Rehabilitation services at 1-year, *n* (%)			0.003*	
None	13 (23)	23 (52)		36
≥1	43 (77)	21 (48)		64
Support from friends at 1-year, *n* (%)			0.054*	
Yes	39 (70)	38 (86)		77
No	17 (30)	6 (14)		23
Individual plan at 1-year, *n* (%)			<0.001*	
Yes	27 (48)	4 (9)		31
No	29 (52)	40 (91)		69
Driving vehicle at 1-year, *n* (%)			<0.001*	
Yes	7 (13)	29 (66)		36
No	49 (88)	15 (34)		64

*$p \leq 0.05$. *p*-values from univariate logistic regression.
SD: standard deviation; GCS: Glasgow Coma Scale.

Univariate logistic regression analyses were conducted to examine differences in personal and environmental factors between unemployed and employed patients (Table I). We conducted a multivariate logistic regression analysis (Backward: Wald method) with employment at the 2-year follow-up as the dependent variable and included independent variables based on the significant factors from the univariate analysis. In addition, the model was adjusted for injury severity by including acute GCS scores as an independent variable. The categories with the highest number of patients were used as reference groups, except for the variables of support from friends, individual plan and pre-injury employment. Two regression models were developed, the first without and the second with employment status pre-injury as an independent variable. The literature indicates that employment before an injury is strongly associated with employment after the injury. Therefore, we chose to run a model without pre-injury employment in order to highlight the relationships of less frequently investigated factors. The results are presented as odds ratios (OR) with 95% confidence intervals (CI) and *p*-values, Nagelkerke and Cox & Snell R^2. Possible multicollinearity and the presence of outliers were examined before running the multivariate logistic regression analysis. The Hosmer-Lemeshow goodness-of-fit statistic was computed.

RESULTS

The study sample had a mean age of 31 years (standard deviation; SD 11.4), and 77% were men. Based on acute GCS scores before intubation, 68% of the patients had severe TBI, and 32% had moderate TBI. At the time of injury, 56 (67.5%) of the individuals in the employment group were working full-time, while 4 (4.8%) were working part-time and 23 (27.7%) were studying.

Table II. *Association between personal and environmental factors and employment 2 years after traumatic brain injury (TBI), model 1*

Variables	Code	OR	95% CI	*p*-values
Friends	0=yes, 1=no	3.455	0.900–1.469	0.071
Individual plan[a]	0=no, 1=yes	4.149	1.081–15.922	0.038*
GCS score	Continuous	1.223	1.018–1.469	0.031*
Driving vehicle	0=no, 1=yes	8.361	2.819–24.798	<0.001*

*$p \leq 0.05$.
[a]An individual plan is established to coordinate the need of long-term healthcare services.
GCS: Glasgow Coma Scale; OR: odds ratio; CI: confidence intervals.

Seventeen patients were categorized as unemployed at the time of injury. Of these patients, 8 were in fact unemployed, 1 was on long-term sick leave, 3 received work assessment allowances, and 5 were on disability pension. Differences in personal and environmental factors at the time of injury and at the 1-year follow-up in relation to employment status 2 years after moderate-to-severe TBI are presented in Table I.

Employment outcome 2 years after injury

Of all the patients, 50% were employed at 1-year follow-up. Eighteen patients (36.0%) worked full-time, 18 (36.0%) worked part-time and 14 (28.0%) were studying. Two years after the TBI, the employment rate had decreased to 44%. Twenty-six (59.1%) patients were working full-time, 15 (34.1%) were working part-time and 3 (6.8%) were studying. Of the 44 patients employed at 2-year follow-up, 40 patients (91%) were stably employed (employed at both follow-up times). Of these, 38 (95%) were working in a similar job at both the 1- and 2-year follow-ups. Of those who were stably employed, 28 patients (70%) had no change in the number of work hours, whereas 11 (28%) experienced an increase in the hours they worked, and only 1 person (3%) had a decrease in work hours. Of the 17 patients who were unemployed before their injury, only 1 was employed at both follow-up times. As shown in Table I, there were statistically significant differences between employed and unemployed patients in terms of personal factors regarding pre-injury employment and injury severity and in the environmental factors of support by friends, use of rehabilitation services, the presence of an individual rehabilitation plan, and driving a vehicle at the 1-year follow-up.

Table III. *Association between personal and environmental factors and employment 2 years post-TBI, model 2*

Variables	Code	OR	95% CI	*p*-values
Pre-injury employment	0=no, 1=yes	25.599	2.763–237.145	0.004*
Individual plan[a]	0=no, 1=yes	5.328	1.325–21.423	0.018*
GCS score	Continuous	1.210	0.994–1.473	0.058
Driving vehicle	0=no, 1=yes	7.851	2.365–26.064	0.001*

*$p \leq 0.05$.
[a]An individual plan is established to coordinate the need of long-term healthcare services.
GCS: Glasgow Coma Scale; OR: odds ratio; CI: confidence intervals.

Predictors of employment 2 years after injury

The first multivariate logistic regression model showed that patients with less severe injuries had a 1.2-times higher probability (OR = 1.2, p=0.03) of being employed at the 2-year follow-up than those with more severe injuries. Patients with support from close friends had a 3.5-times higher probability of being employed at the 2-year follow-up, with a p-value approaching the significance level (OR = 3.5, $p = 0.07$). Patients without an individual plan of rehabilitation had a 4.1-times higher probability of being employed (OR = 4.1, $p = 0.04$), and patients driving a vehicle at the 1-year follow-up had an 8.4-times higher probability (OR = 8.4, $p < 0.001$) of being employed (Table II). Gender and rehabilitation services were clearly not significant in multivariate models ($p = 0.5$ and $p = 0.6$, respectively). The model as a whole explained 38% (Cox and Snell R^2) and 51% (Nagelkerke R^2) of the variance in employment status and correctly classified 79% of cases. The Hosmer-Lemeshow goodness-of-fit test found that the model was good (p=0.28).

When pre-injury employment was included as an independent factor in the second regression analysis, we found that previously employed patients had a 25.6-times higher probability of being employed 2 years post-TBI (OR = 25.6, $p = 0.004$). Injury severity by GCS score was marginally significant ($p = 0.058$). Patients without an individual plan of rehabilitation had a 5.3-times higher probability of being employed (OR = 5.3, $p = 0.02$), and patients driving a vehicle had a 7.9-times higher probability of being employed at the 2-year follow-up (OR = 7.85, $p = 0.001$) (Table III). Gender ($p = 0.5$), friends (p=0.4) and rehabilitation services ($p = 0.4$) were not significant factors. The second model explained 44% (Cox and Snell R^2) and 59% (Nagelkerke R^2) of the variance in employment status and correctly classified 82% of cases. The Hosmer-Lemeshow goodness-of-fit test showed that the second model was also good ($p = 0.20$).

DISCUSSION

This study attempted to describe employment outcomes 2 years after injury, and to assess the role of personal (gender, age, education, work demands, marital status and child-care) and environmental (support by friends, number of rehabilitation services used, individual plan, driving vehicle) factors in predicting employment outcomes 2 years after moderate-to-severe TBI when adjusting for the acute GCS score. The employment rate at the 2-year follow-up was 44%, and the majority of the patients were considered stably employed. Of the personal factors, age, gender, education, work demands, marital status and responsibility for child-care were not significant predictors. Of the environmental factors, the presence of an individual rehabilitation plan and driving a vehicle were significant predictors of employment 2 years after TBI in both multivariate models. As expected, pre-injury employment was a highly significant predictor of employment outcome at the 2-year follow-up.

The employment rate at the 2-year follow-up was similar to those reported in the van Velzen et al review (9). Previous studies have shown an increase in employment rates over time after TBI (10, 11). However, this was not the case in our study, where the employment rate of 50% at 1 year after TBI dropped to 44% 2 years after injury. This decrease may be understood in the context of Norway as a welfare state. A large proportion of the patients with long-lasting impairments will qualify to receive disability pensions within 2 years after TBI and may therefore not have to return to work. It is well known that changes in the economic climate may lead to a fall in employment. The last employed worker who gets into a company is usually the first to go when cuts are made. However, we do not believe that this was the case in the present study, as the global economic crisis in 2008–2009 has had a significantly smaller impact on Norway compared with other European countries. Furthermore, the fact that the majority of employed patients were stably employed at 2 years may indicate that employers are willing to adapt the working situation to keep them in their jobs, thus reflecting the "cooperative agreement for a more inclusive work place" introduced in Norway in 2004 (http://www.nav.no/).

In contrast to other studies (14), gender was found to be a non-significant predictor of employment outcome 2 years after TBI (10, 14). A limited study sample ($n = 100$) and a small amount of women ($n = 23$) may explain this finding. It was more surprising that neither age nor education were significant predictors, a finding that was in contrast to the literature (27). Many researchers have set the age of 40 years as a cut-off for predicting successful RTW after TBI, where patients below the age of 40 years fare better than older adults (28–30). The limited age range and the fact that only 24% of our patient sample was between 40 and 55 years of age are possible explanations for the finding that age was not a significant predictor in this study.

In line with the study by Keyser-Marcus et al. (30), education level was not a significant predictor in this study. A substantial number of studies support the role of education as predictor of employment outcome in patients with TBI. Gollaher et al. (19) found that education, pre-injury productivity (employment/studying) and level of disability correlated significantly with employment status 1–3 years following TBI. Some possible reasons for the discrepancy between our findings and the literature may be the categorization of education used in this study, a similar frequency of high and low educational groups and the stability of the labour market in Norway.

Marital status was not found to be a significant predictor of employment outcome, in line with some studies (21, 31) and in contrast to others (11, 32). Kreutzer et al. (11) found that married couples were more likely to be employed and to remain stably employed. However, the majority of patients in this study had a stable living situation during the first year after the injury.

Work demands, dichotomized into white-collar (professional, managerial or administrative) and blue-collar (manual labour) work, were not a significant predictor of employment status in this study. However, the existing literature reveals a trend in the relationship between work-type and RTW after TBI. Walker et al. (33) showed that individuals with TBI in prior professional/managerial positions were 3.0 times more likely to RTW than those in manual labour positions. Fleming et al. (13) also found that pre-injury occupational status was a significant predictor of RTW, and patients with prior upper-status occupations were more likely to RTW after TBI. A likely explanation for the discrepancy in the findings between our study and other studies is that the majority of patients in both qualification groups had a stable work experience prior to injury.

Pre-injury employment status and injury severity are known to be strong predictors of post-injury return to work (30, 34, 35). In our previous study (18), we found that the probability of being employed 1 year after injury was 95% lower for pre-injury unemployed patients and 74% lower for patients with more severe brain injury. The main explanation for these findings is that individuals with work experience prior to injury and those with less severe injuries cope better with employment reintegration.

Social support, including family members, friends and community members, was viewed as necessary for successful RTW (36). Support by close friends approached the significance level as a predictor in the first regression model. When prior employment status was included in the model, having friends was no longer a significant predictor. A possible reason might be that many of the friendships were established at and maintained through work, so that the effect of having friends coincided with employment status. In fact, three-quarters of the patients who reported no friends support were in the non-employed group. However, very few studies have focused on friendship in relation to TBI. It has previously been reported that persons with severe TBI are at a high risk of social isolation and significantly decrease in their friendships and social support as well as limited opportunities to establish new social contacts and friends (37). A study by Engberg & Teasdale (38) suggested that the ability to retain a network of family and friends may be an important factor for long-term survival after TBI.

Institutional support, such as the number of rehabilitation services, was not a significant predictor in this study. In contrast, the need for well-coordinated healthcare and rehabilitation services was a highly significant predictor. In Norway, the most central rehabilitation tool for patients in need of long-term and well-coordinated healthcare services is the individual plan, in accordance with statutory regulations (Law for patients rights 1999) (39). Patients with an individual plan often used several coordinated rehabilitation services, indicating more severe impairments. Thus, it was not surprising that the presence of an individual plan was a significant negative predictor for RTW after TBI. Our results are in accordance with the study by Bowman (40), which found that individuals who used several rehabilitation services had lower levels of occupational activity. In contrast, Vogenthaler et al. (21) found that a high level of use of rehabilitation adjustment services was associated with greater productivity.

Kreutzer et al. (11) reported that subjects who could drive their own vehicle 1 year after a TBI were more than 4 times more likely to be stably employed than those who had to rely on others for transportation. Klonoff et al. (27) found that returning to driving was significantly related to competitive status (working/in school) at follow-up 1–7 years after brain injury. For those who were unable to drive, the availability of transportation support was noted to be the strongest instrumental element that influenced RTW after TBI (36). We found that patients who had resumed driving at the 1-year follow-up were approximately 8 times more likely to be employed 2 years after moderate-to-severe TBI than those who were dependent on others for transportation. Patients' driver's licences were revoked after their intracranial brain injuries. To obtain permission to resume driving, patients with TBI must undergo multidisciplinary assessments in order to determine whether they are able to drive, including medical evaluations, neuropsychological assessments, driving simulators and on-road evaluations (41). Individuals who resume driving may be less severely injured and more cognitively able to perform the complex task of driving (which transfers to complex work tasks). In addition, having a car would suggest a higher income because it is expensive to pay for both a licence and a car.

This study has limitations that should be considered when interpreting the results. The study included patients aged 16–55 years who experienced a moderate-to-severe TBI 2 years previously. Therefore, the results may not generalize to patients outside this age range, to patients with mild TBI, or to individuals more than 2 years post-injury. Based on the findings of the regression models, there are other unmeasured factors (such as functional status) that may have a significant effect on employment outcomes.

The study results shed light on several environmental factors that could influence vocational outcome after TBI. The findings support existing evidence on relationships between pre-injury employment, injury severity and future employment outcomes. Of the environmental factors, support from close friends tended to be a positive predictor, whereas the presence of an individual rehabilitation plan was a negative predictor of employment outcomes. Access to one's own transportation was a strong positive predictor of employment at the 2-year follow-up. The data reveal that the important personal and environmental factors influencing employment outcome in the welfare state of Norway did not differ from prior studies from the USA. Rehabilitation professionals should be aware not only of the patients' functional status, but also of the physical, social and attitudinal environment, when planning vocational rehabilitation services after TBI. Interventions designed to improve the employment outcome of patients with TBI should integrate this complexity and include rehabilitation efforts targeting social relations in order to secure best outcomes for patients, and future research should focus on such environmental interventions. In addition, future studies with a mixed model design are required to further explore the relationship between environmental factors and employment outcome.

ACKNOWLEDGEMENTS

The authors would like to thank all the patients for their participation. Special thanks to Nini Hammergren for assistance with patient registrations. This study was funded by grants from the Norwegian Health South-East Authority and The Research Council of Norway.

REFERENCES

1. Ghajar J. Traumatic brain injury. Lancet 2000; 356: 923–929.
2. Hoffmann B, Duwecke C, von Wild KR. Neurological and social long-term outcome after early rehabilitation following traumatic brain injury. 5-year report on 240 TBI patients. Acta Neurochir Suppl 2002; 79: 33–35.
3. Arango-Lasprilla JC, Ketchum JM, Williams K, Kreutzer JS, Marquez de la Plata CD, O'Neil-Pirozzi TM, et al. Racial differences in employment outcomes after traumatic brain injury. Arch Phys Med Rehabil 2008; 89: 988–995.
4. Andelic N, Hammergren N, Bautz-Holter E, Sveen U, Brunborg C, Roe C. Functional outcome and health-related quality of life 10 years after moderate-to-severe traumatic brain injury. Acta Neurol Scand 2009; 120: 16–23.
5. Ownsworth T, McKenna K. Investigation of factors related to employment outcome following traumatic brain injury: a critical review and conceptual model. Disabil Rehabil 2004; 26: 765–783.
6. Sigurdardottir S, Andelic N, Roe C, Schanke AK. Cognitive recovery and predictors of functional outcome 1 year after traumatic brain injury. J Int Neuropsychol Soc 2009; 15: 740–750.
7. Shames J, Treger I, Ring H, Giaquinto S. Return to work following traumatic brain injury: trends and challenges. Disabil Rehabil 2007; 29: 1387–1395.
8. Doctor JN, Castro J, Temkin NR, Fraser RT, Machamer JE, Dikmen SS. Workers' risk of unemployment after traumatic brain injury: a normed comparison. J Int Neuropsychol Soc 2005; 11: 747–752.
9. van Velzen JM, van Bennekom CA, Edelaar MJ, Sluiter JK, Frings-Dresen MH. How many people return to work after acquired brain injury?: a systematic review. Brain Inj 2009; 23: 473–488.
10. Franulic A, Carbonell CG, Pinto P, Sepulveda I. Psychosocial adjustment and employment outcome 2, 5 and 10 years after TBI. Brain Inj 2004; 18: 119–129.
11. Kreutzer JS, Marwitz JH, Walker W, Sander A, Sherer M, Bogner J, et al. Moderating factors in return to work and job stability after traumatic brain injury. J Head Trauma Rehabil 2003; 18: 128–138.
12. Olver JH, Ponsford JL, Curran CA. Outcome following traumatic brain injury: a comparison between 2 and 5 years after injury. Brain Inj 1996; 10: 841–848.
13. Fleming J, Tooth L, Hassell M, Chan W. Prediction of community integration and vocational outcome 2–5 years after traumatic brain injury rehabilitation in Australia. Brain Inj 1999; 13: 417–431.
14. Devitt R, Colantonio A, Dawson D, Teare G, Ratcliff G, Chase S. Prediction of long-term occupational performance outcomes for adults after moderate to severe traumatic brain injury. Disabil Rehabil 2006; 28: 547–559.
15. WHO. The International Classification of Functioning, Disability and Health-ICF. Geneva: World Health Organization; 2001.
16. Arango-Lasprilla JC, Rosenthal M, Deluca J, Komaroff E, Sherer M, Cifu D, et al. Traumatic brain injury and functional outcomes: does minority status matter? Brain Inj 2007; 21: 701–708.
17. Arango-Lasprilla JC, Kreutzer JS. Racial and ethnic disparities in functional, psychosocial, and neurobehavioral outcomes after brain injury. J Head Trauma Rehabil 2010; 25: 128–136.
18. Andelic N, Stevens LF, Sigurdardottir S, Arango-Lasprilla JC, Roe C. Associations between disability and employment 1 year after traumatic brain injury in a working age population. Brain

Inj 2012; 26: 261–269.
19. Gollaher K, High W, Sherer M, Bergloff P, Boake C, Young ME, et al. Prediction of employment outcome one to three years following traumatic brain injury (TBI). Brain Inj 1998; 12: 255–263.
20. Whiteneck G, Brooks CA, Mellick D, Harrison-Felix C, Terrill MS, Noble K. Population-based estimates of outcomes after hospitalization for traumatic brain injury in Colorado. Arch Phys Med Rehabil 2004; 85 (4 Suppl 2): S73–S81.
21. Vogenthaler DR, Smith KR Jr, Goldfader P. Head injury, a multivariate study: predicting long-term productivity and independent living outcome. Brain Inj 1989; 3: 369–385.
22. Johansson U, Bernspang B. Predicting return to work after brain injury using occupational therapy assessments. Disabil Rehabil 2001; 23: 474–480.
23. Borg J, Roe C, Nordenbo A, Andelic N, de BC, Af Geijerstam JL. Trends and challenges in the early rehabilitation of patients with traumatic brain injury: a Scandinavian perspective. Am J Phys Med Rehabil 2011; 90: 65–73.
24. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
25. Willer B, Ottenbacher KJ, Coad ML. The community integration questionnaire. A comparative examination. Am J Phys Med Rehabil 1994; 73: 103–111.
26. Sander AM, Fuchs KL, High WM, Jr, Hall KM, Kreutzer JS, Rosenthal M. The Community Integration Questionnaire revisited: an assessment of factor structure and validity. Arch Phys Med Rehabil 1999; 80: 1303–1308.
27. Klonoff PS, Watt LM, Dawson LK, Henderson SW, Gehrels JA, Wethe JV. Psychosocial outcomes 1–7 years after comprehensive milieu-oriented neurorehabilitation: the role of pre-injury status. Brain Inj 2006; 20: 601–612.
28. Ip RY, Dornan J, Schentag C. Traumatic brain injury: factors predicting return to work or school. Brain Inj 1995; 9: 517–532.
29. Ponsford JL, Olver JH, Curran C, Ng K. Prediction of employment status 2 years after traumatic brain injury. Brain Inj 1995; 9: 11–20.
30. Keyser-Marcus LA, Bricout JC, Wehman P, Campbell LR, Cifu DX, Englander J, et al. Acute predictors of return to employment after traumatic brain injury: a longitudinal follow-up. Arch Phys Med Rehabil 2002; 83: 635–641.
31. Dikmen SS, Temkin NR, Machamer JE, Holubkov AL, Fraser RT, Winn HR. Employment following traumatic head injuries. Arch Neurol 1994; 51: 177–186.
32. Greenspan AI, Wrigley JM, Kresnow M, Branche-Dorsey CM, Fine PR. Factors influencing failure to return to work due to traumatic brain injury. Brain Inj 1996; 10: 207–218.
33. Walker WC, Marwitz JH, Kreutzer JS, Hart T, Novack TA. Occupational categories and return to work after traumatic brain injury: a multicenter study. Arch Phys Med Rehabil 2006; 87: 1576–1582.
34. Gary KW, Arango-Lasprilla JC, Ketchum JM, Kreutzer JS, Copolillo A, Novack TA, et al. Racial differences in employment outcome after traumatic brain injury at 1, 2, and 5 years postinjury. Arch Phys Med Rehabil 2009; 90: 1699–1707.
35. Ketchum JM, Almaz GM, Krch D, Banos JH, Kolakowsky-Hayner SA, Lequerica A, et al. Early predictors of employment outcomes 1 year post traumatic brain injury in a population of Hispanic individuals. NeuroRehabilitation 2012; 30: 13–22.
36. Stergiou-Kita M, Dawson DR, Rappolt SG. An integrated review of the processes and factors relevant to vocational evaluation following traumatic brain injury. J Occup Rehabil 2011; 21: 374–394.
37. Morton MV, Wehman P. Psychosocial and emotional sequelae of individuals with traumatic brain injury: a literature review and recommendations. Brain Inj 1995; 9: 81–92.
38. Engberg AW, Teasdale TW. Psychosocial outcome following traumatic brain injury in adults: a long-term population-based follow-up. Brain Inj 2004; 18: 533–545.
39. Tingvoll WA, Snelltvedt T, Haggblom A. Patient rehabilitation in hospitals a prioritized discipline after hospital reform: a Norwegian perspective. J Nurs Manag 2010; 18: 767–775.
40. Bowman ML. Ecological validity of neuropsychological and other predictors following head injury. The Clinical Neuropsychologist 1996; 10: 382–396.
41. Schanke AK, Rike PO, Molmen A, Osten PE. Driving behaviour after brain injury: a follow-up of accident rate and driving patterns 6–9 years post-injury. J Rehabil Med 2008; 40: 733–736.

J Rehabil Med 2013; 45: 808–814

ORIGINAL REPORT

DEPRESSIVE SYMPTOMS AND PSYCHOLOGICAL DISTRESS DURING THE FIRST FIVE YEARS AFTER TRAUMATIC BRAIN INJURY: RELATIONSHIP WITH PSYCHOSOCIAL STRESSORS, FATIGUE AND PAIN

Solrun Sigurdardottir, PhD[1,2], Nada Andelic, MD, PhD[2], Cecilie Røe, MD, PhD[2,3] and Anne-Kristine Schanke, PhD[1,4]

From the [1]Department of Research, Sunnaas Rehabilitation Hospital, Nesoddtangen, [2]Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval, [3]Faculty of Medicine, University of Oslo and [4]Department of Psychology, Faculty of Social Sciences, University of Oslo, Oslo, Norway

Objective: **To determine the prevalence of depressive symptoms among individuals with traumatic brain injury and to identify predictors of depressive symptoms and psychological distress.**

Design: **A longitudinal study with assessments at 3 months, 1 year and 5 years after injury.**

Subjects: **A total of 118 individuals (29% females; mean age 32.5; range 16–55 years) with mild-to-severe traumatic brain injury who were hospitalized in the Trauma Referral Centre from 2005 to 2007.**

Methods: **Self-report assessments using the Hospital Anxiety and Depression Scale, the Symptom Checklist 90-Revised and the Fatigue Severity Scale. Injury severity, trauma scores, pain, fatigue, substance abuse and demographic characteristics were also recorded.**

Results: **The prevalence of depressive symptoms was 18% at 3 months, 13% at 1 year and 18% at 5 years after injury. Only 4% had persistent depressive symptoms at all time-points. At 1 year post-injury, anxiety, age, ongoing stressors and employment status predicted depressive symptoms ($R^2 = 0.43$, $p < 0.001$), and ongoing stressors, employment status, fatigue and pain predicted psychological distress ($R^2 = 0.45$, $p < 0.001$).**

Conclusion: **Psychosocial stressors and employment status contributed to depressive symptoms and psychological distress, whereas injury severity did not have any predictive value. The prevalence of depressive symptoms remained stable over time, emphasizing the importance of recognizing and treating depression early after the injury.**

Key words: traumatic brain injury; depression; anxiety; psychosocial; fatigue; pain.

J Rehabil Med 2013; 45: 808–814

Correspondence address: Solrun Sigurdardottir, Sunnaas Rehabilitation Hospital, NO-1450 Nesoddtangen, Norway. E-mail: solrun.sigurdardottir@sunnaas.no

Accepted March 12, 2013

INTRODUCTION

Traumatic brain injury (TBI), defined as injury to brain tissue caused by an external trauma, is a life-changing event that may result in persistent or progressive psychiatric disturbances. A significant proportion (30%) of individuals with TBI experience psychiatric disorders during the first year after TBI (1). A study found that 65% of individuals with TBI received at least one psychiatric diagnosis up to 5.5 years after injury (2). Most studies that have followed individuals with TBI for 1 year or more after injury have found that anxiety and depression are the most common symptoms reported by these individuals (3–5). The prevalence of depression reported in the literature varies from 17% to 53% (1, 6, 7), and this variation is mostly due to the use of different instruments and procedures, or to differences in the study population and design. Other potential disorders are anxiety, varying from 10% to 29% (1, 6); post-traumatic stress disorder, varying from 10% to 27% (8, 9); and substance abuse disorders, varying from 10% to 25% (1, 5, 10).

The relationships between psychiatric disorders and TBI are multidimensional, with biological, psychological, and social contributors, as demonstrated in reviews of the literature (11, 12). Most researchers consider depression after TBI to have a complex aetiology, in which acute depression is more associated with biological mechanisms (4) and chronic depression is more related to psychosocial factors (13). The literature suggests that factors such as pre-existing psychiatric or depressive disorders (4, 7), female gender (2), increasing age (14), lower education level (2, 15, 16), unemployment (15, 17, 18), pain (2, 13), and substance abuse (3, 7, 15) may play roles in the development of depression after TBI. However, there are inconsistent findings with respect to the relationships between depression and pre-existing psychiatric disorders (5, 13, 15), gender effects (4, 17) and education level (4).

Depression appears to be unrelated to TBI severity and is found in all TBI severity groups (mild, moderate, severe) during the first year or longer after injury (4, 11). One study found that 27% of individuals with moderate-to-severe TBI met the criteria for major depression 10–126 months after injury, and that neither TBI severity nor the time since injury was correlated with depression (17). However, a study of 520 veterans 50 years after head injury (16) indicated that the severity of the head injury was positively related to the lifetime risk of major depression. Several studies that investigated depression beyond 2 years after TBI have assessed patients at one time-point with no longitudinal collection of data (5, 16, 19, 20). However, longitudinal studies are few; some indicate that depression may

increase over time (3, 6), in contrast to other studies (15, 21). Chronically depressed TBI individuals have been found to be more likely to have poorer psychosocial functioning (13) and to experience higher levels of psychological distress compared with their non-depressed counterparts (22). Studies have shown that concurrent psychiatric disorders predict psychosocial and functional outcomes during the first year after TBI (6). However, these relationships are unclear, as depression may either lead to, or be an effect of, poor psychosocial functioning (23).

Some of the trends in epidemiology, acute management and rehabilitation in Scandinavia have been described by Borg et al. (24), who emphasized the importance of a continuous chain of medical care after TBI. However, there have been few longitudinal studies in the areas of psychology and psychiatry in Scandinavia that illustrate the influence of specific injury-related and clinical variables on depressive symptoms after TBI. Moreover, much is known about the point prevalence of depression, but less is known about the long-term course of depressive symptoms. This longitudinal study including individuals with varying TBI severity based on clinical evaluations at 3 different time-points and assessed multiple variables, including injury severity, depressive symptoms, psychosocial stressors, fatigue and pain.

The aims of this study were as follows:

- to determine the prevalence of depressive symptoms after TBI over time (3 months, 1 year and 5 years post-injury);
- to examine changes in depressive symptoms and other symptoms of psychological distress over time (3 months, 1 year and 5 years post-injury);
- to determine if depressive symptoms and psychological distress have overlapping predictors (demographic characteristics, injury-related variables, psychosocial stressors, fatigue and pain).

METHODS

Design and participants

A longitudinal prospective study of individuals admitted to the Trauma Referral Centre of Oslo University Hospital, Ulleval, Norway, with acute TBI during the period May 2005 to May 2007 was conducted. Inclusion criteria were: (*i*) age 16–55 years; (*ii*) admission within 24 h of injury; (*iii*) computed tomography (CT) brain scan performed within 24 h of injury; and (*iv*) fluent Norwegian speaker. Individuals were excluded (non-eligible) if they had any of the following: (*i*) severe substance abuse ($n=14$); (*ii*) a known severe psychiatric disorder ($n=7$) or previous brain pathology ($n=6$); or (*iii*) associated spinal cord injury ($n=3$). Severe substance abuse was defined as a previous diagnosis of illicit substance abuse/dependence or alcohol abuse/dependence according to the International Classification of Diseases (ICD-10) diagnosis of substance use disorders. Severe psychiatric disorders included, for example, schizophrenia or recent attempted suicide. The initial severity of TBI was measured using the Glasgow Coma Scale (GCS) (25) score determined at admission to the emergency department at the hospital or prior to intubation at the accident site. As shown in Fig. 1, 296 individuals fulfilled the inclusion criteria. All potential individuals in the age range 16–55 years ($n=270$) received a letter containing information about the study 4–6 weeks after injury. The participants ($n=118$) and non-participants ($n=133$) did not differ with respect to age, gender, GCS, cause of injury, loss of consciousness, or duration of post-traumatic amnesia (PTA). However, significantly more participants with moderate-to-severe TBI ($n=78$) than non-participants with moderate-to-severe TBI ($n=27$) had an intracranial pathology (85% vs 63%, respectively $\chi^2(1)=6.0$, $p<0.05$). A total of 118 individuals (84 males, 34 females) were included and participated at 3 months after injury. At 1 year, 109 of the 118 originally included individuals (78 males, 31 females) participated and at 5 years 89 individuals (63 males, 26 females) completed the follow-up (see Fig. 1). Individuals lost to follow-up at 5 years were significantly more often unemployed at the time of injury (45%) than those who completed the study (13%) $\chi^2(1)=12.9$, $p<0.001$, and had more often mild TBI (59%) than those who completed the study (26%) $\chi^2(1)=10.5$, $p<0.001$, but those lost to follow-up at 5 years and those who completed the study did not differ significantly with respect to other demographic, substance abuse, or injury-related variables.

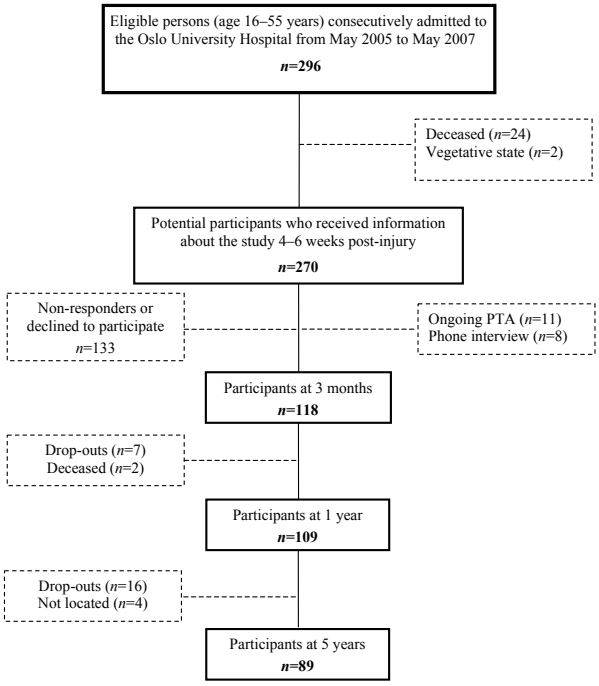


Fig. 1. Included individuals admitted to the hospital after traumatic brain injury. PTA: post-traumatic amnesia.

Evaluations were performed at 3 months, 1 year and 5 years post-injury. Most of the patients were assessed at the out-patient department of Oslo University Hospital. Those participants who received inpatient rehabilitation at 3 months or medical care follow-up at 1 year were assessed during their hospital stay at Sunnaas Rehabilitation Hospital. Participants underwent neuropsychological examinations (collected for a parallel study) before they completed a set of questionnaires. The time required to complete the examination was approximately 3 h. Written consent was obtained from all participants. No control group was used in this study. The Regional Committee for Medical Research Ethics, East-Norway, and the Norwegian Data Inspectorate approved this study according to the Declaration of Helsinki.

Measurements

Individuals with TBI were interviewed at 3 months, 1 year and 5 years after injury to provide information related to demographic characteristics (age, gender, education, and marital status), employment status and psychosocial situation. The pre-injury (for the last year) and post-injury (1 year) employment statuses were dichotomized into productive work/employment (employed full-/part-time or full-/part-time student) and unemployment (unemployed, sick leave, homemaker, disability pension, and other). An inclusive definition of employment was used

that included other productive activities, such as studying, as described in our previous studies on TBI (19, 26).

A semi-structured psychological interview, based on clinical experiences and relevant literature, was developed by a research group of 5 psychologists at Sunnaas Rehabilitation Hospital (27). Previous studies have published this interview on multiple traumas and spinal cord injuries (27) and polio survivors (28). This interview was used in the current study to assess the participants' psychosocial situations and stress loads. The pre-injury (for the last year) and post-injury (1 year) psychosocial factors assessed in this interview were rated as "Yes" or "No" for 8 items (stressors): serious illness, psychiatric illness requiring therapy, serious illness or death of a close family member, marital problems, economic problems, substance abuse, feeling isolated or lonely, and other related problems (27). Substance abuse was evaluated using the Cut down, Annoyed, Guilty, Eye-opener (CAGE cut-off ≥2), and responses were dichotomized into "Yes" or "No". Individuals also completed self-report questionnaires to provide measures of depression, anxiety, psychological distress, fatigue, and pain at 3 months, 1 year and 5 years post-injury. Symptoms of depression and anxiety during the previous 7 days were measured using the validated Norwegian version of the Hospital Anxiety and Depression Scale (HADS) (29). Both HADS subscales consist of 7 items rated on a 4-point scale from 0 (no symptom) to 3 (a severe symptom). The cut-off score >7 was used to indicate at least a mild, but significant, level of depressive symptoms. Distress symptomatology was evaluated using the validated Norwegian translation of the Symptom Checklist 90-Revised (SCL-90-R) (30). This questionnaire measures emotional distress during the previous 7 days and consists of 90 items rated on a 5-point scale from 0 (not at all) to 4 (extremely). The 90 scores are transferred to a profile sheet of 9 symptom dimensions (Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism) and provide a Global Severity Index (GSI) that represents overall psychological distress. In this study, depression was operationalized by scores above the cut-off on 2 scales to avoid false positives: the HADS-Depression subscale (scores >7) and the SCL-90-R Depression symptom dimension (T scores ≥63). This operational definition does not fulfil the ICD-10 criteria for major depression requiring treatment. The severity of fatigue related to daily activities was assessed using the Norwegian translation of the Fatigue Severity Scale (FSS) (31). This scale contains 9 items rated on a 7-point scale, from 1 (strongly disagree) to 7 (strongly agree). The severity of pain during the previous 7 days was measured using a visual analogue scale for pain (VAS-P) and was rated on a 100-mm horizontal line, ranging from 0 (indicating no pain) to 100 (very severe pain).

All persons underwent CT scanning within 24 h after injury. Magnetic resonance imaging (MRI) scans were performed on 104 participants at 1-year follow-up. The trauma scores of the Abbreviated Injury Scale (AIS) (32) and the Injury Severity Score (ISS) (33) were extracted from the Trauma Registry of the Oslo University Hospital, Ulleval. An AIS_{head} score from 3 to 5 indicates increasingly severe intracranial pathology. An ISS greater than 15 is accepted as the definition of major trauma.

Statistical analysis

Chi-square tests were conducted to analyse the frequencies of demographic characteristics, injury-related variables, and psychosocial situations and to compare the percentages of males and females who met the criteria for depression, as stated above. Data obtained from questionnaires (mean, standard deviation (SD)) were analysed by repeated-measures analysis of variance (ANOVA) (within-subjects) at 3 months, 1 year, and 5 years. A total of 89 (of the original 118) individuals participated at 5 years; a response rate of nearly 75%. This reduction affected the power of the statistical analysis and the number of potential predictors in the regression analyses. Regression analyses were therefore performed on the 1-year data of 106 participants. To reduce the effect of multiple comparisons, only two regression models were chosen. The HADS-Depression score was chosen as the dependent variable in the regression analysis because this scale is one of the most common measures of depression used in TBI studies (34). For the first model, linear regression analysis (backward selection) was conducted to explore the associations between the HADS-Depression score at 1 year and demographic variables (age, gender, and education), injury severity (ISS in the acute phase), employment status (pre-injury and at 1 year), psychosocial situation (pre-existing and at 1 year), and scores on the FSS, VAS-P, and SCL-90-R Anxiety scales. For the second model, the associations between GSI (SCL-90-R) at 1 year and demographic variables (age, gender, and education), injury severity (ISS in the acute phase), employment status (pre-injury and at 1 year), psychosocial situation (pre-existing and at 1 year), and scores on the FSS and VAS-P were assessed. The AIS_{head} was excluded from the analyses due to strong correlations ($r > 0.70$) with the GCS and ISS. A sample size of 106 individuals at 1 year, including 11 predictors, had a sufficient power of 0.86 for a medium effect size ($f^2 = 0.20$). Significance was assumed for p-values < 0.05 for all statistical analyses (two-tailed). Data analyses were performed using PASW® Statistics 18.

RESULTS

Characteristics of participants and psychosocial stressors

Individuals' demographic characteristics, pre- and post-injury psychosocial variables, and injury-related data are presented in Table I. The mean age at the time of injury was 32.5 years (SD 11.1) and the mean length of education 13.2 years (SD 2.5). In our sample, 66% of patients sustained a moderate-to-severe TBI (GCS 3–12) and 34% sustained a mild TBI (GCS 13–15). Transport accidents caused the injury in 46% of individuals, followed by falls (27%), assaults (19%) and other causes (8%). A considerable number of individuals had substance abuse problems and unemployment.

Pre-existing psychosocial stressors were summed to provide an overall score, resulting in a mean score of 1.4 (SD 1.4, range 0–6, $n = 117$). Pre-existing stressors were as follows (from most to least frequent): serious illness or death of a close family member (27%), substance abuse CAGE >2 (24%), psychiatric illness requiring

Table I. *Demographics, pre-injury information and injury severity of individuals with traumatic brain injury (*n = *118)*

	TBI sample *n* (%)
Males	84 (71)
Females	34 (29)
Single at the time of injury	82 (70)
Unemployed pre-injury	25 (21)
Unemployed at 1 year[a]	35 (32)
Substance abuse pre-injury[a]	28 (24)
Substance abuse at 1 year[a]	20 (19)
Substance abuse at 5 years[a]	22 (25)
Glasgow Coma Scale score 3–12	78 (66)
Glasgow Coma Scale score 13–15	40 (34)
Traffic accident cause of injury	54 (46)
Abbreviated Injury $Scale_{head}$ ≥3	80 (68)
Injury Severity Score ≥15	72 (61)
CT acute intracranial findings	72 (61)
MRI intracranial findings at 1-year[a]	75 (73)
Post-traumatic amnesia >7 days	51 (43)

[a]Data missing for: unemployed 1 year post-injury ($n = 10$), MRI ($n = 14$), substance abuse pre-injury ($n = 1$), substance abuse at 1 year ($n = 13$), substance abuse at 5 years ($n = 31$).
TBI: traumatic brain injury; CT: computed tomography; MRI: magnetic resonance imaging.

therapy (15%), marital problems (11%), serious medical illness (11%), economic problems (10%), feeling isolated or lonely (9%), and other stressors (20%), such as being in prison (4%), prior trauma (3%) or work-related stress (3%). Psychosocial stressors at 1 year were also summed to provide an overall score used in the regression analysis, resulting in a mean score of 1.3 (SD 1.6, range 0–7, $n=105$). The frequency of these stressors were as follows: psychiatric illness requiring therapy (24%), substance abuse CAGE > 2 (19%), economic problems (19%), feeling isolated or lonely (18%), serious illness or death of a close family member (17%), serious medical illness (11%), marital problems (2%), and other stressors (21%) such as waiting for a trial/serving a sentence (6%), or not having a driving licence (2%).

Frequency and predictors of depressive symptoms

The percentage of individuals reporting depressive symptoms was relatively stable over time from 18% at 3 months ($n=20$), 13% at 1 year ($n=14$), and 18% at 5 years post-injury ($n=16$). No effects of TBI severity (mild vs moderate-to-severe), marital status or education level on depressive symptoms were observed at the 3 time-points (all p-values > 0.05). The prevalence of depressive symptoms differed substantially between genders ($\chi^2=6.5$, $p=0.011$) at 1 year, but not at 3 months or 5 years. Depressive symptoms were observed in 18% of males and none of the females at 1 year. Of the 105 individuals who participated in both the 3- and 12- months follow-up assessments, 22% ($n=23$) reported significant depressive symptoms at least once during the first year. Of the 83 individuals who were assessed at all time-points, 28% ($n=23$) had depressive symptoms at least once during the 5-year period after the injury. Only 4% ($n=3$) had persistent depressive symptoms at all time-points.

Regression analysis was performed using the HADS-Depression score at 1 year as the dependent variable. Because depression and anxiety often co-exist (4), the SCL-90-R Anxiety dimension at 3 months was included in the regression analysis. Pearson's correlation coefficient for the association between the HADS-Depression and SCL-90-R Anxiety scores was $r=0.51$, $p<0.001$. Table II shows that higher levels of anxiety at 3 months (SCL-90-R Anxiety dimension), a high number of ongoing psychosocial stressors, older age, being employed pre-injury and being unemployed post-injury were the main predictors of depressive symptoms. These 5 variables accounted for 43% of the variance ($F_{5,101}=14.7$, $p=0.001$). *Post-hoc* analysis using *t*-tests showed that individuals who had high levels of depressive symptoms at 1 year (HADS-Depression > 7 and SCL-90-R Depression ≥ 63), had significantly higher numbers of pre-existing psychosocial stressors (2.1 (SD 1.7)) compared with those with low levels of depressive symptoms (1.1 (SD 1.2)) ($p<0.01$). Individuals who had high levels of depressive symptoms at 1 year also had higher numbers of ongoing psychosocial stressors (2.9 (SD 1.7)) than their counterparts (1.1 (SD 1.3)) ($p<0.001$).

Table II. *Regression coefficients (B,β) with 95% confidence intervals (CI) for predictors of depressive symptoms (HADS-Depression) at 1 year after injury*

Independent variables	B	β	95% CI (B)	*p*-value
Constant	–4.55		–7.29 to –1.83	
SCL-90-R Anxiety at 3 months	0.08	0.38	0.04 to 0.11	0.001
Psychosocial stressors at 1 year[a]	0.70	0.28	0.25 to 1.15	0.003
Employment at 1 year	1.93	0.24	0.38 to 3.47	0.015
Age at injury	0.06	0.19	0.01 to 0.12	0.021
Employment pre-injury	–1.70	–0.18	–3.58 to 0.19	0.078

$R^2=0.43$, adjusted $R^2=0.40$.
HADS: Hospital Anxiety and Depression Scale; SCL-90-R: Symptom Checklist 90-Revised.
[a]Medical or psychiatric illness, serious illness or death in family, marital problems, economic problems, substance abuse, feeling isolated or other problems.

Table III. *Results of questionnaires at 3 months, 1 year and 5 years post-injury, as calculated with repeated measures of analysis of variance (*n = *83)*

	3 months Mean (SD)	1 year Mean (SD)	5 years Mean (SD)	*F*	*p*-value
Hospital Anxiety and Depression Scale					
Anxiety (total score)	4.6 (3.8)	4.6 (4.2)	5.8 (4.5)	5.89	0.01*
Depression (total score)	3.7 (3.5)	3.2 (3.5)	4.4 (3.8)	4.51	0.01*
Symptom checklist-90-R (T-scores)					
Global Severity Index	55.6 (15.1)	54.8 (12.5)	58.6 (17.2)	2.82	0.07
Somatization	57.3 (14.5)	55.2 (13.8)	57.0 (15.1)	1.20	0.30
Obsessive-Compulsive	58.4 (15.7)	59.0 (15.5)	62.1 (17.6)	3.27	0.05*
Interpersonal Sensitivity	50.3 (11.5)	51.1 (10.4)	54.8 (15.4)	7.75	0.001*
Depression	57.3 (15.5)	54.9 (13.6)	59.3 (18.4)	4.09	0.02*
Anxiety	55.6 (16.4)	53.7 (15.4)	57.2 (18.0)	2.89	0.06
Hostility	49.9 (10.0)	50.3 (9.6)	54.3 (14.0)	8.39	0.001*
Phobic Anxiety	56.9 (20.9)	54.7 (17.2)	59.3 (27.9)	2.21	0.12
Paranoid Ideation	50.7 (13.1)	49.9 (9.6)	53.3 (15.3)	3.68	0.03*
Psychoticism	51.4 (14.3)	50.3 (11.0)	52.7 (13.4)	1.74	0.18
Fatigue Severity Scale (total score)	3.8 (1.8)	3.8 (1.8)	4.0 (1.7)	0.45	0.62
Pain Visual Analogue Scale (1–100 mm)	25 (25)	20 (25)	24 (27)	1.60	0.21

*Significant within-subjects effect.
SD: standard deviation.

Table IV. *Regression coefficients (B,β) with 95% confidence intervals (CI) for predictors of psychological distress (SCL-90-R: Global Severity Index) at 1 year after injury*

Independent variables	B	β	95% CI (B)	*p*-value
Constant	28.12		19.09 to 37.15	
Psychosocial stressors at 1 year[a]	4.73	0.43	2.66 to 6.81	0.001
Fatigue Severity Scale	2.88	0.31	1.33 to 4.43	0.001
Employment pre-injury	9.64	0.23	2.40 to 16.89	0.010
Psychosocial stressors pre-existing[a]	–2.35	–0.20	–4.65 to –0.05	0.045
Visual analogue scale for pain	1.04	0.23	–0.05 to –2.11	0.054

R^2=0.45, adjusted R^2=0.42.
SCL-90-R: Symptom Checklist 90-Revised.
[a]Medical or psychiatric illness, serious illness or death in family, marital problems, economic problems, substance abuse, feeling isolated or other problems.

Changes in psychological distress

Table III presents the results obtained from the questionnaires addressing aspects of psychological distress (SCl-90-R), fatigue (FSS) and pain (VAS-P). A total of 83 individuals completed the SCL-90-R at all time-points. The raw SCL-90-R scores were converted into gender-adjusted T-scores as suggested by Derogatis (30). Repeated-measures ANOVA (within-subjects) using the Greenhouse-Geisser adjustment revealed a significant increase in the scores from 3 months to 5 years for 5 dimensions of the SCL-90-R. The FSS and VAS-Pain scores did not vary significantly over time ($p > 0.05$). The mean FSS scores were similar to the mean score of 3.98 for the Norwegian population (31).

Predictors of psychological distress

Regression analysis was performed using the GSI (SCL-90-R) at 1 year as the dependent variable. Table IV shows that a high number of ongoing psychosocial stressors, a low number of pre-existing stressors, being unemployed before injury, and higher levels of fatigue and pain at 3 months, emerged as the best predictors of psychological distress at 1 year, explaining 45% of the variance ($F_{5,101}$=15.6, p=0.001).

Correlations between measurements are reported in Table V. The data from questionnaires investigating depressive symptoms were highly correlated with the GSI (SCL-90-R) and psychosocial stressors at 1 year (Pearson's two-tailed correlations). Substance abuse at 1 year was correlated with psychosocial stressors (Spearman's two-tailed correlations).

DISCUSSION

This longitudinal study investigated the relationships between depressive symptoms and potential predictors in a sample of hospitalized individuals with mild to severe TBI. The prevalence of depressive symptoms was found to be stable over a 5-year period. High levels of depressive symptoms were a significant problem in 18% of individuals at 3 months, 13% at 1 year, and 18% at 5 years after injury. Among demographic, injury-related and clinical factors, anxiety and ongoing psychosocial stressors were the strongest predictors of depressive symptoms (HADS), together with increasing age, being employed before injury and being unemployed post-injury. Psychological distress symptoms (SCL-90-R GSI) were more strongly predicted by ongoing psychosocial stressors than by pre-existing stressors, together with pre-injury unemployment and higher levels of fatigue and pain.

In our study, the frequencies of depressive symptoms were similar to those found by Bryant et al. (1), who reported that 18% of patients had depression at 3 months and 17% had depression at 1 year after mild TBI. Our results are also consistent with those of another study (15), which found that 17% of patients had depression 3–5 years after moderate-to-severe TBI. In a recent longitudinal study, the prevalence of depression was found to be 26% at both 1 and 2 follow-up years after injury and 75% of those with depression at 1 year had significant symptoms at 2 years (6). Another study assessed depression at 3 months up to 4 years after TBI, using repeated clinical interviews 1 year apart (21), and 35% of subjects reported depression at the initial assessment, 24% at the second, and 21% at the third. A Norwegian study found a prevalence of depressive symptoms of 31% at 10 years after moderate-to-severe TBI (19). Currently, there is firm evidence that the prevalence of depression (> 30–50%) is high after TBI (1, 6, 7, 19, 21) relative to the 12-month prevalence rates of 4.2%–10.3% for the general population (35, 36). In this study, 22% of patients developed high levels of depressive symptoms at least once during the first year after injury and 28% at least

Table V. *Correlations between measures of depressive symptoms (HADS and SCL-90-R), Global Severity Index (GSI: SCL-90-R), FSS, VAS-P, CAGE, and psychosocial stressors*

	GSI	FSS	VAS-P	CAGE	Stressors pre-injury	Stressors at 1 year	HADS-Depression
Depression dimension (SCL-90-R)	0.94***	0.41***	0.27***	0.11	0.23*	0.46***	0.72***
Global Severity Index (SCL-90-R) at 1 year		0.45***	0.39***	0.11	0.22*	0.48***	0.72***
Fatigue Severity Scale (FSS) at 3 months			0.42***	0.05	0.17	0.12	0.28**
VAS-Pain at 3 months				–0.05	0.20*	0.24*	0.31**
CAGE at 1 year					0.22[a]	0.28[b]	0.04
Psychosocial stressors pre-injury						0.59***	0.28**
Stressors at 1 year							0.50***

*Pearson's correlation (p <0.05), **Pearson's correlation (p <0.01), ***Pearson's correlation (p <0.001).
[a]Spearman's correlation (p <0.05), [b]Spearman's correlation (p <0.01).
SCL-90-R: Symptom Checklist 90-Revised; VAS-P: visual analogue scale for pain; CAGE: Cut down, Annoyed, Guilty, Eye-opener.

once during the 5-year period after injury. Overall, 4% reported high levels of depressive symptoms at all time-points (chronic cases). Other studies found that 33–53% of subjects met the criteria for depression during the first year after TBI (4, 7) and 46–52% during the first 5 years (5, 13), with 14% defined as chronic cases (13). The results of our study are consistent with previous findings, indicating that injury severity (ISS) does not predict depressive symptoms (1, 13, 15, 17).

According to the literature, females are expected to experience depression more often than males (35). However, in this study males reported more depressive symptoms than females at 1 year. Another study found this same gender difference in the TBI population (15) and regarded it as a finding of chance. Several possibilities could explain this difference. First, males may not be receiving medical or psychological treatment for their depression during the first year, in contrast to females, who may receive more attention and treatment for their depression. Secondly, the number of females in this study was small at one year ($n = 31$) and, by chance, none had experienced depressive symptoms.

Anxiety was expected to contribute to depressive symptoms, as a high frequency of depression and anxiety co-morbidity (73.5%) was documented in the study by Whelan-Goodinson et al. (5). In the present study, anxiety at 3 months was identified as the strongest predictor for depressive symptoms at 1 year. Another study found that individuals with co-existing depression and anxiety had longer durations of symptoms than those who were only depressed (4). Other studies have found that depression can co-exist with other psychiatric conditions, such as substance abuse and post-traumatic stress disorder (1, 3, 6, 7, 9).

In this study, repeated measures revealed that neither pain scores nor scores for fatigue (FSS) or somatic complaints (somatization dimension SCL-90-R) exhibited significant increases over time. In this study, fatigue and pain correlated moderately with depressive symptoms at 1 year, reflecting the complex interactions between physical and psychological disturbances in individuals with TBI. The most frequent symptom of depression is fatigue (20). Englander et al. (37) found that patients with TBI taking anti-depressant medications had higher fatigue scores, probably because of medication side-effects or that depression contributed to fatigue. Only a few studies have focused on pain and depression in the TBI population (13, 37, 38). Hibbard et al. (13) noted that pain had a greater impact on chronic depression after TBI, suggesting that pain served as a stimulus or maintainer of depressive symptoms. Another study (38) reported a higher prevalence rate of pain (66.7%) among TBI patients 1 year after injury, and found that depression was strongly associated with poorer pain outcomes. These findings are partly in contrast to those of the current study, which found that pain was not significantly associated with depression in the regression analysis but only on a bivariate level.

An important implication of the current study is that the employment status represents a sensitive indicator of depressive symptoms, in agreement with other studies (15, 17, 18). On the one hand, depression may delay or hinder recovery from TBI and may complicate the process of returning to work, school and social life (4, 13). On the other hand, an individual's decreased ability to function at work and at home due to biological, interpersonal and social disruptions may cause emotional distress that may further lead to the development of mood disorders (13, 23).

Disturbances in psychosocial function affecting employment situation and rehabilitation are often described in the TBI literature (13). As noted above, psychosocial stressors were not frequent in individuals without depressive symptoms and perhaps in some cases these stressors were normal psychological reactions. This study did not determine the type of stressors involved in depressive symptoms related to family (e.g. marital, economic problems) or psychological (e.g. substance abuse, previous psychiatric illness). At 5 years, 25% of individuals reported substance abuse (CAGE), i.e. approximately at the same level as pre-injury, but substance abuse was not found to correlate with depressive symptoms or general distress.

This study has a number of limitations. First, because of the small size of the sample, which was representative of the population (aged 16–55 years) in eastern Norway, caution should be exercised in when generalizing results to other populations. The sample attrition rate over time was systematic, not random; the participants that tended to stay in the study had moderate-to-severe TBI, thus biasing the long-term data toward more severe cases. Secondly, the exclusion of previous severe substance abuse or known previous psychiatric disorders ($n = 21$) may have resulted in the underestimation of pre-existing psychosocial stressors and psychiatric problems. Thirdly, the present study used two subscales of depression to estimate the prevalence of depressive symptoms. It is not known if these levels of depressive symptoms are sufficient to warrant a diagnosis of major depressive disorder. Recently, the HADS has been recognized to have a high rate of false negatives and to exhibit inconsistency in differentiating anxiety and depression (39). In this study, the HADS-Depression score was highly correlated with the GSI (SCL-90-R), a result that may support the finding that depressive items on the HADS consist of a non-specific component of general emotional reactions. The SCL-90-R has been divided into the "Brain Injury Scale" with 14 items and the remaining 76 SCL-90-R items. A previous study did not support this distinction (40) as the ratings for both scales were equally related to affective reactions, cognitive performance and behavioural disturbances related to brain injury. The findings of Hoofien et al. (40) indicate that the SCL-90-R is a valid measure of psychological distress for individuals with TBI.

The findings of this study indicate that psychosocial stressors and employment status contributed to depressive symptoms and psychological distress at 1 year after injury, whereas injury severity did not have any predictive value. The prevalence of depressive symptoms remained stable over time, emphasizing the importance of recognizing and treating depressive symptoms early after injury.

ACKNOWLEDGEMENTS

The authors are grateful to all the persons for their participation. The study was supported by grants from the South-Eastern Norway Regional Health

Authority. Thanks to Morten Hestnes and Nils Oddvar Skaga from the Oslo University Hospital's Trauma Registry, for the extraction of trauma scores, and Tone Jerstad, neuroradiologist, for the CT and MRI assessments.

REFERENCES

1. Bryant RA, O'Donnell ML, Creamer M, McFarlane AC, Clark CR, Silove D. The psychiatric sequelae of traumatic injury. Am J Psychiatry 2010; 167: 312–320.
2. Whelan-Goodinson R, Ponsford JL, Schonberger M, Johnston L. Predictors of psychiatric disorders following traumatic brain injury. J Head Trauma Rehabil 2010; 25: 320–329.
3. Hart T, Hoffman JM, Pretz C, Kennedy R, Clark AN, Brenner LA. A longitudinal study of major and minor depression following traumatic brain injury. Arch Phys Med Rehabil 2012; 93: 1343–1349.
4. Jorge RE, Robinson RG, Moser D, Tateno A, Crespo-Facorro B, Arndt S. Major depression following traumatic brain injury. Arch Gen Psychiatry 2004; 61: 42–50.
5. Whelan-Goodinson R, Ponsford J, Johnston L, Grant F. Psychiatric disorders following traumatic brain injury: their nature and frequency. J Head Trauma Rehabil 2009; 24: 324–332.
6. Gould KR, Ponsford JL, Johnston L, Schonberger M. Relationship between psychiatric disorders and 1-year psychosocial outcome following traumatic brain injury. J Head Trauma Rehabil 2011; 26: 79–89.
7. Bombardier CH, Fann JR, Temkin NR, Esselman PC, Barber J, Dikmen SS. Rates of major depressive disorder and clinical outcomes following traumatic brain injury. JAMA 2010; 303: 1938–1945.
8. Bryant RA, Marosszeky JE, Crooks J, Gurka JA. Posttraumatic stress disorder after severe traumatic brain injury. Am J Psychiatry 2000; 157: 629–631.
9. Bombardier CH, Fann JR, Temkin N, Esselman PC, Pelzer E, Keough M, et al. Posttraumatic stress disorder symptoms during the first six months after traumatic brain injury. J Neuropsychiatry Clin Neurosci 2006; 18: 501–508.
10. Ponsford J, Whelan-Goodinson R, Bahar-Fuchs A. Alcohol and drug use following traumatic brain injury: a prospective study. Brain Inj 2007; 21: 1385–1392.
11. Hesdorffer DC, Rauch SL, Tamminga CA. Long-term psychiatric outcomes following traumatic brain injury: a review of the literature. J Head Trauma Rehabil 2009; 24: 452–459.
12. van Reekum R, Cohen T, Wong J. Can traumatic brain injury cause psychiatric disorders? J Neuropsychiatry Clin Neurosci 2000; 12: 316–327.
13. Hibbard MR, Ashman TA, Spielman LA, Chun D, Charatz HJ, Melvin S. Relationship between depression and psychosocial functioning after traumatic brain injury. Arch Phys Med Rehabil 2004; 85: S43–S53.
14. Levin HS, McCauley SR, Josic CP, Boake C, Brown SA, Goodman HS, et al. Predicting depression following mild traumatic brain injury. Arch Gen Psychiatry 2005; 62: 523–528.
15. Dikmen SS, Bombardier CH, Machamer JE, Fann JR, Temkin NR. Natural history of depression in traumatic brain injury. Arch Phys Med Rehabil 2004; 85: 1457–1464.
16. Holsinger T, Steffens DC, Phillips C, Helms MJ, Havlik RJ, Breitner JC, et al. Head injury in early adulthood and the lifetime risk of depression. Arch Gen Psychiatry 2002; 59: 17–22.
17. Seel RT, Kreutzer JS, Rosenthal M, Hammond FM, Corrigan JD, Black K. Depression after traumatic brain injury: a National Institute on Disability and Rehabilitation Research Model Systems multicenter investigation. Arch Phys Med Rehabil 2003; 84: 177–184.
18. Franulic A, Carbonell CG, Pinto P, Sepulveda I. Psychosocial adjustment and employment outcome 2, 5 and 10 years after TBI. Brain Inj 2004; 18: 119–129.
19. Andelic N, Hammergren N, Bautz-Holter E, Sveen U, Brunborg C, Roe C. Functional outcome and health-related quality of life 10 years after moderate-to-severe traumatic brain injury. Acta Neurol Scand 2009; 120: 16–23.
20. Kreutzer JS, Seel RT, Gourley E. The prevalence and symptom rates of depression after traumatic brain injury: a comprehensive examination. Brain Inj 2001; 15: 563–576.
21. Ashman TA, Spielman LA, Hibbard MR, Silver JM, Chandna T, Gordon WA. Psychiatric challenges in the first 6 years after traumatic brain injury: cross-sequential analyses of Axis I disorders. Arch Phys Med Rehabil 2004; 85: S36–S42.
22. Bay E, Donders J. Risk factors for depressive symptoms after mild-to-moderate traumatic brain injury. Brain Inj 2008; 22: 233–241.
23. Taylor CA, Jung HY. Disorders of mood after traumatic brain injury. Semin Clin Neuropsychiatry 1998; 3: 224–231.
24. Borg J, Roe C, Nordenbo A, Andelic N, de Boussard C, af Geijerstam J-L. Trends and challenges in the early rehabilitation of patients with traumatic brain injury: a Scandinavian perspective. Am J Phys Med Rehabil 2011; 90: 65–73.
25. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
26. Sigurdardottir S, Andelic N, Roe C, Schanke AK. Cognitive recovery and predictors of functional outcome 1 year after traumatic brain injury. J Int Neuropsychol Soc 2009; 15: 740–750.
27. Quale AJ, Schanke AK, Froslie KF, Roise O. Severity of injury does not have any impact on posttraumatic stress symptoms in severely injured patients. Injury 2009; 40: 498–505.
28. Schanke AK. Psychologcial distress, social support and coping behaviour among polio survivors: a 5-year perspective on 63 polio patients. Disabil Rehabil 1997; 19: 108–116.
29. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the hospital anxiety and depression scale. An updated literature review. J Psychosom Res 2002; 52: 69–77.
30. Derogatis LR. SCL-90-R. Administration, scoring and procedures manual. Baltimore, MD: Clinical Psychometric Research Inc.; 1983.
31. Lerdal A, Wahl A, Rustoen T, Hanestad BR, Moum T. Fatigue in the general population: a translation and test of the psychometric properties of the Norwegian version of the fatigue severity scale. Scand J Public Health 2005; 33: 123–130.
32. Association for the Advancement of Automotive Medicine. The Abbreviated Injury Scale, revision 1998. Des Plains, IL: 1990.
33. Baker SP, O'Neill B, Haddon WJr, Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 1974; 14: 187–196.
34. Steel JL, Dunlavy AC, Stillman J, Pape HC. Measuring depression and PTSD after trauma: common scales and checklists. Injury 2011; 42: 288–300.
35. Kringlen E, Torgersen S, Cramer V. A Norwegian psychiatric epidemiological study. Am J Psychiatry 2001; 158: 1091–1098.
36. Gould KR, Ponsford JL, Johnston L, Schonberger M. The nature, frequency and course of psychiatric disorders in the first year after traumatic brain injury: a prospective study. Psychol Med 2011; 41: 2099–2109.
37. Englander J, Bushnik T, Oggins J, Katznelson L. Fatigue after traumatic brain injury: Association with neuroendocrine, sleep, depression and other factors. Brain Inj 2010; 24: 1379–1388.
38. Hoffman JM, Ragulayan KF, Zawaideh N, Dikmen S, Temkin N, Bell KR. Understanding pain after traumatic brain injury: impact on community participation. Am J Phys Med Rehabil 2007; 86: 962–969.
39. Cosco TD, Doyle F, Ward M, McGee H. Latent structure of the Hospital Anxiety And Depression Scale: a 10-year systematic review. J Psychosom Res 2012; 72: 180–184.
40. Hoofien D, Barak O, Vakil E, Gilboa A. Symptom checklist-90 revised scores in persons with traumatic brain injury: affective reactions or neurobehavioral outcomes of the injury? Appl Neuropsychol 2005; 12: 30–39.

J Rehabil Med 2013; 45: 815–819

ORIGINAL REPORT

FIFTEEN-YEAR FOLLOW-UP OF UPPER LIMB FUNCTION IN CHILDREN WITH MODERATE TO SEVERE TRAUMATIC BRAIN INJURY

Anne-Christine Åhlander, MD, PhD[1], Marika Persson, OT[1] and Ingrid Emanuelson, MD, PhD[2]

From the [1]Queen Silvia Children's Hospital and [2]Institution for Clinical Sciences, Department of Paediatrics, University of Gothenburg, Gothenburg, Sweden

Objective: **To describe the impaired fine-motor skills in patients with traumatic brain injury acquired in childhood.**

Design: **A total of 165 patients with traumatic brain injury, aged 0–17 years, injured during the period 1987–1991, were identified. Fifteen years post-injury a questionnaire was sent to the patients. Twenty-six of the subjects had upper limb problems, 15 of whom agreed to participate and 12 attended an evaluation.**

Methods: **The Sollerman test was administered. This test consists of 20 activities, of which 7 hand-grips were used (pulp-pinch, lateral pinch, tripod pinch, 5-finger pinch, diagonal, transverse and spherical volar grip). Each sub-test was scored from 0 to 4 points. Each task must be performed within 20 s. The maximum score was 80. Bimanual fine motor skills were classified by Bimanual Fine Motor Function (BFMF). BFMF consists of 5 levels of function of each hand. Level I is normal function, level II–V means subnormal function in an increasing grade. Co-ordination, spasticity, 2PD and stereognosis were also measured.**

Results: **All patients had subnormal results on the Sollerman test. Fifty-eight percent had abnormal scores on the BFMF test.**

Conclusion: **The Sollerman test seemed to be reliable at picking up hand motor problems, as all subjects who reported such problems scored subnormally. This is in contrast to the BFMF test findings, where only 60% of our group scored subnormally.**

Key words: long-term follow-up; upper limb function; traumatic brain injury.

J Rehabil Med 2013; 45: 815–819

Correspondence address: Ingrid Emanuelson, Habilitering och Hälsa, Näverlursgatan 38, SE-421 44 Västra Frölunda, Sweden. E-mail: ingrid.emanuelson@vgregion.se

Accepted June 4, 2013

INTRODUCTION

Children and adolescents who experience severe traumatic brain injury (TBI) comprise a group that requires not only medical resources in the acute phase, but also long-term rehabilitation because of remaining cognitive and motor deficits. There are some studies that have examined the long-term outcome in children with severe TBI, but they are few in number, have a short-term follow-up and do not always specify upper limb dysfunction. The Westmead Pediatric Multidisciplinary Outcome Study (1) is a prospective cohort study from a tertiary paediatric trauma centre in Australia, which followed 81 consecutive admissions (26 severe TBI, 41 mild TBI, 30 non-TBI controls) aged 0–14 years, 2 years after injury. Thirty-six percent of the severe subjects continued to have upper limb motor difficulties (muscle tone and arm/hand difficulties, poor handwriting, abnormal hand grasp, subnormal bilateral activity) (1). Mild TBI and control subjects had no or very few difficulties. Overall, half of the subjects in the severe TBI group had persistent fine motor difficulties at 2 years post-injury (1). In 2003, Kuhtz-Buschbeck (2) reported that hand motor skills had improved less than gait within 5 months of the injury. Functional motor function and control were affected 1–2 years after a TBI (2, 3) with reaction time and movement duration being prolonged. Co-ordination deficits were also frequent (2). In 2004 Gölge and co-workers (3) investigated recovery of precision grip in children after TBI. In this study 13 children, 5–14 years of age, with moderate to severe TBI were examined. The first date of examination was defined by Barthel index (part B > 20 points). Re-examinations followed after 1 and 5 months. Four different grips were measured. The children had deficits in force regulation, but weakness of the hand muscles did not seem to be a problem. This persisting physical disability in the severe TBI group is consistent with the findings of other researcher (4–7). The late outcome for children with severe TBI is thought to be dependent on the age at which the child was injured, so that those who experience TBI at an early age have more severe sequelae, compared with children who are older at the time of injury (3, 8). This study was initiated as the literature lacks descriptions of the long-term results with respect to fine-motor function.

This study was undertaken to clarify the complex pattern of impaired fine-motor skills in the long-term perspective in children with TBI. In the present study, patients have been followed for 15 years to determine their upper limb function after a moderate or severe TBI.

MATERIAL AND METHODS

Patients

A total of 165 survivors of moderate and severe TBI, aged between 0 and 17 years, injured during the period 1987–1991, were identified in the former south-west Sweden healthcare region, which has a popula-

Table I. *Severity parameters at injury 15 years before follow-up for the 29 patients with upper limb dysfunction and the 12 who attended the investigation*

Severity parameter	Group $n=29$ Mean (SD)	Group $n=12$ Mean (SD)	p-value Mean (SD)
GCS	4.63 (2.69)	5.88 (3.61)	n.s.
LOC, h	230 (218.01)	181 (148.25)	n.s.
Acute care, days	29.65 (40.49)	26.36 (23.16)	n.s.
Rehabilitation duration, days	8.31 (144.85)	59.08 (148.75)	n.s.
GOS	4.41 (0.68)	4.58 (0.67)	n.s.

SD: standard deviation; GCS: Glasgow Coma Scale: GOS: Glasgow Outcome Scale; LOC: loss of consciousness; n.s.: not significant.

tion of 1.7 million. Inclusion criteria were the above-mentioned and documented moderate or severe brain injury: ≥1 h of unconsciousness and/or neurophysiological, neuroradiological or neurological signs of a brain contusion or haemorrhage. The exclusion criterion was a diagnosis of concussion. This population has previously been presented in an epidemiological study and a study of health-related quality of life (9, 10). The traceable individuals (149) were invited to take part in a follow-up investigation 10 years after injury. Twenty individuals did not reply, 16 did not want to participate, 2 had died and 2 had moved abroad. A total of 109 individuals answered a questionnaire on symptoms and health-related quality of life (10).

Of these 109, 29 had problems with upper limb function. A new questionnaire with questions about upper limb function was sent 15 years after the injury and 26 subjects agreed that they still had these problems and were invited to participate in a clinical investigation. All 26 belonged to the group of 29 who had replied at the 10-year follow-up, that they had upper limb problems. Fifteen agreed to attend an assessment and were called for an interview and a clinical examination. Twelve subjects (age range 16–32 years) (8 males, 4 females) finally attended the evaluation, and the examination of upper limb function was performed a mean of 15.11 years (standard deviation (SD) 1.44, range 14.19–16.03 years) after the injury. The 12 individuals who finally attended the evaluation did not differ significantly in terms of severity of injury from the 29 who originally stated that they had problems with upper limb function (Tables I and II).

Identification of children

The children were identified primarily by the International Classification of Diseases (ICD)-9 diagnosis classification system and hospital death records, including the records from the forensic department. The study was approved by the ethics committee of the University of Gothenburg.

Table II. *Demographic data for the examined group of 12 patients*

Patient number	Age at injury, years	External cause	Traffic category	Sequelae at discharge from acute care
1	10.9	Fall		None
2	15.2	Traffic	Moped	Motor+medical+behaviour
3	15.7	Traffic	Motor vehicle	Motor+speech
4	8.4	Traffic	Pedestrian	Motor
5	8.5	Traffic	Motor vehicle	Motor+behaviour
6	13.0	Traffic	Motor vehicle	None
7	11.2	Traffic	Pedestrian	Motor+behaviour
8	2.5	Traffic	Motor vehicle	Medical+motor+behaviour +cognive+speech
9	0.3	Violence		Motor+behaviour
10	4.4	Traffic	Cyclist	Motor
11	13.9	Traffic	Cyclist	Motor+cognitive
12	17.0	Traffic	Cyclist	Motor+vision

Table III. *Bimanual Fine Motor Function classification (BFMF)*

Level I	One hand: manipulates without restrictions. The other hand: manipulates without restrictions or limitations in more advanced fine motor skills.
Level II	a) One hand: manipulates without restrictions. The other hand: only ability to grasp or hold. b) Both hands: limitations in more advanced fine motor skills.
Level III	a) One hand: manipulates without restrictions. The other hand: no functional ability. b) One hand: limitations in more advanced fine motor skills. The other hand: only ability to grasp or worse.
Level IV	a) Both hands: only ability to grasp. b) One hand: only ability to grasp. The other hand: only ability to hold or worse.
Level V	Both hands: only ability to hold or worse.

Measurements

Hand function was evaluated using the standardized Sollerman hand function test (11). The test was developed for measuring hand function in healthy adult populations and has been used for tetraplegic individuals, for individuals with rheumatic illnesses and for those with chronic stroke (12). This test consists of 20 different activities of daily living (ADL), of which 7 main hand-grips are used to the same extent (pulp-pinch, lateral pinch, tripod pinch, 5-finger pinch, diagonal, transverse and spherical volar grip) (Fig. 1).

Each subtest is scored by the examiner (according to the guidelines for scoring subtests) (11) on a 0–4-point scale. The ratings are based on the time and quality of performance of the hand-grip. Each of the tasks must be performed within 20 s to be given a score, giving a maximum score of 80, and the estimated time for performing the test was 20 min (according to the instructions given by the author). The subjects' bimanual fine-motor skills were classified using the Bimanual Fine Motor Function (BFMF) classification system (13). BFMF consists of 5 levels describing the grade of function of the hands separately, and was developed for children with cerebral palsy (Table III). This is the first study describing the use of their classification in a TBI population. Levels II–V mean restrictions of functions in daily life.

Grip strength was measured with the Grippit instrument (AB Detektor, Göteborg, Sweden). The instrument estimates peak grip strength over a 10-s period, and sustained grip strength averaged across the

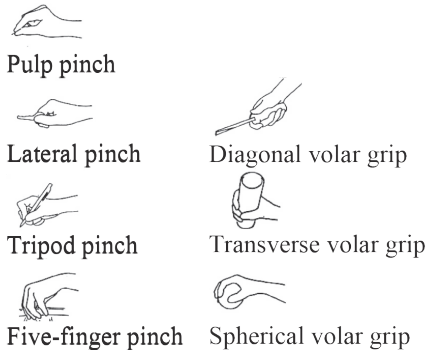


Fig. 1. The 7 grips in the Sollerman test.

10 s. The instrument has been found to have good reliability in healthy adults (14, 15).

Tactile sensibility was measured by tactile gnosis and 2-point discrimination (2PD). Tactile gnosis was measured by the Shape-Texture Identification test (STI), where 6 standardized objects of different shape, texture and size should be identified with each hand in a bag without seeing the objects (16, 17). Two-point discrimination was tested for all fingers at a distance of 3–4 mm between the points, using the method developed by Moberg (18).

The clinical examination also included estimation of spasticity and co-ordination. Spasticity was measured using the modified Ashworth scale (19).

Procedure

The follow-up examination included an interview with the patients about problems in fine-motor skills in daily life, a clinical assessment using the Sollerman test, co-ordination (diadochokinesis, finger-nose and tremor) spasticity and tactile gnosis. The procedure was videotaped. A thorough review of the video film was carried out later and the raters also noticed problems during the test procedure. Both the dominant and the non-dominant hand were tested in all the tests.

The assessment was performed by an experienced paediatric neurologist and an occupational therapist. The whole procedure was performed in a quiet environment, in a hospital setting and took 3–4 h.

Statistical analysis

Data calculations were performed using Excel software and descriptive statistics only were used. For comparisons of injury groups, non-parametric statistical methods were used.

RESULTS

The mean age of the patients at injury was 10 years, and they were evaluated between 14.19 and 16.03 years after the injury.

Table IV. *Test results for fine-motor function in the upper limb in 12 patients with traumatic brain injury*

Patient	Sollerman total score		Stereognosis		2PD		Grip strength		BFMF
number	R	L	R	L	R	L	R	L	level
1	75	74	n	n	n	n	n	n	1
2	55	71	n	n	n	n	A	n	2b
3	40	48	n	n	A dig1–5	n	A	n	3b
4	74	69	n	n	A dig4,5	n	n	n	2b
5	70	66	n	n	n	n	n	n	2b
6	79	72	n	n	n	n	ı	n	1
7	69	10	n	A	n	A dig1–5	n	A	3b
8	59	74	n	n	n	n	A	n	2a
9	73	33	n	A	A dig1–5	A dig3,5	A	A	3a
10	70	70	n	n	n	n	n	n	1
11	78	71	n	n	A dig5	A dig3,5	n	n	1
12	76	70	n	n	A dig5	n	n	n	1

BFMF: Bimanual Fine Motor Function (see Table III); dig: digits; A: abnormal; n: normal; R: right; L: left.

At the 10-year follow-up 27% (29/109) had hand motor problems and 5 years later, 24% (26/109) still had these problems. With regard to gross motor function all the patients were ambulatory without any technical aids.

All the patients had subnormal test results on the Sollerman test (maximum score 80 per hand). Eleven hands scored 71–79 (subnormal), and the remaining 13 hands scored below 71 (Table IV).

Of the total of 240 rated items, 97 had a score of 3 out of 4. In as many as 38 items (39%) the subnormal score was due to more than 20 s being needed to perform the task (see methods). For a score of 3, either more than 20 s but less than 40 s were needed for performance, or the test was performed with some difficulty in the hand grip. The examiners ($n=2$) noticed the need for repeated instructions, guidance during the test, impaired task performance and the need for pauses during the test.

On the BFMF test 7/12 patients (58%) had abnormal scores. Of these 7 patients, 5 had subnormal grip strength in 1 or both hands. Only 3 patients with IIIa or IIIb score for BFMF had increased muscle tone (Table IV); of these, 1 patient had undergone hand surgery. Patients scoring between 70 and 79 on the Sollerman test were classified as level I in the BFMF test.

During the clinical examination and when viewing the video of the Sollerman test we also noted that the patients had problems with co-ordination (8 patients), hand manipulation (8 patients), needed more than 20 min for performance (10 patients), needed repeated instructions (9 patients) and had impaired performance of task (9 patients) (Table V). All patients were able to complete the tests.

The current life situation of the patients was distributed so that 7 patients were employed and, of the other 5, 3 attended school (2 in special school, 1 in mainstream school) and 2 had a disability pension. Five were married (4 had children), 4 lived alone (1 needed support in ADL activities) and the 3 who attended school lived with their parents.

Table V. *Results of the clinical assessment of co-ordination (dysmetria, ataxia and tremor), spasticity, in-hand manipulation, need for repeated instructions and performance of task*

	Coordination		Spasticity		Manipulation		Repeated	Instruction
Pat.no	R	L	R	L	R	L	performance	about task
1	A	n	n	n	n	n	A	n
2	n	n	n	n	n	A	n	n
3	A	A	A	n	A	A	A	A
4	n	A	n	n	A	A	A	n
5	A	A	n	n	A	A	A	A
6	n	n	n	n	n	n	A	A
7	n	n	n	A	n	n	A	A
8	A	A	n	n	A	A	A	A
9	n	A	n	A	n	A		A
10	n	A	n	n	A	n	A	A
11	n	n	n	n	n	A	A	A
12	n	A	n	n	n	n	A	A

Pat.: patient; no; number: A: abnormal; n: normal; R: right; L: left.

DISCUSSION

After a brain injury the outcome varies depending on the location and severity of injury and is unpredictable; thus it is difficult to develop specific tests for TBI, and there is no generally accepted standard test for the evaluation of upper limb function after a TBI. The tests used are the same as those used for other neurological dysfunctions. When reviewing the literature there is, to our knowledge, no earlier study using the Sollerman test and the BFMF test for evaluating the late effects on upper limb function after TBI.

The overall experience to be seems that the Sollerman test is relatively reliable at picking up hand motor problems relevant to activities of daily living in the studied group, as all those who subjectively reported such problems scored subnormally. This is in contrast to the findings in the BFMF test, in which 60% scored subnormally. In the clinical tests of co-ordination 8/12 had such problems, in contrast to the assessment of 2PD and tactile gnosis.

The Sollerman test is sensitive enough to capture the hand function problems related to speed and performance of grasp, but does not describe the reason for the problem. Upper limb tempo was a problem for 10/12 patients. This is in concordance with the findings presented by Chaplin and co-workers (20), who evaluated 14 patients 16 months or later after injury with the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP), and described that upper limb tempo and dexterity were significantly lower than the other fine-motor subtests in the BOTMP.

The BFMF test is designed for the classification of upper limb dysfunction in patients with cerebral palsy (13). The advantage of using this test is that it describes the hands separately, is easy to perform and takes only a short time to administer; however, this test does not identify all those with scores between 70 and 79 on the Sollerman test.

Despite a duration of 15 years post-injury, the limitations of upper limb function remained in 24% of the patients, according to the questionnaires, and we have no reason to believe that the group not examined had recovered with regard to hand function during the follow-up time.

Our study also highlights that patients with TBI have persistent upper limb functional limitations, implying a need for tests which could be used to assess all patients. As these limitations interfere with activities of daily living there is a constant need for support. In the literature descriptions of upper limb dysfunction after TBI are sparse, and those that exist have short follow-up times. In this respect our study emphasizes the role of an individualized, non-structured evaluation. This study highlights the need for both qualitative and quantitative tests to be able to administer adequate support and rehabilitation for these patients.

The limitation of this study is the small number of clinically evaluated patients. This is a part of a larger population-based long-term follow-up study, in which the drop-out rate was 50% for those with anamnestic upper limb problems in the 15-year follow-up group ($n = 26$). The drop-outs ($n = 14$) did not differ from the evaluated group ($n = 12$) in terms of severity of injury (Tables I and II). The group has been followed by a team that has had the same principal investigator for 15 years (IE).

Of the 26 patients in the group, we examined only 12, partly because of memory problems among the patients approached (i.e. they forgot the time of appointments). There were originally 29/109 (27%) with upper limb problems at the 10-year follow-up of children with TBI (8), and in this 15-year follow-up there were 26/109 (24%) according to questionnaire ratings by the patients. In this study the exact nature of the upper limb problems were assessed only on a single occasion, which did not reveal the natural history of these complaints. Furthermore, it is sometimes impossible to discriminate what is the limitation of performance of hand function and what is due to cognitive and perceptual difficulties.

REFERENCES

1. O'Flaherty SJ, Chivers A, Hannan TJ, Kendrick LM, Mccartney LC, Wallen MA, et al. The Westmead Pediatric TBI Multidisciplinary Outcome Study; use of functional outcomes data to determine resource prioritization. Arch Phys Med Rehabil 2000; 81: 723–729.
2. Kuhtz-Buschbeck J, Hoppe B, Gölge M, Dreesmann M, Damm-Stunitz U, Ritz A. Sensorimotor recovery in children after traumatic brain injury: analysis of gait, gross motor, and fine motor skills. Dev Med Child Neurol 2003; 45: 821–828.
3. Gölge M, Muller M, Dreesmann M, Hoppe B, Wenzelburger R, Kuhtz-Buschbeck JP. Recovery of the precision grip in children after traumatic brain injury. Arch Phys Med Rehabil 2004; 85: 1435–1444.
4. Wallen M, Mackay S, Duff S, McCartney L, O'Flaherty S. Upper-limb function in Australian children with traumatic brain injury: a controlled, prospective study. Arch Phys Med Rehabil 2001; 82: 642–649
5. Ewing-Cobbs L, Miner ME, Fletcher JM, Levin HS. Intellectual motor and language sequelae following closed head injury in infants and preschoolers. J Pediatr Psychol 1989; 14: 531–547.
6. Fay GC, Jaffe KM, Polissar NL, Liao S, Pivara JB, Martin KM. Outcome after pediatric traumatic brain injury at three years; a cohort study. Arch Phys Med Rehabil 1994; 75: 733–741.
7. Jaffe KM, Fay GC, Polissar NL, Martin KM, Shurleff H, Rivara JB. Severity of pediatric traumatic brain injury and early neurobehavioural outcome; a cohort study. Arch Phys Med Rehabil 1992; 73; 540–547.
8. Koskiniemi M, Kyykkä T, Nybo T, Jarho L. Long-term outcome after severe brain injury in preschoolers is worse than expected. Arch Pediatr Adolesc Med 1995; 149: 249–254.
9. Emanuelson I, and von Wendt L. Epidemiology of traumatic brain injury in children and adolescents in south-western Sweden. Acta Paediatr 1997; 86: 730–735.
10. Horneman, G, Folkesson, P, Sintonen, H., von Wendt, L, Emanuelson, I. Health related quality of life of adolescents and young adults 10 years after serious traumatic brain injury. Intl J Rehab Res 2005; 28: 245–249.
11. 11.Sollerman C, Ejeskär A. Sollerman hand function test. A standardized method and its use in tetraplegic patients. Scand J Plast Recontr Surg Hand Surg 1995; 29: 167–176.
12. Brogårdh C, Persson AL, Sjölund BH. Intra- and inter-rater reliability of the Sollerman hand function test in patients with chronic stroke. Disabil Rehabil 2007; 29: 145–154.
13. Beckung E, Hagberg G. Neuroimpairments, activity limitations

and participation restrictions in children with cerebral palsy. Dev Med Child Neurol 2002; 44: 309–316.
14. Nordenskiöld U, Grimby G. Grip force in patients with rheumatoid arthritis and fibromyalgia and in healthy subjects. A study with the Grippit instrument. Scand Rheumatol 1993; 22: 14–19.
15. Lagerström C, Nordgren B. On the reliability and usefulness of methods for grip strength measurements. Scand J Rehabil Med 1998; 30: 113–119.
16. Rose'n B, Lundborg G. A new tactile gnosis instrument in sensibility testing. J Hand Ther 1998; 11: 251–257.
17. Rose'n B, Jerosch-Herold C. Comparing the responsiveness over time of two tactile gnosis tests: two-point discrimination and the STI-test. Br J Hand Ther 2000; 5: 114–119.
18. Moberg E. Two-point discrimination test. A valuable part of hand surgical rehabilitation, e.g. in tetraplegic. Scand J Rehabil Med 1990; 22: 127–134.
19. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther 1987; 67: 206–207.
20. Chaplin D, Deitz J, Jaffe KM. Motor performance in children after traumatic injury. Arch Phys Med Rehabil 1993; 74: 161–164.

J Rehabil Med 2013; 45: 820–826

ORIGINAL REPORT

CLINICALLY SIGNIFICANT CHANGES IN THE EMOTIONAL CONDITION OF RELATIVES OF PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY DURING SUB-ACUTE REHABILITATION

Anne Norup, PhD[1], Karin Spangsberg Kristensen, MPH[1], Ingrid Poulsen, PhD[1], Christina Löfvquist Nielsen, MSc[1] and Erik Lykke Mortensen, MSc[2]

From the [1]Research Unit on BRain Injury rehabilitation, Copenhagen (RUBRIC), Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen, University Hospital, Glostrup and [2]Institute of Public Health and Center for Healthy Aging, University of Copenhagen, Copenhagen, Denmark

Objective: **To investigate clinically significant change in the emotional condition of relatives of patients with severe traumatic brain injury during sub-acute rehabilitation.**

Methods: **Participants were 62 pairs of relatives and patients. Relatives completed the anxiety and depression scales from the Symptom Checklist-90-R (SCL-90-R) when the patients were admitted to sub-acute rehabilitation and at discharge. Improvement in emotional condition was investigated using the following criteria: (*i*) statistically reliable improvement; and (*ii*) clinically significant change (CSC).**

Results: **At admission, 53.2% and 58.1% of relatives had scores above cut-off values on the anxiety and depression scales, respectively. On the anxiety scale 69.7% of these experienced a reliable improvement according to the Reliable Change Index (RCI) and 45.5% also obtained CSC, as their end-point was below the cut-off value. On the depression scale the corresponding figures were 44.4% and 41.7%, respectively. When comparing relatives with and without CSC, we found that CSC in symptoms of anxiety was associated with significantly better functional improvement during rehabilitation and a shorter period of post-traumatic amnesia in the patients.**

Conclusion: **Of the relatives who reported scores above cut-off values on the anxiety and depression scales at patient's admission, approximately 40% experienced CSC in anxiety and depression during the patient's rehabilitation. Relatives of patients experiencing improvement during inpatient rehabilitation are more likely to experience CSC in anxiety.**

Key words: emotional distress; anxiety; depression; relatives; sub-acute rehabilitation; traumatic brain injury; clinically significant change; reliable change index; functional improvement; SCL-90-R.

J Rehabil Med 2013; 45: 820–826

Correspondence address: Anne Norup, Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen University Hospital, Glostrup, Denmark. E-mail: anne.norup@regionh.dk

Accepted April 25, 2013

INTRODUCTION

A number of studies has provided evidence that relatives of patients with brain injury experience significant emotional distress (e.g. 1–3), and high frequencies of anxiety and depression have been reported in the years following a family member acquiring a brain injury (4, 5). Studies have indicated that long-term deficits in the patient, such as changes in personality, behaviour and social cognition, are among the most distressing changes for the family (6–8). Mixed results have been found regarding associations between the patient's level of consciousness and function and the emotional condition of the relatives (2, 9). Cross-sectional studies conducted in the early phases of rehabilitation have indicated an association between the patient's level of consciousness and function and the emotional condition of the closest relative (10–13). These mixed results might be due to the fact that different predictors are important in different phases of rehabilitation. So far, no studies have investigated the possible associations between patient's recovery and changes in the emotional condition of the closest relative. To investigate causal inferences requires a longitudinal design, and only a few longitudinal studies have been conducted (13–16), with even fewer studies in the early phases of rehabilitation (15, 17). These longitudinal studies have reported a decrease in distress over the years following brain injury, as would be expected as the situation stabilizes and the family adapts. However, it is difficult to assess whether the reported decrease is clinically meaningful. Despite families experiencing a significant decrease in distress, they may still be living with severe distress caused by the continuing consequences of brain injury. Thus, there is a need to investigate the magnitude of the change and to evaluate whether the end-point is below the cut-off for pathology established in reference populations.

In 1984, the term clinically significant change (CSC) was introduced by Jacobson et al. (18). CSC was defined as the extent to which a subject moves outside the range of the dysfunctional population or within the range of the functional population. Some years later, Jacobson & Truax (19) elaborated by publishing a paper introducing ways of operationalizing the term. In this paper, the authors proposed

the term Reliable Change Index (RCI) as a means of determining whether the magnitude of change is statistically reliable. The introduction of this term led to the two-fold criterion for CSC used in this paper.

Aims

The current study aimed to investigate change in the emotional condition of relatives of patients with severe traumatic brain injury (TBI) during inpatient rehabilitation using the following criteria: (*i*) statistically reliable improvement; and (*ii*) CSC. Moreover, group differences were investigated between relatives who experienced change and those who did not.

METHODS

Participants

The study sample consisted of relatives of patients with severe TBI admitted to intensive specialized sub-acute rehabilitation at a TBI unit. A relative was defined as a child, parent, spouse, boyfriend, girlfriend or sibling. Relatives who did not speak Danish, and relatives with a psychiatric diagnosis or a progressive brain disease were excluded from the study. If more than one relative was present the family decided which relative should complete the questionnaire. Relatives of patients fulfilling the following criteria were included:

- Diagnosis of TBI.
- Aged 16 years or older.
- Glasgow Coma Scale (GCS) (20) score during the first 24 h after injury ≤ 8.

Patients were excluded if they met any of the following criteria:

- Violence-related cause of TBI (with the exception of war-related violence).
- Serious conditions causing mental disability prior to the TBI, such as developmental handicap (e.g. Down's syndrome), residual disability after previous TBI, confirmed dementia, or serious chronic mental illness (schizophrenia, psychosis or confirmed bipolar disorder).

Measures

Demographics. Data concerning gender, age and employment status of the patient and the relative were collected at admission. Moreover, cohabitant status and relationships were registered.

Relatives' emotional well-being. The emotional well-being of the relatives was investigated at patients' admission and discharge and assessed with measures of anxiety and depression. Symptoms of anxiety and depression were evaluated with the relevant scales of the Symptom Checklist (SCL), a self-report checklist designed to reflect symptom patterns and levels of distress (21). Each item is scored on a scale of 0 ("not at all") to 4 ("extremely"), indicating the degree of distress, and the respondents are asked to answer according to their condition over the previous 7 days. The anxiety and depression scale scores were evaluated using the gender-specific norms for a Danish population sample provided by Olsen et al. (22). The Danish population study revealed high alpha coefficients of the two scales used in this study, depression and anxiety: 0.91 and 0.86, respectively (22).

Neuropsychological support. The amount of contact that relatives of patients admitted to the unit had with a neuropsychologist was recorded. Both individual sessions and participation in group sessions were registered during the patient's hospitalization. The contact time was registered in units of 15 min. Scheduled contacts with the relative, unplanned or informal contacts, and phone contacts regarding patient's treatment were registered. The number of sessions with the neuropsychologist was also registered.

Patient's condition. As a standard procedure, relevant data were collected regarding the patient's condition. Severity of injury was assessed using GCS (20) and Injury Severity Score (ISS) (23).

GCS scores range from 3 to 15. Patients with scores of less than 9 are considered to be in a coma, and patients with scores of 15 have spontaneous eye opening, are able to follow commands and are fully oriented. According to criteria for injury severity, patients with GCS scores of 8 or less are classified as having severe brain injuries. GCS scores were rated by the treating physician at admission. The treating physician also calculated the ISS, which consists of an anatomical scoring system that provides an overall score for patients with multiple traumatic injuries. The ISS ranges from 0 to 75. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to 1 of 6 body regions: head, face, chest, abdomen, extremities and skin. Only the highest AIS score in each region of the body is used. The scores of the 3 most severely injured regions are added together to produce the ISS score.

At admission and discharge, the patient's level of consciousness was assessed by a neuropsychologist using the Rancho Los Amigos Levels of Cognitive Functioning Scale (RLA) (24). Scores on this scale range from Level 1, which describes a comatose condition with no observable response, to Level 8, which is a condition with purposeful and appropriate responses.

The scale measuring Early Functional Abilities (EFA) (25) is an assessment tool used in the early neurological rehabilitation stage, which describes clinically observable change in the early functional abilities of the patient. The EFA Scale contains 20 items and assesses early basic abilities related to 4 functional areas: vegetative, face and oral, sensory-motor, and sensory cognitive functions. Each item is rated on a 5-point scale, from "not obviously observable" to "no essential functional limitation". The total score ranges from 20 to a maximum of 100, where higher scores indicate better functional ability.

The Functional Independence Measure (FIM) (26) is an 18-item rating scale assessing activities of daily living (ADL): self-care, bowel and bladder management, mobility, communication, cognition, and psychosocial adjustment. Each item is rated on a 7-point scale, from "total assistance" to "complete independence". A total FIM score ranges from 18 to 126, with higher scores indicating greater independence. The FIM Scale has been shown to be valid and reliable for measuring functional outcome after TBI (27).

Both the FIM and the EFA were assessed within 72 h of admission and discharge by the nurses, physiotherapists and occupational therapists.

Procedure

A total of 77 pairs of patients and relatives were included in the study during the enrollment period from 1 October 2007 to 31 December 2011. The relatives were contacted when the patient was admitted and were given oral and written information about the study. If the relatives gave consent to participate in the study, they were enrolled.

As the aim was to investigate changes from admission to discharge based on the difference between the 2 assessments, only complete data were used. Eight relatives were excluded because of missing data (2 did not return the admission questionnaire, and 6 did not return the discharge questionnaire). Four relatives of patients were excluded because the patient died during hospitalization, and one relative chose to withdraw consent to participate and was therefore excluded. Two patients were transferred to a psychiatric ward, and thus their relatives were excluded, as we expected that the situation of these relatives was not similar to those of patients discharged to further rehabilitation. In total, 15 pairs of relatives and patients were excluded, and data are reported for the 62 remaining pairs.

No significant differences were found between excluded patients and relatives and the included sample with respect to the patient's age, GCS score and level of consciousness, or the age and gender of the relatives.

The study was approved by the Committees on Biomedical Research Ethics of the Capital Region of Denmark and the Danish Data Protection Agency.

Table I. *Demographics*

Characteristics	Patient ($n=62$)	Relative ($n=62$)
Age, years, mean (SD)	35.10 (18.68)	50.21 (11.37)
Range, years	16–82	27–78
Gender, *n* (%)		
Male	50 (80.6)	11 (17.7)
Female	12 (19.4)	51 (82.3)
Employment status, *n* (%)		
Full-time work/studying	52 (83.9)	
Unemployed/pension	10 (16.1)	
Cohabitants, *n* (%)		
Yes		41 (66.1)
No		21 (33.9)
Relationship, *n* (%)		
Spouse/cohabitant		19 (30.6)
Parent		36 (58.1)
Children		3 (4.8)
Others		4 (6.4)

SD: standard deviation.

Statistical analysis

Data are described with means (standard deviation (SD) and range, and categorical data with frequencies and percentages. Mean raw scores were calculated on each of the two outcome measures and compared with the Danish reference population (22), and the number of cases above cut-off was counted.

Analyses of change were conducted in a series of steps: firstly, the RCI was used to assess whether the individual change was statistically significant. The RCI is defined as the change in scores divided by the standard error of the difference for the test being used (19). The standard error of difference was calculated based on the standard deviation and the reliability coefficient (Cronbach's alpha) given in the Danish SCL-manual (28). The cut-off for statistical significance on the RCI is 1.96, which equates to the 95% confidence interval (CI).

Secondly, the number of participants obtaining CSC, defined as subjects improving significantly reliably and obtaining a raw score below cut-off at patient's discharge, was investigated. Evaluation of CSC requires participants to be above cut-off for caseness (e.g. in the dysfunctional range) at admission, and consequently all relatives below the cut-off were excluded from these analyses. Thirdly, the sample of relatives reported as cases initially were categorized according to the RCI, and, finally, the number of relatives experiencing a CSC and relatives not experiencing such a change were counted.

Statistical differences between groups were calculated using Wilcoxon signed-rank tests when comparing ordinal data, and McNemar's tests when proportions of cases were investigated. Effect sizes within groups were expressed as the difference between means at admission and discharge, divided by the SD at admission (29).

Group differences were investigated using χ^2 tests and independent samples *t*-tests.

For significance test, alpha was set at 0.05. All statistical analyses were conducted with SPSS version 19.0.

RESULTS

Description of the sample

The sample of relatives consisted of 82.3% females, who were primarily parents (58.1%) or spouses (30.6%) of the patients. The mean age of the sample was 50.21 years (SD 10.37; range 27–78 years). Most of the relatives were living with the patient at time of injury (66.1%).

The sample of patients was primarily male (80.6%) and had a mean age of 35.10 years (SD 18.68; range 16–82 years). The sample of patients was transferred to sub-acute rehabilitation 19.02 days after injury (SD 10.02 days), and the relatives completed the admission questionnaire 6.31 days after admission (SD 6.69 days). Patients had a mean length of stay of approximately 92.29 (SD 50.83) days, and the relatives completed the discharge questionnaire 10.98 (SD 19.67) days after discharge. Consequently, the mean follow-up time between admission and discharge questionnaires was 96.96 days (Table I).

The clinical status of the patients at admission and discharge is shown in Table II.

During rehabilitation the relatives received the standard intervention provided by the neuropsychologists working in the unit. On average, the relatives were provided with 15 units (SD 10; range 0–46 units) of 15 min duration during the patient's hospitalization, corresponding to a total of approximately 4 h. The amount of time was averagely spent in approximately 5 sessions.

Condition of relatives at admission and discharge

Raw scores on the anxiety and depression scales are shown in Table III. One sample *t*-test showed that the sample had significantly higher scores on both the depression and the anxiety scales at both admission and discharge, compared with Danish norms (28). When comparing scores at admission and discharge, change effect sizes for the total sample were 0.64

Table II. *Clinical status at admission and discharge*

	Admission			Discharge			Difference		
Variable	Median	IQR	Range	Median	IQR	Range	Median	IQR	Range
ISS ($n=62$)	29	25–38	16–59	–	–		–	–	
GCS ($n=62$)	11	8–14	5–15	–	–		–	–	
RLA ($n=62$)	4	2.75–5	2–7	8	6–8	3–8	3**	2–4	0–6
EFA ($n=62$)	39	29.75–72.5	21–98	99	76.50–100	43–100	42**	24–56.50	2–75
FIM ($n=62$)	18	18–25	18–115	104	44.75–117.50	18–125	68.50**	13.75–90.25	0–104

*$p<0.05$, **$p<0.01$.

Difference refers to the difference between patient's admission and discharge scores, and the statistical significance of this difference was calculated using Wilcoxon signed-rank test.

ISS: Injury Severity Score; GCS: Glasgow Coma Scale; RLA: Rancho Los Amigos; EFA: Early Functional Abilities; FIM: Functional Independence Measure; IQR: interquartile range.

Table III. *Emotional condition of relatives at admission and discharge*

	Anxiety					Depression				
	Mean (SD)	Range	D	*t*	*p*-value	Mean (SD)	Range	D	*t*	*p*-value
Admission ($n=62$)	1.32 (0.72)	0–3.36	0.88	9.61	<0.001	1.68 (0.67)	0.15–3.15	1.09	12.76	<0.001
Discharge ($n=62$)	0.86 (0.69)	0–3.27	0.42	4.85	<0.001	1.33 (0.83)	0–3.31	0.74	7.04	<0.001
Effect size	0.64					0.52				

p-values: 1-sample *t*-test.
D: difference to Danish norms; SD: standard deviation.

and 0.52 for anxiety and depression, respectively, indicating a moderate to large effect size (Table III).

The number of cases above cut-off levels on the 2 scales were counted, and it was found that 53.2% scored above cut-off on the anxiety scale at admission and 29.0% scored above at discharge (cut-off = 1.15 for females, and 0.94 for males). On the depression scale, 58.1% scored above cut-off at admission and 40.3% at discharge (cut-off = 1.60 for females, and 1.29 for males) (Table IV). The differences between the number of cases at admission and discharge were significant for both anxiety ($p=0.003$) and depression ($p=0.019$).

No significant group differences were found when comparing cases vs. no-cases on anxiety or depression with respect to the relative's gender, age, relationship to the patient or the patient's age, GCS, ISS, EFA, FIM or RLA scores at admission.

Changes in the condition of relatives during patients' rehabilitation

Total sample. The RCI was calculated for the total sample and, based on these calculations, the relatives were divided into 3 groups; deteriorating, no reliable change, and reliably improved (see Table IV). On the anxiety scale, 50.0% experienced a statistically reliable improvement, as did 32.3% on the depression scale.

No significant group differences between sub-samples with and without RCI on anxiety or depression were found with respect to the relative's gender, age, relationship to the patient, amount of neuropsychological support or the patient's age, GCS score, ISS score, duration of post traumatic amnesia (PTA) or progress on the EFA, FIM or RLA during admission.

Table IV. *Changes in emotional condition of relatives during patient's rehabilitation*

	Anxiety ($n=62$)		Depression ($n=62$)	
	% (*n*)	95% CI	% (*n*)	95% CI
Number of cases				
Admission	53.2 (33)	41.0–65.1	58.1 (36)	45.7–69.5
Discharge	29.0 (18)	19.2–41.4	40.3% (25)	29.0–52.8
Significance of change	0.003		0.019	
Change status (RCI)				
Deteriorated	8.1 (5)	3.1–17.9	8.1 (5)	3.1–17.9
No reliable change	41.9 (26)	30.5–54.3	59.7 (37)	47.2–71.0
Reliably improved	50.0 (31)	37.9–62.1	32.3 (20)	21.9–44.7

Cases were defined as a raw score above the cut-off: 1.15 for females and 0.94 for males on the anxiety scale, and 1.60 for females and 1.29 for males on the depression scale. Significance of change was calculated using McNemar's test.
RCI: Reliable Change Index, CI: confidence interval.

Analysis of cases. The classification of CSC necessitates initial case status (e.g. at patient's admission) and, consequently, all no-cases were excluded from the rest of the analyses. When investigating the remaining proportion of the relatives (cases; anxiety: $n=33$, depression: $n=36$) (Table V), we found that 69.7% experienced a reliable improvement according to the RCI, and 45.5% also obtained CSC, as their end-point was below cut-off on the anxiety scale. On the depression scale, 44.4% experienced a statistically significant improvement, and 41.7% also obtained CSC.

After the exclusion of relatives below the cut-off, effect sizes increased compared with the total sample. The effect sizes for the case sample were 1.21 and 1.02 for anxiety and depression, respectively, indicating a large change effect size.

When comparing relatives who experienced CSC with those who did not, in relation to anxiety we found that CSC was associated with significantly shorter duration of PTA ($t=2.964$, $p=0.007$) and significantly more improvement on the FIM during rehabilitation ($t=2.324$, $p=0.027$) in the patients. Patients of relatives experiencing CSC in relation to anxiety had a mean PTA duration of 45 (SD 31) days, whereas patients of relatives not experiencing CSC had a duration of 114 (SD 94) days. This pattern was also seen in relation to functional improvement, where patients of relatives experiencing CSC had a median improvement on the FIM of 87 points (interquartile range (IQR) 78–92) during rehabilitation, and patients of relatives not experiencing CSC had a median improvement on the FIM of 62 points (IQR 78–92).

No significant differences were observed between relatives with and without CCS in relation to depression.

DISCUSSION

Condition of relatives at admission and discharge

The results of this study revealed that the sample had significantly more symptoms of anxiety and depression at both patients' admission and discharge compared with a reference population. In the total sample, 53.2% and 58.1% scored above cut-off on the anxiety and depression scales, respectively. These numbers are comparable with our previous results (10, 30). In spite of the obvious limitations when comparing results of studies with methodological differences, these results do support the few studies conducted in the early phases of rehabilitation showing increased levels of both depression and

Table V. *Change status in the case "group" (after excluding no-cases at admission)*

	Anxiety ($n=33$)		Depression ($n=36$)	
	Mean (SD)	95% CI	Mean (SD)	95% CI
Admission	1.83 (0.57)	1.63–2.01	2.12 (0.45)	1.97–2.27
Discharge	1.14 (0.71)	0.9–1.38	1.66 (0.83)	1.39–1.93
	% (*n*)	95% CI	% (*n*)	95% CI
Change status (RCI)				
Deteriorated	6.1 (2)	0.7–20.6	11.2 (4)	3.8–25.9
No reliable change	24.2 (8)	12.6–41.2	44.4 (16)	29.4–60.5
Reliably improved	69.7 (23)	52.5–82.8	44.4 (16)	29.4–60.5
Clinically significant change (CSC)	45.5 (15)	29.8–62.0	41.7 (15)	27.1–57.8
Effect size	1.21		1.02	

A participant is classified as experiencing clinically significant change when the magnitude of change should be statistically significant and symptoms are reduced to an end-score (discharge) below the cut-off for caseness. RCI: Reliable Change Index; CI: confidence interval: SD: standard deviation.

anxiety. Oddy et al. (17) reported that 39% of the relatives were above the cut-off score for clinical depression 1 month after injury, in comparison with the present study, in which more than half of the relatives scored above the cut-off in this sample approximately 3 weeks after injury. However, the patients in Oddy et al.'s sample had less severe injuries than the patients in our sample.

Novack et al. (15) found that 9% of patients were clinically depressed and 33% of caregivers were clinically anxious at admission (46 days post-injury). The levels reported in this study were low compared with those in our study and the study of Oddy et al. (17). However, the caseness criteria used were higher (Beck Depression Inventory > 18, State-Trait Anxiety Inventory > 90th percentile) than recommended (31).

Changes in the condition of relatives during patients' rehabilitation

Total sample. Using the RCI, we found that, of the total sample, 50.0% experienced a statistically reliable improvement on the anxiety scale, and 32.3% experienced a statistically reliable improvement on the depression scale. A relatively large proportion of these relatives reported no measurable degree of change (anxiety 41.9% and depression 59.7%).

Despite the relatively large percentages experiencing no reliable change, effect sizes indicated moderate-to-large effects. This emphasizes how large effect sizes do not reflect improvement for all relatives, as more than half of the sample did not report any reliable change. These results emphasize the need for a clinically meaningful definition of change.

Analysis of cases. When we excluded the no-cases at admission from the further analyses and once again calculated the RCI, we found that only 24.2% and 44.4% reported no reliable change on anxiety and depression scales, respectively. This indicates that the majority of relatives experiencing pathological symptoms of anxiety and depression did report a reliable improvement. Moreover, in the "case" group 45.5% reported CSC on anxiety and 41.7% on depression. In the sub-sample with case status, change effect sizes for both anxiety and depression were large.

To the authors' knowledge, no other studies in the field of brain injury have used the concept CSC to investigate changes in the wellbeing of relatives. Most relatives do experience a decrease in symptoms of distress, anxiety and depression during the patients' rehabilitation, which is to be expected as the patient recovers and the situation stabilizes (3, 13, 15, 17, 32, 33). However, whether this decrease is statistically reliable and clinically important has not been investigated. A significant decrease in score level may not be clinically significant if the end-point is still above the cut-off for pathology. Thus, the evaluation of change in symptomatology should include both the magnitude and reliability of the improvement, as well as the end-point score of relatives.

Investigating group differences

We found that patients with relatives who experienced a CSC in relation to anxiety experienced a larger functional improvement during in-patient rehabilitation and a shorter period of post-traumatic amnesia. This emphasizes the associations between patient's recovery and the well-being of the relative. To the authors' knowledge, no other studies have investigated associations between the patients' functional improvement and emotional improvements in relatives. Previous studies have used a cross-sectional design revealing associations between indices of severity of injury (e.g. GCS (12, 13)), level of function (e.g. Disability Rating Scale (EFA) (2, 9, 10, 34)) and the emotional condition of family members. The results of these cross-sectional studies have been mixed, as authors have also reported no associations between functional level (e.g. FIM (9)) and the condition of relatives. As mentioned in the Introduction, the innate problem of cross-sectional studies is that they do not provide information about changes over time, e.g. improvement in patients' status in relation to the emotional condition of relatives. The present study is the first to report such an association in the early phases of rehabilitation, and this underlines how the wellbeing of relatives is connected to the physical condition of patients. Some authors have pointed out that this association might be reciprocal, indicating that the emotional condition of relatives might influence the final outcome after the patient's rehabilitation (35). However, this issue needs further investigation.

Thus, the improvement in the emotional condition of the relatives was expected, but the reported association between relatives with CSC and patient's recovery is interesting, and to the authors' knowledge this has not been demonstrated before. However, no associations were found between patient's recovery and the change in relatives' depression scores. Moreover, no associations were found between the amount of neuropsychological intervention and the improvement in relatives' condition. This might suggests that the recovery observed is primarily spontaneous, reflecting that the relatives gradually adapt to the new life situation with a close family member who is seriously ill. The relatives are likely to be in

a crisis during the most acute phase of the patient's illness, and their emotional state improves as they gradually learn to cope with the situation and adapt to the long-term perspective.

Limitations

In the current study changes in emotional distress were investigated, but no assessments of social support were carried out. Social support is known to have an impact on emotional well-being (22). Moreover, both coping style and personality affect how relatives deal with the situation facing a close relative with a severe brain injury. For example, the broad personality dimension of neuroticism is known to be related not only to health-related quality of life (HRQoL), anxiety and depression, but also to coping strategies (36, 37). Thus, the inclusion of a personality inventory would have strengthened the study.

Another limitation is the registration of the neuropsychological intervention, which was recorded as duration in minutes as well as number of sessions. This is not an adequate way of measuring a psychological intervention, as duration does not necessarily equate to quality. However, this method was used for pragmatic reasons, as the data were collected as part of another study (30). A different research design and methods are required to evaluate the true effect of the neuropsychological intervention administered and associations with changes in the emotional condition of the relative. Randomized studies could include relative's ratings of the benefits from various elements in the intervention. This procedure has been used by other family intervention researchers (38). Moreover, it appears that the timing of the intervention is critical. This is discussed further in another paper in this special issue (39).

Moreover, we did not register the support administered by other professionals, e.g. nurses, physicians, therapists, or the support that relatives received from their families, which is known to be important.

Clinical implications

When investigating change in relatives' wellbeing, previous studies have neglected to evaluate whether the reported change is clinically meaningful. Reporting this dimension of research reduces the gap between clinicians and researchers. This enables and assists the researchers and clinicians in translating the results into clinical practice (40).

There has not been sufficient focus on the importance of the condition of the relatives during the early phases of rehabilitation in rehabilitation research. Since symptoms of anxiety and depression influence the collaboration between staff and families as family members, it is important that clinicians are aware of the distress that families experience, when a patient is admitted to rehabilitation (41). Furthermore, the symptoms of distress experienced by relatives may have important long-term consequences for the family and the patient with respect to employment, quality of life, and prevention of marital disruption.

Moreover, results have indicated that the association between the condition of the family and the patient is reciprocal; meaning that the distress that the family experiences also influences the condition of the patient (35). This has emphasized the need and importance of early detection of symptoms of distress and the necessity for emotional support, which may, to some extent, prevent the more long-term symptoms of depression.

This study has also emphasized the fact that relatives of patients who do not make progress with respect to functional level, have higher risk of experiencing anxiety and depression. This emphasizes the need for specific support for families of patients without functional progress during rehabilitation. These families may also need substantial support after the patient's discharge, which might be provided by more systematic follow-up of patients and families.

Future research

Future studies should assess the changes over time in the emotional condition of relatives of patients with severe brain injury using a reliable threshold for change and examining whether the reported change is statistically reliable and clinically important.

There is a lack of research describing the early impact of brain injury on family members, thus future studies should focus on the early phases of rehabilitation. Exploring associations between the functional improvement in patients and the relatives' wellbeing will enable professionals to identify relatives and families who are at risk of developing or maintaining high levels of anxiety and depression throughout the early phases of rehabilitation. This is important for the triangle in rehabilitation: patients, relatives and professionals. Healthcare professionals and health organizations need to establish support systems that can adequately meet the needs of the families. Support systems should be based on clinical experience, while they still lack evidence-based supported interventions in the early phases of rehabilitation. Health organizations and rehabilitation services should have a structured approach towards supporting the family during and after the patient's rehabilitation. The support system can include professionals working in the rehabilitation settings or provide relatives with links to other public or voluntary organizations.

Conclusion

Of the relatives reporting scores above the cut-offs on the anxiety and depression scales at patient's admission, the majority experienced reliable improvement according to the RCI, and approximately half of the relatives also obtained CSC, as their end-point was below the cut-off score on the anxiety scale. On the depression scale, just under half of the relatives experienced a statistically significant improvement, and approximately 40% also obtained CSC. The study also found that relatives of patients who had a shorter duration of PTA and who experienced functional improvement, were more likely to experience CSC in symptoms of anxiety. This emphasizes the need for increased awareness about families of patients who are not progressing or who are progressing slowly during rehabilitation.

ACKNOWLEDGEMENTS

The authors would like to thank participants in the study, and additionally acknowledge the data collection conducted by the staff at the Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen University Hospital, Glostrup. The authors would also like to thank Dr John Whyte and Dr Tessa Hart, Moss Rehabilitation Institute, Philadelphia, USA, for kind permission to use data on neuropsychological support collected in a collaborative study.

REFERENCES

1. Brooks N, Campsie L, Symington C, Beattie A, McKinlay W. The 5 year outcome of severe blunt head-injury – a relative's view. J Neurol Neurosurg Psychiatry 1986; 49: 764–770.
2. Kreutzer JS, Rapport LJ, Marwitz JH, Harrison-Felix C, Hart T, Glenn M, et al. Caregivers' well-being after traumatic brain injury: a multicenter prospective investigation. Arch Phys Med Rehabil 2009; 90: 939–946.
3. Livingston MG, Brooks DN, Bond MR. Patient outcome in the year following severe head–injury and relatives psychiatric and social functioning. J Neurol Neurosurg Psychiatry 1985; 48: 876–881.
4. Machamer J, Temkin N, Dikmen S. Significant other burden and factors related to it in traumatic brain injury. J Clin Exp Neuropsychol 2002; 24: 420–433.
5. Rivera P, Elliott TR, Berry JW, Grant JS, Oswald K. Predictors of caregiver depression among community-residing families living with traumatic brain injury. Neurorehabilitation 2007; 22: 3–8.
6. Ergh TC, Rapport LJ, Coleman RD, Hanks RA. Predictors of caregiver and family functioning following traumatic brain injury: social support moderates caregiver distress. J Head Trauma Rehabil 2002; 17: 155–174.
7. Groom KN, Shaw TG, O'Connor ME, Howard NI, Pickens A. Neurobehavioral symptoms and family functioning in traumatically brain-injured adults. Arch Clin Neuropsychol 1998; 13: 695–711.
8. Ponsford J, Olver J, Ponsford M, Nelms R. Long-term adjustment of families following traumatic brain injury where comprehensive rehabilitation has been provided. Brain Inj 2003; 17: 453–468.
9. Douglas JM, Spellacy FJ. Correlates of depression in adults with severe traumatic brain injury and their carers. Brain Inj 2000; 14: 71–88.
10. Norup A, Siert L, Mortensen E.L. Emotional distress and quality of life in relatives of patients with severe brain injury: the first month after injury. Brain Inj 2010; 24: 81–88.
11. Norup A, Welling KL, Qvist J, Siert L, Mortensen EL. Depression, anxiety and quality-of-life among relatives of patients with severe brain injury: the acute phase. Brain Inj 2012; 26: 1192–2000.
12. Pielmaier L, Walder B, Rebetez MM, Maercker A. Post-traumatic stress symptoms in relatives in the first weeks after severe traumatic brain injury. Brain Inj 2011; 25: 259–265.
13. Turner B, Fleming J, Parry J, Vromans M, Cornwell P, Gordon C, et al. Caregivers of adults with traumatic brain injury: the emotional impact of transition from hospital to home. Brain Impairment 2010; 11: 281–292.
14. Marsh NV, Kersel DA, Havill JA, Sleigh JW. Caregiver burden during the year following severe traumatic brain injury. J Clin Exp Neuropsychol 2002; 24: 434–447.
15. Novack TA, Bergquist TF, Bennett G, Gouvier WD. Primary caregiver distress following severe head injury. J Head Trauma Rehabil 1991; 6: 69–77.
16. Oddy M. 7 years after – a follow-up-study of severe head-injury in young adults. J Clin Exp Neuropsychol 1985; 7: 165.
17. Oddy M, Humphrey M, Uttley D. Stresses upon relatives of head-injured patients. Br J Psychiatry 1978; 133: 507–513.
18. Jacobson NS, Follette WC, Revenstorf D. Psychotherapy outcome research: methods for reporting variability and evaluating clinical significant change. Behavior Therapy 1984; 17: 308–311.
19. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol 1991; 59: 12–19.
20. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–44.
21. Derogatis LR. SCL-90-R: Symptom Checklist-90-R. Administration, scoring and procedures manual. 3rd edn. Minneapolis: National Computer Systems; 1994.
22. Olsen LR, Mortensen EL, Bech P. Mental distress in the Danish general population. Acta Psychiatr Scand 2006; 113: 477–484.
23. Baker SP, Oneill B, Haddon W, Long WB. Injury severity score – method for describing patients with multiple injuries and evaluating emergency care. J Trauma-Inj Infect Crit Care 1974; 14: 187–196.
24. Hagen C, Malkmus D, Durham P. Levels of cognitive function. Downey, CA: Rancho Los Amigos Hospital Communication Disorders Service; 1972.
25. Heck G, Schmidt T, Steiger-Bachler G. Early functional abilities (EFA) – eine Skala zur Evaluation von Behandlungsverlaufen in der neurologischen Fruhrehabiltation. Neurol Rehabil 2000; 6: 125–133.
26. Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. Adv Clin Rehabil 1987; 1: 6–18.
27. Corrigan JD, Smith-Knapp K, Granger CV. Outcomes in the first 5 years after traumatic brain injury. Arch Phys Med Rehabil 1998; 79: 298–305.
28. Bech P, Olsen LR, Poulsen A, Mortensen EL, Munk V. [SCL-90-R Manual.] Virum: Dansk Psykologisk Forlag; 2006 (in Danish).
29. Cohen J. Quantitative methods in psychology: a power primer. Psychol Bull 1992; 112: 155–159.
30. Norup A, Kristensen KS, Siert L, Poulsen I, Mortensen EL. Neuropsychological support to relatives of patients with severe traumatic brain injury in the sub-acute phase. Neuropsychol Rehabil 2011; 21: 306–321.
31. Beck AT, Steer RA. Beck Depression Inventory – manual. San Antonio: Psychological Corp.; 1987.
32. Marsh NV, Kersel DA, Havill JH, Sleigh JW. Caregiver burden at 6 months following severe traumatic brain injury. Brain Inj 1998; 12: 225–238.
33. Marsh NV, Kersel DA, Havill JH, Sleigh JW. Caregiver burden at 1 year following severe traumatic brain injury. Brain Inj 1998; 12: 1045–1059.
34. Livingston LA, Kennedy RE, Marwitz JH, Arango-Lasprilla JC, Rapport LJ, Bushnik T, et al. Predictors of family caregivers' life satisfaction after traumatic brain injury at one and two years post-injury: a longitudinal multi-center investigation. NeuroRehabil 2010; 27: 73–81.
35. Lehan T, Arango-Lasprilla JC, de los Reyes CJ, Quijano MC. The ties that bind: the relationship between caregiver burden and the neuropsychological functioning of TBI survivors. NeuroRehabilitation 2012; 30: 87–95.
36. Gunthert KC, Cohen LH, Armeli S. The role of neuroticism in daily stress and coping. J Pers Soc Psychol 1999; 77: 1087–1100.
37. McCrae RR, Costa PT. Personality, coping, and coping effectiveness in an adult sample. J Personality 1986; 54: 385–405.
38. Kreutzer JS, Stejskal TM, Godwin EE, Powell VD, Arango-Lasprilla JC. A mixed methods evaluation of the Brain Injury Family Intervention. NeuroRehabil 2010; 27: 19–29.
39. Norup A, Siert L, Lykke Mortenensen E. Neuropsychological intervention in the acute phase: A pilot study of emotional well-being of relatives of patients with severe brain injury. J Rehabil Med 2013; 45: 827–834
40. Evans C, Margison F, Barkham M. The contribution of reliable and clinically significant change methods to evidence-based mental health. Evidence-Based Mental Health 1998; 1: 70–72.
41. Kross EK, Curtis JR. Burden of psychological symptoms and illness in family of critically ill patients: what is the relevance for critical care clinicians? Crit Care Med 2008; 36: 1955–1956.

J Rehabil Med 2013; 45: 827–834

ORIGINAL REPORT

NEUROPSYCHOLOGICAL INTERVENTION IN THE ACUTE PHASE: A PILOT STUDY OF EMOTIONAL WELLBEING OF RELATIVES OF PATIENTS WITH SEVERE BRAIN INJURY

Anne Norup, PhD[1], Lars Siert, MSc[1] and Erik Lykke Mortensen, MSc[2]

From the [1]Research Unit on BRain Injury rehabilitation, Copenhagen (RUBRIC), Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen, University Hospital, Glostrup and [2]Institute of Public Health and Center for Healthy Aging, University of Copenhagen, Copenhagen, Denmark

Objective: **This pilot study investigated the effects of acute neuropsychological intervention for relatives of patients with severe brain injury.**

Methods: **Participants were enrolled in an intervention group comprising 39 relatives, and a control group comprising 47 relatives. The intervention consisted of supportive and psycho-educational sessions with a neuropsychologist in the acute care setting. The intervention group completed self-report scales in the acute setting and after the intervention at admission to sub-acute rehabilitation. The control group completed the self-report scales only at admission to sub-acute rehabilitation. Outcome measures included selected scales from the Symptom Checklist Revised 90 (SCL-90-R), the Short Form 36 (SF-36), and a visual analogue quality of life scale.**

Results: **The intervention group showed a significant decrease in anxiety scores from the acute to the sub-acute setting ($t = 2.70$, $p = 0.010$, $d = 0.30$), but also significantly lower Role Emotional scores ($t = 2.12$, $p = 0.043$, $d = 0.40$). In the sub-acute setting, an analysis of covariance model showed a borderline significant difference between the intervention and the control group on the anxiety scale ($p = 0.066$, $d = 0.59$).**

Conclusion: **Any effects of the acute neuropsychological intervention were limited. Further research is needed to explore the effects of different interventions in more homogenous and larger groups of relatives.**

Key words: acute neuropsychological intervention; relatives; severe brain injury; anxiety; depression; quality of life.

J Rehabil Med 2013; 45: 827–834

Correspondence address: Anne Norup, Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen University Hospital, Glostrup, Denmark. E-mail: anne.norup@regionh.dk

Accepted April 23, 2013

INTRODUCTION

Emotional strain and distress in relatives of patients with brain injury have been documented in a number of studies (1–8). The majority of studies have focused on the long-term impact on family members, and there has been a lack of studies investigating the early effects of brain injury and the family's condition during hospitalization. Only two studies have been identified investigating relatives of patients with severe brain injury in the early phases of hospitalization (9, 10). Pielmaier et al. (10) reported that more than half of relatives of patients with severe traumatic brain injury (TBI) admitted to critical care had clinically significant post-traumatic stress symptoms shortly after the injury, which is in concordance with our findings in a neuro intensive care unit (NICU) reporting high frequencies of anxiety and depression (9). These results are consistent with research with longer follow-up investigating the condition of the relatives (6, 11–14).

A review concerning the emotional condition of relatives of critically ill patients in intensive care units (ICUs) and NICUs found that most relatives needed "to have questions answered honestly" and "to know specific facts regarding what is wrong with the patient and the patient's progress". The review concluded that information was the most important need identified in critical care, when the patient's situation is unstable. The families sought honest and frequent information about progress, status and prognosis (15).

A few intervention studies have been conducted investigating different types of interventions for families of brain injury survivors in outpatient centres years after injury (16–21). Despite knowledge of the distress and needs of families of patients admitted to NICUs (3, 9, 10, 15), no studies have investigated and evaluated intervention for families of brain injury survivors in the early phases of rehabilitation.

Present study

The present pilot study was designed in an attempt to meet the needs of the relatives in the early phases of rehabilitation. When receiving the families at admission to sub-acute rehabilitation most families expressed a need for support and information that they felt had not been met in the acute setting. Therefore, this pilot study tried to meet the needs of the relatives in the acute setting based on our clinical experience.

The purpose of the study was to investigate the effects of neuropsychological intervention for relatives of patients with severe brain injury in the acute care setting. The intervention consisted of supportive sessions with a trained neuropsychologist, and the sessions were a flexible mixture of both psycho-education and emotional support. The sessions were

 doi: 10.2340/16501977-1181

 ISSN 1650-1977

individualized and focused primarily on the family's immediate situation with a close family member in hospital.

The aims of the pilot study were to investigate whether:

- a group of relatives receiving neuropsychological intervention in the acute setting experienced a decrease in symptoms of anxiety and depression and an increase in quality of life;
- the group receiving intervention had significantly fewer symptoms of anxiety and depression and better quality of life compared with a control group at admission to sub-acute rehabilitation.

MATERIAL AND METHODS

Participants

Two groups of relatives of patients with a severe brain injury were included: an intervention group receiving acute neuropsychological intervention and a control group receiving no intervention in acute care. The intervention group initially comprised 46 relatives, but because 4 patients died and 3 relatives did not return follow-up questionnaires at admission to rehabilitation, data are reported for only 39 relatives. The control group comprised 47 relatives, who completed the questionnaires only when included at admission to sub-acute rehabilitation.

All patients had severe brain injury and a need for intensive neurorehabilitation. Patients admitted for rehabilitation have to fulfil the admission criteria of the unit, where the highest priority is given to patients who after initial treatment in a neurosurgical or other clinic have a Glasgow Coma Score (GCS) in the range 3–12 one day after cessation of sedation. All such survivors are transferred as soon as they breathe spontaneously, even if the prognosis for recovery may appear extremely bad.

Secondly, the unit admits patients with a GCS of 13–14 one day after cessation of sedation. These patients are admitted only if they have severe focal neurological deficits, such as aphasia, hemiparesis and/or are severely agitated (the admission criteria are more thoroughly described in previous publications (22, 23)).

Exclusion criteria were: relatives who did not speak Danish, those who had a psychiatric diagnosis, or a progressive brain disease.

Procedure

The two groups of relatives were included at two different time-points and allocated to the two groups depending on time of enrolment. Despite the different time of enrolment, all patients had been through the same pathway of care in the acute setting.

The intervention group was included at the neuro-intensive care unit (T1), when the patient's condition was stabilized, and the control group was included at admission to the sub-acute rehabilitation (T2). Patients were included only if they fulfilled the criteria above, and if the relative did not meet any of the exclusion criteria. Both groups were admitted for intensive neurorehabilitation in the sub-acute phase at the traumatic brain injury unit (Fig. 1).

Oral consent to participate was obtained by a neuropsychologist, when the relative was included. If more than one relative was present at the time of inclusion, the family decided who should participate in the study.

The study was approved by the Committees on Biomedical Research Ethics of the Capital Region of Denmark (journal number H-KF-311150) as the Danish Data Protection Agency (journal number 2007-41-0583).

Intervention

Method. The intervention group received neuropsychological support during acute care, conducted by neuropsychologists trained in dealing with psychological trauma and having years of experience in the field of brain injury rehabilitation. The sessions did not follow a specific treatment manual, as the emotional condition, and consequently the needs, of relatives differed considerably. In each session the neuropsychologist decided on the most beneficial structure of the session according to the needs of the relatives, balancing between psychological support and psycho-education. This method was chosen after conducting a few pilot sessions facing the very different situations and needs of the families. The intervention was administered during the first 3 weeks after the injury.

Purpose and expected benefits. The purpose of the intervention was two-fold, and consequently it was a flexible mixture of both emotional support and psycho-education. The sessions were targeted on the family's immediate situation with a close family member severely ill in hospital. The first purpose of the intervention was providing psychological support to the family in terms of dealing with the distressing situation of having a critically ill family member. The primary objective for the neuropsychologist was to listen and to instil hope in the families by identifying progress in the patient's condition and personal strengths in the relatives. This was expected to help families regain hope in the future, and indirectly cause emotional relief. The second purpose of the session was psycho-educational, providing information about treatment in the acute setting and the consequences of brain injury. Giving needed information was expected to improve understanding of the patient's condition and reduce anxiety and more general symptoms of distress. The relatives were only given information they requested, and in each session the neuropsychologist carefully evaluated how much information the relatives were capable of receiving without causing further distress (Table I).

Content and topics. The topics of the sessions depended on the relatives' specific needs. Every session began with the neuropsychologist asking the family how they experienced the accident, if they witnessed it or were involved. In cases in which the relatives had not been present, they were asked to share how they received the message about the accident. The relatives often needed immediate psychological support to help them deal with their own emotional reactions and needs during the first critical phases of the patient's stay in the acute setting. Topics often addressed in the supportive part of the sessions were how to handle each day with a close family member in hospital, feelings of isolation, guilt and emotional distress. The second part of the sessions was psycho-educational, and the relatives were able to ask any questions regarding treatment in the acute setting, the first period of unconsciousness, post-traumatic amnesia, consequences of brain injury and recovery from brain injury.

In some cases, the relatives had obvious symptoms of anxiety, being tense, physically restless and almost unable to sit still. In such sessions, the focus remained on the immediate situation and how to handle this. In cases, where the families were more calm and able to receive information, the neuropsychologist tried to answer the relatives' questions about prognosis, treatment in the acute setting, etc. However, it was very important that each session was finished properly, making sure that the relatives had no further questions or queries.

Outcome measures. Effects of the intervention were assessed by having the relatives complete standardized questionnaires regarding anxiety, depression and quality of life (information regarding the specific measures is given below). Anxiety and depression were chosen, as these symptoms have been described in families of brain injury survivors

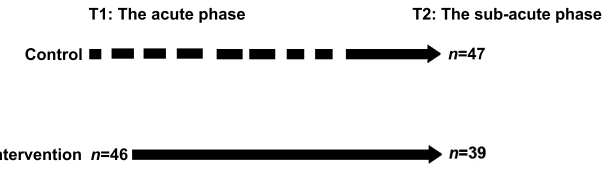


Fig. 1. Inclusion procedure.

Table I. *Overview of intervention*

Purpose	Objective	Expected benefits	Examples of topics
Emotional support	Identifying progress in the patient's condition and emotional strength in the relative by listening and instilling hope	Regain hope in the future and indirectly causing emotional relief	Handling each day with a family member in hospital Feelings of isolation, guilt and distress
Psycho-education	Improve understanding of the patient's condition by providing information	Reduce anxiety and general symptoms of distress	Treatment in the acute setting; monitoring of intracranial pressure, decompressive surgery, etc. The first period of unconsciousness, vegetative and minimally conscious state Post-traumatic amnesia, consequences and recovery from brain injury

for years (15, 24–27). We expected anxiety to be more sensitive to the intervention, as information is known to be able to reduce anxiety.

A quality of life measure was also included; as research has shown that quality of life can be high in caregivers despite high levels of distress (28).

Amount of intervention. The duration of the sessions was 1–1.5 h, depending on the relatives and their ability to maintain concentration throughout the session. In some cases, the relatives were very restless, as described above, and the sessions were kept brief. However, more often the family enjoyed the respite from the bedside and the possibility to talk about their loved one and their current situation. The majority of the relatives (67.4%) received 1 session. Of the relatives, 17.4% had 2 sessions, 13.0% had 3 sessions, and 1 relative had 4 sessions (2.2%).

An independent samples *t*-test showed no difference in the relatives' emotional wellbeing on T2 depending on whether or not the relative received more than 1 session of intervention.

Assessment of relatives

Outcome measures were administered at T1 and T2 in the intervention group and at T2 in the control group, as described below.

Quality of life. Each relative was asked to complete the Short Form 36 (SF-36), a measure of self-reported health-related quality of life. The questionnaire comprises 36 items addressing 8 dimensions of health. Scores in each domain of the SF-36 range from 0 to 100, with higher scores indicating better health. Only 4 scales were used in the present study: Role Emotional (RE), Social Function (SF), Mental Health (MH) and Vitality (VT). The scores of the relatives were evaluated in terms of available Danish norms (29). This normative study showed high Cronbach's alpha coefficients on all the subscales used in this study ranging from 0.75 to 0.85 (29).

The relatives were also asked to rate their own perception of quality of life on a visual analogue scale (VAS) with a range from 0 to 10; 0 indicating "very dissatisfied" and 10 indicating "very satisfied".

Anxiety and depression. The relatives' symptoms of anxiety and depression were evaluated by the relevant scales of Symptom Check List 90 Revised (SCL-90-R); a self-report checklist designed to reflect the symptom pattern and level of distress (30). Each item is scored on a scale of 0 ("not at all") to 4 ("extremely"), indicating the degree of distress for that particular item. The respondents are asked to answer each item according to their condition during the past 7 days. Raw-scores were converted into T-scores, and evaluated in terms of the gender-specific norms for a Danish sample. This Danish population study revealed high alpha coefficients on all the SCL subscales, and in particular for the depression and anxiety scales used in this study ($\alpha = 0.91$ and $\alpha = 0.86$, respectively) (30).

We also registered the relatives' social support and prior life events, as both factors are known to influence emotional reactions (1, 30–32).

Social support and life events. Questions regarding the relatives' social support included a question about how often they had contact with different people (parents, children, other family, colleagues after work, neighbours, childhood friends, other friends, professional caregiver), and how satisfied the relative was with this contact. The relatives also reported how many people they were able to share very personal matters with.

Questions about traumatic life events over the past year and over the entire life-span included 5 work-related questions (unemployment, not being promoted, conflicts with colleagues, superiors or subordinates) and 7 questions related to events in the family (children severely ill, severe educational problems for children, severe conflicts with grown-up children, severe problems in marriage, own severe illness, severe illness or death among relatives, severe economical problems). We counted the total amount of traumatic events in the past year and over the entire life.

The questions were modified versions of questions used in the Copenhagen City Heart Study and were administered, when the relatives were enrolled (33).

Assessment of patients

As a standard procedure during admission, relevant data were collected regarding the patient's condition: severity of injury, level of consciousness and function. Data regarding the condition of the patients were included in the study, as previous research has shown how the condition of the patient and the relative are entangled (3, 9, 24).

Severity of injury. The severity of injury was assessed by two well-known and validated scales: The Glasgow Coma Score (34) and the Injury Severity Score (ISS) (35). GCS is scored from 3 to 15. Patients with scores less than 9 are considered to be in coma, and patients with scores of 15 have spontaneous eye opening, are able to follow commands and are fully oriented. According to criteria for injury severity, GCS scores of 8 or less are classified as severe injuries. The treating physician assessed GCS at admission to the traumatic brain injury unit.

The treating physician also estimated the ISS, which consists of an anatomical scoring system that provides an overall score for patients with multiple traumatic injuries. The ISS ranges from 0 to 75. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to 1 of 6 body regions (head, face, chest, abdomen, extremities and skin). Only the highest AIS score in each region of the body is used. The scores of the 3 most severely injured regions are added together to produce the ISS. The ISS was only assessed for patients with a traumatic brain injury.

Level of consciousness. Rancho Los Amigos (RLA) score (36, 37) was assessed by a neuropsychologist at admission to sub-acute rehabilitation. This score ranges from level 1, which describes a comatose condition with no observable response, to level 8, which is a condition with purposeful and appropriate responses. This scale was designed for use on patients with a traumatic brain injury.

Functional level. The patient's functional level at admission was assessed with the Early Functional Abilities (EFA) and the Functional Independence Measure (FIM).

The EFA is an assessment tool for patients with severe cerebral impairments in the early neurological rehabilitation stage, which

Table II. *Characteristics of the relatives and the patients retrieved at baseline* p-*values from Student's* t-*test for continuous data, from* χ^2 *tests (or Fisher's exact test) for categorical characteristics and Mann-Whitney for ordinal data*

Characteristics of the relatives	Intervention group ($n=39$)	Control group ($n=47$)	p-value[a]
Female, *n* (%)	31 (80)	32 (69)	0.211
Cohabitant at time of injury, *n* (%)	23 (59)	28 (58)	0.820
Working at time of injury, age 16–66 years, *n* (%)	34 (87)	40 (83)	0.683
Relationship, *n* (%)			
Spouse	8 (20)	21 (44)	0.002
Parent	24 (61)	13 (27)	
Sibling	1 (3)	2 (4)	
Child	5 (13)	8 (17)	
Boy-/girlfriend	0 (0)	3 (6)	
Other	1 (3)	1 (2)	
Social support			
Very satisfied, %	82	80	0.855
People to talk with about personal matters, median (range)	4 (1–6)	3 (1–8)	0.377
Life events, median (range)			
Last year	0 (0–2)	1 (0–4)	0.434
Entire life	2 (0–5)	2 (0–5)	0.651
Completion of questionnaires, mean (SD) [range]			
T1: NICU, days after injury	16 (6) [5–32]	–	–
T2: Sub-acute rehab, days after injury	24 (8) [11–41]	35 (18) [9–77]	0.001
Characteristics of the patients, *n* (%)			
Male	31 (80)	32 (68)	0.145
Traumatic brain injury	31 (80)	31 (66)	0.211
Clinical status at admission to rehabilitation, mean (SD) [range]			
Admission, number of days after injury	17 (6) [7–34]	24 (16) [8–68]	0.013
Age	31.35 (17.02) [4–71]	45.51 (19.62) [1–82]	<0.001
Glasgow Coma Score	10.44 (2.96) [4–15]	11.05 (3.25) [5–15]	0.402
Early Functional Abilities	42.47 (17.42) [23–90]	44.80 (19.81) [22–91]	0.784
Functional Independence Measure	22.11 (12.06) [18–74]	24.36 (13.82) [18–68]	0.451
Rancho Los Amigo	3.86 (1.68) [2–8]	4.00 (1.39) [2–7]	0.805
Injury severity	34.90 (10.94) [25–66]	28.58 (7.09) [10–43]	0.009

SD: standard deviation.

describes clinically observable changes in a patient's early functional abilities (38) The EFA Scale contains 20 items and assesses early basic abilities related to 4 functional areas: vegetative, face and oral, sensory-motor, and sensory cognitive functions. Each item is rated on a 5-point scale from "not obviously observable" to "no essential functional limitation". The total score is the sum of the item scores, ranging from 20 to a maximum of 100. High scores indicate better functional ability.

The FIM (39) is an 18-item rating scale assessing activities of daily living (ADL): self-care, bowel and bladder management, mobility, communication, cognition, and psychosocial adjustment. Each item is rated on a 7-point scale, from "total assistance" to "complete independence". A total FIM score ranges from 18 to 126 with higher scores indicating greater independence. The FIM Scale has been shown to be valid and reliable for measuring functional outcome after TBI.

Both FIM and EFA scores assessed by physiotherapists and occupational therapists, who were trained users of the scales.

Data analysis

Descriptive statistics were used; results are presented as percentages and means with standard deviation and range. Categorical and ordinal data were analysed using χ^2 and Mann-Whitney tests. Changes in the relatives' emotional condition between T1 and T2 were analysed with paired *t*-tests and the emotional condition of the intervention and control group were compared using independent samples *t*-tests. ANCOVA was used to adjust for the relatives' gender and for the observed group differences on variables with significantly different distributions in the two patient groups. We calculated Cohen's *d* to estimate effect size.

All data was analysed using two-tailed testing, and $p=0.05$ as a threshold for statistical significance. The statistical software used was SPSS version 19.0.

RESULTS

Description of the intervention and the control group

The intervention group consisted primarily of parents (61%) and spouses (20%), and most relatives were female (80%). The majority of the relatives (59%) were living with the patient at time of injury and most (87%) were working at time of injury. The majority of the patients was male (80%) and had sustained a TBI (80%). A fifth of the intervention group had sustained a non-traumatic brain injury (NTBI) caused by spontaneous intracranial haemorrhage (2.5%), subarachnoid haemorrhage (5%), brain tumour (2.5%) and major cerebral infarction (10%). The mean age of the patients in the intervention group was 31 years (standard deviation (SD) 17; range 4–71 years) (Table II).

The control group consisted primarily of females (69%), and most relatives were spouses (44%) or parents (27%). The majority of the relatives (58%) were living with the patient at time of injury, and the majority (83%) was working at time of injury.

Most patients in the control group were male (68%) and had acquired a TBI (66%). Of the patients in the control group, 16 had acquired a NTBI caused by cardiac arrest (8%), spontaneous intracranial haemorrhage (4.5%), subarachnoid haemorrhage (4.5%), major cerebral infarction (11%), tumour (2%) and meningitis (2%). The mean age of the patients in the control group was approximately 46 years (SD 20; range 1–82) (Table II).

The relatives in the intervention group completed questionnaires regarding emotional wellbeing in the acute phase (T1) on average 16 days (SD 6; range 5–32) after injury, and once again when the patient was transferred to sub-acute rehabilitation (T2) about 24 days (SD 8; range 11–41) after injury. The patients in the intervention group were admitted to rehabilitation 17 days (SD 6; range 7–34) after injury.

The patients in the control group were admitted to sub-acute rehabilitation 24 days (SD 16; range 8–68) after injury on average, and their relatives completed the questionnaires at admission to sub-acute rehabilitation (T2) 35 days (SD 18; range 9–77) days after injury.

Condition of the relatives

The condition of the relatives in the two groups was assessed and compared with the relevant Danish norms (29, 30) using one-sample *t*-tests. The relatives in both groups had significantly higher scores on the depression and anxiety scales and significantly lower quality of life at T2 compared with Danish norms, and this was also the case for the intervention group at T1. Means, SD and range can be seen in Table III.

Changes in emotional wellbeing from T1 to T2

Quality of life. The intervention group became significantly worse from T1 to T2 ($t=2.12$, $p=0.043$, $d=0.40$) on the RE-scale, but a trend towards improvement on the VT-scale was found ($t=-2.02$, $p=0.051$, $d=0.18$). No change from T1 to T2 was observed on the MH-scale and SF-scale.

On the VAS, the relatives in the acute group rated their quality of life slightly better on T2 compared with T1 (Table III).

Emotional distress. The intervention group experienced significantly less anxiety at T2 compared with T1 ($t=2.70$, $p=0.010$, $d=0.30$), and scored lower on depression at T2 compared with T1, although not significantly lower ($t=1.77$, $p=0.085$, $d=0.29$) (Table III).

Comparisons between the intervention and the control group

Group differences. The control group was admitted to rehabilitation and completed the questionnaires later than the intervention group (see Table II). The groups did not differ significantly with regards to occupational status, cohabitation status or gender distribution.

The relative's relationship to the patient was re-coded into 3 categories; parents, spouses and others (siblings, children, boy-/girlfriends), and a χ^2 test showed that the relatives' relationship to the patient was distributed significantly different in the 2 groups (see Table II). The groups did not differ significantly with regards to social support or experienced life events.

The patients in the intervention group were significantly younger than the control group, and the intervention group had a significantly higher ISS score than the control group, indicating that patients in the intervention group had more severe injuries (Table II for results regarding group differences).

Quality of life. A significant difference was found on the RE-scale; the control group had significantly better scores on T2 ($t=-1.99$, $p=0.05$, $d=0.39$) than the intervention group. No difference was observed between the two groups on the MH-, SF- or VT-scales.

No difference was found when comparing the VAS scores of the intervention group with the VAS scores of the control group scores at T2 (Table III).

Table III. *Emotional condition of the relatives at the acute phase (T1) and the sub-acute phase (T2)*

	The intervention group				The control group	
	T1 ($n=39$)		T2 ($n=39$)		T2 ($n=47$)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Quality of life						
SF-36						
VT	28.38 (19.62)	0–75	31.84 (17.45)	10–75	33.04 (20.48)	0–75
SF	53.62 (30.05)	0–100	50.96 (30.40)	0–100	56.12 (27.69)	0–100
MH	33.58 (17.61)	4–76	34.39 (14.67)	13–77	32.00 (16.52)	3–73
RE	26.01 (31.38)	0–100	13.54 (20.49)	0–67*	25.83 (31.57)	0–100***
VAS	6.40 (3.01)	1–10	6.43 (2.8)	1–10	6.27 (2.77)	0–10
Emotional distress						
SCL-90-R						
Anxiety	64.08 (7.75)	45–80	61.72 (8.31)	36–73**	61.91 (9.89)	36–80
Depression	64.00 (6.94)	47–80	61.95 (7.56)	41–80	61.96 (8.29)	43–75

*Significant decrease from T1 to T2, $p=0.043$, Cohen's $d=0.40$. **Significant decrease from T1 to T2, $p=0.010$, Cohen's $d=0.30$. ***Significant difference comparing the groups at T2, $p=0.05$, Cohen's $d=0.39$.

SD: standard deviation; SF-36: Short Form 36; VT: Vitality; SF: Social Function; MH: Mental Health; RE: Role Emotional; VAS: Visual Analogue Scale; SCL-90-R: Symptom Checklist Revised.

Table IV. *Raw and adjusted means for emotional distress and quality of life at sub-acute phase*

	The intervention group		The control group		*p*-values	
Quality of life	Raw mean	Adjusted mean[b]	Raw mean	Adjusted mean[b]	Unadjusted[a]	Adjusted[b]
VT ($n=59$)	30.86	34.34	38.00	34.64	0.776	0.925
SF ($n=61$)	47.17	53.24	62.50	58.56	0.413	0.558
MH ($n=58$)	32.87	37.05	32.76	28.58	0.493	0.070
RE ($n=47$)	15.94	22.45	31.94	25.70	0.061	0.710
VAS ($n=59$)	6.46	6.81	6.38	6.04	0.788	0.354
Emotional distress						
Anxiety ($n=61$)	61.73	59.46	62.03	64.23	0.922	0.066
Depression ($n=61$)	62.17	61.02	61.90	63.01	0.996	0.338

[a]Unadjusted *p*-values calculated from independent *t*-tests.
[b]Adjusted for the relative's gender and relationship to the patient (spouse vs other), the patient's age, number of days after injury that questionnaire was completed and the patient's the injury severity score.
VAS: visual analogue scale; VT: Vitality; SF: Social Function; MH: Mental Health; RE: Role Emotional.

Emotional distress. No difference was found with regards to symptoms of anxiety or depression, when comparing the two groups at T2 (Table III).

Adjusted differences between groups

An ANCOVA model was used to adjust for gender and variables showing significantly different distribution in the intervention and the control group. The model adjusted for the relative's gender, the relatives' relationship to the patient (spouse vs other), the patient's age and the number of days after injury that the relatives completed the questionnaire. The model also adjusted for the ISS, and this reduced our sample, as it is only applicable to patients with TBI (see Table IV for raw and adjusted means).

No significant differences were found, but we did find a non-significant trend towards higher anxiety ($p=0.066$, $d=0.59$) and depression scores ($p=0.338$, $d=0.31$) in the control group at T2. With regards to quality of life, the control group showed lower adjusted VAS scores ($p=0.351$, $d=0.30$), but non-significant, and this was also the case on the MH-scale ($p=0.070$, $d=0.61$). Scores on the anxiety and MH-scale were borderline significant. Table IV shows that the control group obtained higher scores on the remaining SF-36 scales, however non-significant.

Supplementary analyses

The age of the patient was significant in the model, and consequently possible interactions between the age of the patient and the effect of the intervention were tested. However, the differences were not significant, and analyses including only patients above the age of 15 years showed results similar to those obtained for the full sample.

However, in the full sample, the age of the patient was important in relation to anxiety ($p<0.001$) and depression ($p<0.001$), indicating that relatives of older patients experienced less anxiety and depression. The relatives of older patients had higher scores on the VAS ($p=0.001$), RE- ($p=0.001$), MH- ($p<0.001$) and VT-scales ($p<0.001$), indicating better quality of life.

We also found that spouses had higher levels of depression ($p<0.001$) and anxiety ($p=0.001$) and reported lower quality of life at MH- ($p=0.002$) and VT-scale ($p=0.007$) compared with other relatives.

DISCUSSION

Changes in emotional wellbeing from T1 to T2

We found a significant decrease in symptoms of anxiety from T1 to T2 and a decrease in symptoms of depression; however, this decrease was not significant. We found a borderline significant increase in Vitality scores, but the only significant change on the SF-36 scales was a decrease in RE scores from T1 to T2, indicating lower quality of life at T2.

Anxiety probably reflects acute worries about the patient and the future, and these symptoms may decrease more rapidly than symptoms of depression, as other studies have shown that symptoms of depression can persist for years after injury (2, 5–7, 25, 31). The decrease in symptoms of anxiety and depression and improvement in vitality could be caused by the intervention, but it is very likely that the decrease is a consequence of a more spontaneous improvement in the emotional state of the relatives related to the patient's more stable and perhaps improved condition (40).

Low scores on the RE-scale reflect problems with work or other daily activities as a result of emotional problems. It is very likely that relatives rate this score lower at T2 because at this point they realize the severity of the injury and the long-term care and rehabilitation needed.

Because of the intervention as well as the stabilization of the patient's condition, an improvement in the condition of the relatives from T1 to T2 was anticipated, and the control group was included in attempt to obtain a more realistic picture of the effects of the intervention.

Comparisons between the intervention and the control group

The control group was included at admission to rehabilitation in hospital and had not received any kind of intervention in the acute setting. Unfortunately, there were many differences between the two groups: the intervention group completed the questionnaire earlier, the patients were younger and had more severe injuries, and the distribution of parents and spouses was significantly different in the two groups. When adjusting for these differences more anxiety and depression were found in the control group as well as lower VAS and MH-scores. The results regarding anxiety and the scores on the MH-scale were borderline significant, but the others were non-significant. We also found a non-significant tendency towards higher scores on the RE- and SF-scales in the control group.

The results are somewhat mixed when comparing the 2 groups, but it is clear that any effects of the intervention were

small. Other factors appeared to be more important since the age of the patient and the relatives' relationship to the patient overrode any effects of the intervention.

This result was unexpected, and in contrast to what most relatives had expressed, since the majority spontaneously expressed satisfaction with the information and support received during the sessions. However, it is likely that the intervention should have been provided even earlier than it was administered. Many relatives pointed out that their need for psychological support as well as information had been more critical earlier during the patient's stay in acute care. Moreover, in most cases the intervention was limited to only one session, and this may not be enough to produce detectable effects. This indicates that both the timing of and the amount of intervention are important parameters if effects should be detectable.

To the authors' knowledge, this study is the only one investigating the effect of an early intervention study and therefore adds to the knowledge available regarding the condition of the relatives in the early phases of rehabilitation. Nevertheless, the intervention conducted only had limited effects on emotional distress. The intervention studies previously conducted regarding psychological support have also had difficulties proving effects on standardized measures of psychological distress (16, 18, 21, 41). Intervention effects seem to be more detectable on more subjective measures (17, 42, 43).

Methodological considerations

The aim of this study was to examine the effects of neuropsychological intervention in the acute setting, but a variety of circumstances influenced our data collection and the two groups differed on a number of key variables.

In many cases, one of several eligible relatives volunteered to participate at the critical time of enrolment, and it was not deemed justifiable to ask specific members of the families to participate. Of course, this choice may have resulted in bias, as we might primarily have included resilient and emotionally strong relatives, which may indirectly have influenced the effects of intervention. In addition, this choice made it impossible to stratify the relatives according to their relationship to the patient.

Our samples were relatively small, and it is likely that statistical power was not sufficient to detect small effects of the intervention.

It is also a limitation that we used general measures of mental symptoms and quality of life, since it is possible that outcome measures specifically aimed at detailed description of the immediate emotional distress and concrete worries and concerns of the relatives may be more sensitive to the effects of interventions.

Implications

This pilot study has emphasized the emotionally straining situation of families of brain injury survivors in the early phases of rehabilitation and the need for early intervention. No other studies have investigated the effects of early psychological intervention despite the call for early supportive intervention demonstrated in previous research (3, 9, 10, 44).

Future research should focus on obtaining larger samples and investigating intervention characteristics, such as timing, number of sessions and follow-up time. Randomized studies should be considered, but if this is considered unethical, efforts should be made to obtain more comparable intervention and control groups than we were able to obtain in the present study. Larger samples should enable better statistical control of background variables, but individual matching is also a possibility. Choice of outcome measures, as well as follow-up time after intervention, should be considered thoroughly, as changes in distress might require a longer follow-up time to be measurable. Moreover, it would be relevant to include families' ratings of their gains and the beneficial components of the intervention.

Conclusion

In the intervention group, a decrease in symptoms of anxiety and depression from T1 to T2 was observed, and this group also showed less anxiety than the control group. However, most effects were small, and consequently the study did not demonstrate convincing effects of a short neuropsychological intervention administered early in the acute phase. Despite the negative results, psychological intervention of sufficient duration is likely to reduce emotional strain and distress, and this possibility should be explored further in future studies.

ACKNOWLEDGEMENTS

The authors would like to thank all participants in the study, and additionally acknowledge the support of the staff at the NICU, Department of Neuroanaesthesiology, Rigshospitalet, Copenhagen University Hospital, in particular Karen-Lise Welling, PhD, and Jesper Qvist, MD. The authors would also like to thank the staff at the Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen University Hospital, Glostrup, Denmark.

Conflicts of interest. No commercial party had direct influence on the results of the research supporting this article. The study was supported in part by a grant from Aase and Ejnar Danielsens Foundation.

REFERENCES

1. Harris JK, Godfrey HP, Partridge FM, Knight RG. Caregiver depression following traumatic brain injury (TBI): a consequence of adverse effects on family members? Brain Inj 2001; 15: 223–238.
2. Machamer J, Temkin N, Dikmen S. Significant other burden and factors related to it in traumatic brain injury. J Clin Exp Neuropsychol 2002; 24: 420–433.
3. Norup A, Siert L, Mortensen EL. Emotional distress and quality of life in relatives of patients with severe brain injury: the first month after injury. Brain Inj 2010; 24: 81–88.
4. Panting A, Merry PH. The long term rehabilitation of severe head injuries with particular reference to the need for social and medical support for the patient's family. Rehabilitation 1972; 38: 33–37.
5. Perlesz A, Kinsella G, Crowe S. Psychological distress and family satisfaction following traumatic brain injury: injured individuals

and their primary, secondary, and tertiary carers. J Head Trauma Rehabil 2000; 15: 909–929.
6. Ponsford J, Olver J, Ponsford M, Nelms R. Long-term adjustment of families following traumatic brain injury where comprehensive rehabilitation has been provided. Brain Inj 2003; 17: 453–468.
7. Schonberger M, Ponsford J, Olver J, Ponsford M. A longitudinal study of family functioning after TBI and relatives' emotional status. Neuropsychol Rehabil 2010; 20: 813–829.
8. Thomsen IV. The patient with severe head injury and his family. A follow-up study of 50 patients. Scand J Rehabil Med 1974; 6: 180–183.
9. Norup A, Welling KL, Qvist J, Siert L, Mortensen EL. Depression, anxiety and quality-of-life among relatives of patients with severe brain injury: the acute phase. Brain Inj 2012; 26: 1192–1200.
10. Pielmaier L, Walder B, Rebetez MM, Maercker A. Post-traumatic stress symptoms in relatives in the first weeks after severe traumatic brain injury. Brain Inj 2011; 25: 259–265.
11. Douglas JM, Spellacy FJ. Indicators of long-term family functioning following severe traumatic brain injury in adults. Brain Inj 1996; 10: 819–839.
12. Marsh NV, Kersel DA, Havill JH, Sleigh JW. Caregiver burden at 6 months following severe traumatic brain injury. Brain Inj 1998; 12: 225–238.
13. Marsh NV, Kersel DA, Havill JH, Sleigh JW. Caregiver burden at 1 year following severe traumatic brain injury. Brain Inj 1998; 12: 1045–1059.
14. Turner B, Fleming J, Parry J, Vromans M, Cornwell P, Gordon C, et al. Caregivers of adults with traumatic brain injury: the emotional impact of transition from hospital to home. Brain Impairment 2010; 11: 281–292.
15. Hickey M. What are the needs of families of critically ill patients? A review of the literature since 1976. Heart Lung 1990; 19: 401–415.
16. Acorn S. Assisting families of head-injured survivors through a family support programme. J Adv Nurs 1995; 21: 872–877.
17. Kreutzer JS, Stejskal TM, Godwin EE, Powell VD, Arango-Lasprilla JC. A mixed methods evaluation of the brain injury family intervention. NeuroRehabilitation 2010; 27: 19–29.
18. Kreutzer JS, Stejskal TM, Ketchum JM, Marwitz JH, Taylor LA, Menzel JC. A preliminary investigation of the brain injury family intervention: impact on family members. Brain Inj 2009; 23: 535–547.
19. Brown R, Pain K, Berwald C, Hirschi P, Delehanty R, Miller H. Distance education and caregiver support groups: comparison of traditional and telephone groups. J Head Trauma Rehabil 1999; 14: 257–268.
20. Carnevale GJ, Anselmi V, Busichio K, Millis SR. Changes in ratings of caregiver burden following a community-based behavior management program for persons with traumatic brain injury. J Head Trauma Rehabil 2002; 17: 83–95.
21. Liamaki G, Bach L. Group intervention for carers of brain injured relatives: thoughts and suggestions. Clinical Psychol 2003; 26: 28–31.
22. Engberg AW, Liebach A, Nordenbo A. Centralized rehabilitation after severe traumatic brain injury – a population-based study. Acta Neurol Scand 2006; 113: 178–184.
23. Engberg AW. A Danish national strategy for treatment and rehabilitation after acquired brain injury. J Head Trauma Rehabil 2007; 22: 221–228.
24. Livingston MG, Brooks DN, Bond MR. Patient outcome in the year following severe head-injury and relatives psychiatric and social functioning. J Neurol Neurosurg Psychiatry 1985; 48: 876–881.
25. Marsh NV, Kersel DA, Havill JA, Sleigh JW. Caregiver burden during the year following severe traumatic brain injury. J Clin Exp Neuropsychol 2002; 24: 434–447.
26. Oddy M, Humphrey M, Uttley D. Stresses upon relatives of head-injured patients. Br J Psychiatry 1978; 133: 507–513.
27. Oddy M. Seven years after – A follow-up-study of severe head-injury in young-adults. J Clin Exper Neuropsychol 1985; 7: 165.
28. Wells R, Dywan J, Dumas J. Life satisfaction and distress in family caregivers as related to specific behavioural changes after traumatic brain injury. Brain Inj 2005; 19: 1105–1115.
29. Bjorner JB, Damsgård MT, Watt T, Bech P. [Danish manual for SF-36. A health-related questionnaire]. Copenhagen: Medif; 1997 (in Danish).
30. Olsen LR, Mortensen EL, Bech P. Mental distress in the Danish general population. Acta Psychiatrica Scand 2006; 113: 477–184.
31. Douglas JM, Spellacy FJ. Correlates of depression in adults with severe traumatic brain injury and their carers. Brain Inj 2000; 14: 71–88.
32. Ergh TC, Rapport LJ, Coleman RD, Hanks RA. Predictors of caregiver and family functioning following traumatic brain injury: social support moderates caregiver distress. J Head Trauma Rehabil 2002; 17: 155–174.
33. Sethi AA, Nordestgaard BG, Agerholm-Larsen B, Frandsen E, Jensen G, Tybjaerg-Hansen A. Angiotensinogen polymorphisms and elevated blood pressure in the general population: the Copenhagen City Heart Study. Hypertension 2001; 37: 875–881.
34. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
35. Baker SP, Oneill B, Haddon W, Long WB. Injury severity score – method for describing patients with multiple injuries and evaluating emergency care. J Trauma-Inj Infect Crit Care 1974; 14: 187–196.
36. Hagen C, Malkmus D, Durham P. Levels of cognitive function. Downey (CA): Rancho Los Amigos Hospital; 1972.
37. Hagen C. Language disorders secondary to closed head injury: diagnosis and treatment. Top Lang Dis 1981; 1: 73–87.
38. Heck G, Schmidt T, Steiger-Bachler G. Early functional abilities (EFA) – eine Skala zur Evaluation von Behandlungsverlaufen in der neurologischen Fruhrehabiltation. Neurol Rehabil 2000; 6: 125–133.
39. Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. Adv Clin Rehabil 1987; 1: 6–18.
40. Norup A, Spangsberg Kristensen K, Poulsen I, Löfvquist Nielsen C, Lykke Mortensen W. Clinically significant changes in the emotional condition of relatives of patients with severe traumatic brain injury during sub-acute rehabilitation. J Rehabil med 2013; 45: 820–826.
41. Backhaus SL, Ibarra SL, Klyce D, Trexler LE, Malec JF. Brain injury coping skills group: a preventative intervention for patients with brain injury and their caregivers. Arch Phys Med Rehabil 2010; 91: 840–848.
42. Albert SM, Im A, Brenner L, Smith M, Waxman R. Effect of a social work liaison program on family caregivers to people with brain injury. J Head Trauma Rehabil 2002; 17: 175–189.
43. Sander AM, Clark AN, Atchison TB, Rueda M. A web-based videoconferencing approach to training caregivers in rural areas to compensate for problems related to traumatic brain injury. J Head Trauma Rehabil 2009; 24: 248–261.
44. Mauss-Clum N, Ryan M. Brain injury and the family. J Neurosurg Nurs 1981; 13: 165–169.

J Rehabil Med 2013; 45: 835–842

ORIGINAL REPORT

QUALITY OF LIFE AFTER TRAUMATIC BRAIN INJURY: FINNISH EXPERIENCE OF THE QOLIBRI IN RESIDENTIAL REHABILITATION

Sini-Tuuli Siponkoski, MAPsych[1], Lindsay Wilson, PhD[2], Nicole von Steinbüchel, PhD[3], Jaana Sarajuuri, LicPsych[1] and Sanna Koskinen, PhD[1]

From the [1]Käpylä Rehabilitation Centre, Helsinki, Finland, Department of Psychology, [2]University of Stirling, Stirling, UK and [3]Department of Medical Psychology and Medical Sociology, Georg-August-University, Goettingen, Germany

Objective: **To evaluate health-related quality of life of traumatic brain injury patients who have received intensive multidisciplinary residential rehabilitation. To examine the psychometric characteristics of the Finnish Quality of Life after Brain Injury (QOLIBRI) questionnaire.**

Subjects: **A total of 157 adults with TBI, up to 15 years post-injury, who had been treated in the Käpylä Rehabilitation Centre, Helsinki, Finland.**

Methods: **Functional status was assessed using the Extended Glasgow Outcome Scale. Emotional state was evaluated using the Hospital Anxiety and Depression Scale. Health-related quality of life was measured using a generic measure (Short Form-36) and the QOLIBRI.**

Results: **Quality of life was related to depression, amount of help needed, anxiety, education level and age at injury. Quality of life was not associated with time since injury, but a paradoxical relationship was found with injury severity. Internal consistency (alpha = 0.79–0.95) and test-retest reliability (rtt = 0.75–0.87) of the Finnish QOLIBRI met standard psychometric criteria.**

Conclusion: **Quality of life remained relatively stable in the long term. Milder injuries were associated with lower life satisfaction, and careful follow-up is recommended to target patients in special need. This study confirms the reliability and validity of the Finnish QOLIBRI.**

Key words: health-related quality of life; traumatic brain injury; rehabilitation; outcome assessment; psychometrics.

J Rehabil Med 2013; 45: 835–842

Correspondence address: Sini-Tuuli Siponkoski, Käpylä Rehabilitation Centre, Nordenskiöldinkatu 18 B, Box 103, FIN-00251 Helsinki, Finland. E-mail: stsipo@gmail.com

Accepted April 30, 2013

INTRODUCTION

Traumatic brain injury (TBI) affects many domains of life, and impacts the quality of life (QoL) experienced by the injured person (1). A central aspect of QoL is subjective well-being, and overall QoL is related to the person's individual expectations and achievements and their culture and value systems (1). Subjective health-related quality of life (HRQoL) refers to human life experiences, including health status, subjective well-being and life satisfaction (2). Earlier studies have shown that HRQoL after TBI is linked to changes in emotional status (3–6), neurobehavioral disturbances (7, 8), cognitive impairments (9), sleep-wake disturbances and fatigue (10, 11), pain (12), loss of communication skills (13), loss of autonomy in advanced activities of daily living (ADL) (9), changes in the level of participation (14) and vocational status (3, 5).

In recent years HRQoL has become an important outcome variable after TBI (2, 15–18) alongside the more traditional outcome measures, such as physical independence and return to work. This reflects an underlying paradigm shift in the evaluation of outcomes in TBI: capturing the patient's own perspective has become increasingly essential (15). HRQoL is also viewed as a central end-point of rehabilitation, and appropriate measures are needed for the development and evaluation of effective treatments.

Generic HRQoL measures do not capture the full spectrum of effects of brain injury, and the need for a disease-specific measure was identified (16, 17). The Quality of Life after Brain Injury (QOLIBRI) was created to fill this gap. It is a HRQoL instrument specifically developed for persons after TBI (19–21). The validity and psychometric properties of the QOLIBRI have been investigated recently in a multi-centre international study with 795 adults with TBI (19–21). The use of the QOLIBRI in clinical settings has also been described previously in detail; the QOLIBRI provides information about the patient's subjective perception of his/her HRQoL, allows the identification of personal needs, and aids in the prioritization of therapeutic goals and evaluation of individual progress (21).

The Finnish version of the QOLIBRI questionnaire was originally translated in 2004 according to linguistic validation guidelines (20) and was revised in 2006. The Finnish QOLIBRI validation study presented here was conducted using a convenience sample of patients with TBI, who had all participated in residential rehabilitation. This strategy creates some limitations for the study, but simultaneously provides an opportunity to explore the HRQoL in a pure rehabilitation sample with its own distinctive characteristics. The present study also covers an exceptionally long follow-up time of up to 15 years after TBI. The aims of the present study were: (*i*) to examine the HRQoL of patients with TBI who have received residential rehabilitation; and (*ii*) to assess the psychometric properties and validity of the Finnish QOLIBRI.

 doi: 10.2340/16501977-1189

 ISSN 1650-1977

MATERIAL AND METHODS

Participants

The Finnish sample of the international QOLIBRI validation study consisted of 157 patients with TBI who had received intensive multidisciplinary residential rehabilitation during 1993–2006 at the Käpylä Rehabilitation Centre, Helsinki. Patients are referred to the centre from all over Finland by the clinicians responsible for their care. They stay in the centre for 2–8 weeks depending on their individual needs and goals. The multidisciplinary rehabilitation consists of neuropsychological rehabilitation, physiotherapy, occupational therapy, speech and language therapy, as well as the services provided by social workers, nurses and medical doctors. The support provided by peers is essential. After the rehabilitation period the patients return to home. Inclusion criteria were: (*i*) diagnosis of traumatic brain injury according to ICD-10; (*ii*) Glasgow Coma Scale score (24 h worst) obtained; (*iii*) time since injury between 3 months and 15 years; (*iv*) aged 15 years or more at injury; (*v*) outpatient status; (*vi*) aged 17–69 years at interview; and (*vii*) able to give informed consent. Exclusion criteria were: (*i*) Extended Glasgow Outcome Scale (GOSE) <3; (*ii*) spinal cord injury; (*iii*) significant current or pre-injury psychiatric history; (*iv*) ongoing severe addiction; (*v*) inability to understand, cooperate and answer; and (*vi*) having terminal illness. The Finnish sample is part of the larger international QOLIBRI development and validation data (19, 20) and it was collected during 2006–2007.

Measures

The QOLIBRI (19–21) gives a profile of HRQoL in domains relevant to TBI, together with a total HRQoL score. The measure consists of 37 items which form 6 scales: Cognition; Self; Daily life and autonomy; Social relationships; Emotions; and Physical problems. Four of the scales contain "How satisfied are you with..." items, and two have "How bothered are you with..." items. Responses are given on a 5-point Likert scale, from "not at all" to "very".

The GOSE was used as an assessment of functional status (22). Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS) (23). The Short-Form 36 (SF-36) (24) was used as a patient-reported generic health outcome measure, which gives information on both physical and mental HRQoL (25). Data were also gathered concerning social and demographic information, including age, gender, relationship status, educational background, occupation, level of independence, number of social contacts, participation in leisure activities, and the use of alcohol and recreational drugs. A health questionnaire was used to assess health status and comorbid health conditions and problems. Information was also gathered concerning help needed in daily life. Clinicians collected clinical data, including level of consciousness after injury (the worst GCS score in the first 24 h), length of post-traumatic amnesia, location of injury, current medication, and a rating of disorders in 10 areas (epilepsy, hemiparesis, visual and auditory deficit, extra-cerebral injuries, communication problems, attention dysfunction, memory dysfunction, executive dysfunction, affective and behavioural disorders).

Ethical approval

The QOLIBRI study was approved by the ethical committee of the Käpylä Rehabilitation Centre.

Data analysis

The data was analysed using SPSS 18.0. Missing responses on the QOLIBRI-scale were imputed per participant by substituting the missing value by the scale mean rounded to an integer. The scale scores were transformed to 100-point scale (i.e. percentage scale).

RESULTS

Descriptives

A total of 157 participants were enrolled, 14 subjects were excluded due to missing GCS. Demographic and clinical characteristics of the sample are shown in Table I. Both age (mean 43.10 years [SD 10.78]) and the years since injury (mean 8.03 years [SD 3.99]) were somewhat higher than in the international data (age: mean 39.0 years [SD 13.30]; years since injury: mean 5 years [SD 3.9]). Coma length (mean 3.90 days [SD 6.68]) was obtained from 149 participants

Table I. *Demographic and clinical characteristics of the sample*

Characteristics	*n* (%)
Gender	
Male	101 (64.3)
Female	56 (35.7)
Age	
20–30 years	23 (14.6)
31–44 years	62 (39.5)
45–63 years	72 (45.9)
Employment status	
Employed full-time	7 (4.5)
Employed part-time	15 (9.6)
Self-employed	13 (8.3)
Voluntary work	22 (14.0)
Unemployed	6 (3.8)
Retired	100 (64.7)
Relationship status	
Single	34 (21.7)
Married or partnered	100 (63.7)
Separated/divorced or widowed	23 (14.6)
Living arrangements	
Independent	103 (65.6)
Supported	54 (34.4)
Glasgow Coma Scale score (24 h worst)	
Severe: 3–8	93 (59.2)
Moderate: 9–12	8 (5.1)
Mild: 13–15	56 (35.7)
Time since injury	
<1 years	5 (3.2)
1 to <2 years	4 (2.5)
2 to <4 years	19 (12.1)
4–15 years	129 (82.2)
Glasgow Outcome Scale Extended	
Severe disability	19 (12.1)
Moderate disability	136 (86.6)
Good recovery	2 (1.3)

Table II. *Regression model for Finnish Quality of Life after Brain Injury (QOLIBRI) questionnaire total score*

Variable	Standardized coefficient (beta)	Proportion of explained variance (cumulative adjusted R^2)	Change in R^2	Significance of change in R^2
HADS depression	–0.45	0.49	0.50	<0.001
Help needed	–0.21	0.55	0.06	<0.001
HADS anxiety	–0.25	0.57	0.03	0.006
Education level	0.14	0.59	0.02	0.030
Age at TBI	–0.13	0.60	0.02	0.031

TBI: traumatic brain injury; HADS: Hospital Anxiety and Depression Scale.

and the length of post-traumatic amnesia (mean 26.42 days [SD 35.63]) was obtained from 150 participants. The highest education levels were: primary school (14.5%), secondary school (5.1%), trade or technical certificate (28.0%), college diploma or degree (33.1%), university degree (17.2%) and other (1.9%). Again compared with the international data, both lower primary school-group and higher college- and university groups were larger, and therefore the variance was greater (19). For further analysis, the education level "other", which was chosen by 3 participants, was replaced by mean rank (3.) of the 5 clearly ordinal education levels. This was also considered case by case to be the best match.

Predictors of health-related quality of life

Stepwise linear regression analysis was conducted to examine predictors of quality of life. The following variables were entered into the analysis: coma length, GCS, length of post-traumatic amnesia, GOSE, number of comorbid health conditions, number of clinical disorders, number of leisure activities, anxiety and depression measured by HADS, age, rounded age at TBI, rounded years since injury, alcohol use, education level, employment status and amount of received rehabilitation. Since most of the variables were skewed, the analysis was conducted using ranked data (26). Variables were excluded if they explained less than 1% of the variance. Five

Table III. *Item characteristics*

Scale	Item	Mean	SD	Skewness	CITC	Cronbach's Alpha if item removed	*n*
Cognition							
	Concentrate	2.96	1.16	0.76	0.74	0.91	156
	Express yourself	3.33	1.05	–0.12	0.78	0.90	156
	Remember	2.86	1.23	0.06	0.73	0.91	156
	Plan and problem solve	3.42	1.20	–0.24	0.81	0.90	156
	Decisions	3.28	1.13	–0.24	0.75	0.90	156
	Find way	3.76	1.20	–0.70	0.67	0.91	156
	Speed of thinking	3.12	1.24	–0.15	0.75	0.90	156
Self							
	Energy	2.76	1.22	0.25	0.65	0.90	157
	Motivation	2.97	1.22	–0.08	0.70	0.88	157
	Self-esteem	3.11	1.22	–0.15	0.72	0.88	157
	Way you look	3.27	1.12	–0.24	0.61	0.89	157
	Achievements	3.28	1.30	–0.29	0.67	0.89	157
	Self-perception	3.15	1.07	–0.25	0.82	0.87	157
	Own future	3.10	1.24	–0.10	0.76	0.88	157
Daily life and autonomy							
	Independence	3.41	1.16	–0.32	0.67	0.86	157
	Get out and about	3.59	1.20	–0.34	0.74	0.85	157
	Domestic activities	3.52	1.22	–0.47	0.70	0.85	157
	Run personal finances	3.80	1.30	–0.89	0.63	0.86	157
	Participation in work or education	2.55	1.38	0.40	0.51	0.88	157
	Social–leisure activities	3.15	1.35	–0.11	0.66	0.86	157
	In charge of life	3.64	1.14	–0.41	0.76	0.85	157
Social relationships							
	Affection towards others	3.49	1.28	–0.38	0.67	0.84	156
	Family members	3.86	1.08	–0.74	0.73	0.84	155
	Friends	3.54	1.19	–0.52	0.70	0.84	155
	Partner	3.53	1.43	–0.57	0.66	0.85	155
	Sex life	2.94	1.47	0.09	0.70	0.84	155
	Attitudes of others	3.25	1.10	–0.06	0.57	0.86	155
Emotions							
	Loneliness	4.01	1.14	–1.19	0.48	0.84	156
	Boredom	3.76	1.13	–0.83	0.65	0.79	156
	Anxiety	3.73	1.26	–0.71	0.75	0.76	156
	Depression	3.58	1.24	–0.59	0.73	0.77	156
	Anger/aggression	3.88	1.23	–0.91	0.55	0.82	156
Physical problems							
	Slowness/clumsy	3.86	1.17	–0.95	0.56	0.76	157
	Other injuries	3.41	1.39	–0.46	0.61	0.74	157
	Pain	3.41	1.38	–0.41	0.57	0.75	157
	See/hear	3.89	1.05	–0.93	0.52	0.77	157
	TBI–effects	2.81	1.13	–0.05	0.60	0.74	157

SD: standard deviation; TBI: traumatic brain injury; CITC: corrected item-total correlations.

Table IV. *Scale properties*

	Mean, %	SD	Cronbach's alpha
Cognition	56.11	23.20	0.92
Self	52.28	23.68	0.90
Daily life and autonomy	59.49	23.73	0.88
Social relationships	60.92	24.53	0.87
Emotions	69.84	23.23	0.83
Physical problems	61.89	22.71	0.79
QOLIBRI total	59.41	19.19	0.95

CITC: corrected item-total correlations; SD: standard deviation; QOLIBRI: Finnish Quality of Life after Brain Injury.

variables reached significance as predictors of the total QOLIBRI score: depression; the amount of help needed; anxiety; education level; and age at injury. These variables accounted for 60.1% of the variance (Table II).

Education level and age at injury were examined further, since these were specific predictors from the Finnish sample not found in the international study. A statistically significant correlation was found between the total QOLIBRI scale and age at TBI (r=–0.177, p=0.027). When examined more closely, two of the QOLIBRI subscales were significantly correlated with age at TBI: the Cognition scale (r=–0.226, p=0.005) and the Physical problems scale (r=–0.162, p=0.043). The association between the total QOLIBRI and education level, on the other hand, did not reach statistical significance when measured by Spearman's rho (r=0.108, p=0.179). However, the Physical problems (r=0.206, p=0.010) and Daily life and autonomy subscales (r=0.163, p=0.041) correlated significantly with education level.

Psychometric properties of the Finnish QOLIBRI

There were a maximum of 18.9% and a median of 6.1% missing responses per participant. Item characteristics of the QOLIBRI-items are shown in Table III. All of the corrected item-total correlations (CITCs) were 0.48 or greater: it is conventionally accepted that they should be greater than 0.4 (27). Internal consistency of the scales and the total score estimated by Cronbach's alpha met standard psychometric criteria (Table IV). An endorsement index was used for item frequency analysis: distributions were checked for frequency problems and no 2 adjacent response categories had a sum of less than 10% of the total number of responses (28).

Test-retest reliability. A total of 49 subjects completed the QOLIBRI again after a 2-week interval. The test-retest intraclass correlations (ICC) of the Finnish QOLIBRI, which have previously been reported by Steinbüchel et al. (20), ranged from 0.75 to 0.83 for separate scales. The ICC for the total QOLIBRI was 0.87. Test-retest change was examined by paired sample t-testing (Table V). Because most of the scale-variables were skewed, a square-root transformation was applied before carrying out the statistical comparisons. The total QOLIBRI score was consistent over the 2 measurements (p=0.478). Two of the scales ("Daily life and autonomy" and "Emotions") differed statistically between the 2 measurements (p=0.035; p=0.032), but the effect sizes were small (–0.176; –0.213).

Structure of the measure. To confirm the dimensionality and structure of the QOLIBRI, principal component analysis was conducted using oblique rotation (promax method with Kaiser Normalization based on the assumption of correlated scales). A forced 6-factor solution was produced to compare the structure of Finnish QOLIBRI with the international analysis. As shown in Table VI, most of the QOLIBRI scales load on appropriate factors and the PCA reproduces the overall structure of the QOLIBRI. The Daily life and autonomy scale had most cross loadings, and the reliability of this scale was therefore examined more closely. The overall alpha of the scale was good (0.877) and the corrected item total correlations were all 0.512 or greater.

Validity of the Finnish QOLIBRI

Construct validity was assessed by examining correlations between the QOLIBRI scale and other assessments (GOSE, HADS, SF-36) plus demographic and clinical factors. Since the variables were not normally distributed, Spearman correlations were used (Table VII). The results indicate that emotional state is strongly associated with the overall QOLIBRI. In addition, significant correlations were found between the QOLIBRI and the SF-36, a general HRQoL-measure; the mental scale of the SF-36 correlated most strongly with the Emotions-scale of the QOLIBRI, and the physical scale of the SF-36 correlated most strongly with the Physical scale as expected. No association between the years since injury and the QOLIBRI was found and there was no overall trend for change in HRQoL over the long follow-up. The QOLIBRI

Table V. *Test-retest comparisons*

	Paired samples n	Test Mean (SD)	Re-test Mean (SD)	t-value	p-value	Effect size (Cohen's d)
Cognition	48	55.58 (21.45)	54.19 (21.04)	0.648	0.520	0.07
Self	49	53.18 (22.18)	50.87 (21.45)	1.263	0.213	0.11
Daily life and autonomy	49	55.83 (22.01)	59.84 (23.49)	–2.165	0.035	–0.18
Social relationships	49	58.95 (23.51)	58.45 (24.22)	0.202	0.841	0.02
Emotions	49	67.65 (22.66)	72.47 (22.67)	–2.209	0.032	–0.21
Physical problems	49	60.92 (21.47)	62.65 (21.77)	–0.873	0.387	–0.08
QOLIBRI total	49	58.16 (16.63)	59.06 (17.19)	–0.715	0.478	–0.05

QOLIBRI: Finnish Quality of Life after Brain Injury; SD; standard deviation.

Table VI. *Principal component analysis of the Finnish Quality of Life after Brain Injury (QOLIBRI) items. Factor loadings ≥ 0.25 are shown*

Scale	Item	Communality	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
Cognition								
	Concentrate	0.66	0.75					
	Express yourself	0.72	0.83					
	Remember	0.66	0.70			0.25		
	Plan and problem solve	0.76	0.81					
	Decisions	0.72	0.77			–0.27		
	Find way	0.58	0.90					
	Speed of thinking	0.68	0.88					
Self								
	Energy	0.64		0.55		0.30		
	Motivation	0.63		0.67				
	Self-esteem	0.70		0.80				
	Way you look	0.47		0.68				
	Achievements	0.55		0.64				
	Self-perception	0.75		0.86				
	Own future	0.67		0.80				
Daily life								
	Independence	0.64						0.57
	Get out and about	0.69		0.25				0.54
	Domestic activities	0.63		0.25		0.43		0.31
	Run personal finances	0.69						0.78
	Participation work	0.37		0.38				
	Social & leisure activities	0.66		0.55		0.26		
	In charge of life	0.74						0.64
Social								
	Affection towards others	0.67			0.73	0.26		
	Family members	0.69			0.77			
	Friends	0.70		0.33	0.65			
	Partner	0.65			0.86			
	Sex life	0.61			0.72			
	Attitudes of others	0.54		0.39	0.47			
Emotions								
	Loneliness	0.63			0.54	0.32		–0.36
	Boredom	0.60					0.65	
	Anxiety	0.80					0.83	
	Depression	0.79					0.86	
	Anger/aggression	0.70			–0.29		0.80	
Physical								
	Slow/clumsiness	0.57				0.81		
	Other injuries	0.59				0.83		
	Pain	0.64				0.78		
	See/hear	0.49		–0.42		0.49		
	TBI effects	0.64				0.55		

Table VII. *Spearman correlations*

	Cognition	Self	Daily life	Social	Emotions	Physical problems	QOLIBRI total
Age	–0.18	–0.10	–0.09	–0.01	–0.01	–0.13	–0.12
Education level	0.13	0.07	0.16*	0.08	0.12	0.21**	0.15
Glasgow Coma Scale	–0.25**	–0.17*	–0.23**	–0.08	–0.10	–0.24**	–0.21**
Time since injury	–0.02	0.02	0.02	0.08	0.06	0.10	0.01
Age at injury	–0.23**	–0.14	–0.15	–0.06	–0.04	–0.16*	–0.18*
Coma length	0.31**	0.24**	0.31**	0.19*	0.18*	0.30**	0.32**
GOSE	0.22**	0.17*	0.28**	0.17*	0.23**	0.27**	0.27**
HADS depression	–0.57	–0.64**	–0.65**	–0.59**	–0.61**	–0.55**	–0.74**
HADS anxiety	–0.48**	–0.51**	–0.50**	–0.39**	–0.64**	–0.48**	–0.60**
SF-36 MCS	0.40**	0.56**	0.54**	0.54**	0.67**	0.35**	0.63
SF-36 PCS	0.38**	0.27**	0.30**	0.15	0.15	0.62**	0.39**

*$p<0.05$; **$p<0.01$.

QOLIBRI: Finnish Quality of Life after Brain Injury; GOSE: Extended Glasgow Outcome Scale; HADS: Hospital Anxiety and Depression Scale; SF-36: Short-Form 36; PCS: physical component summary scores; MCS: mental component summary scores.

total was 59.4 (SD = 14.5) at 0 to < 4 years ($n = 28$), 58.1 (SD = 19.5) at 4–9 years ($n = 72$), and 61.0 (SD = 21.0) at 10–15 years ($n = 57$).

DISCUSSION

The first aim of this study was to evaluate HRQoL and its predictors in patients with TBI, who have received residential rehabilitation. In this group depression was found to be the strongest predictor of HRQoL. Other significant predictors were the amount of help needed, anxiety, age at injury, and education level. Time after injury was not related to reported HRQoL. Milder injuries were paradoxically associated with lower life satisfaction. The other main goal of this study was to assess the reliability and validity of the Finnish version of the QOLIBRI questionnaire. The results show that the psychometric properties of the Finnish QOLIBRI met standard psychometric criteria. The construct validity of the measure was confirmed by examining its relationship with other measures, including the HADS, SF-36 and GOSE; the relationships found are consistent with expectations for a HRQoL scale.

The strong association between the QOLIBRI and emotional state was expected on the basis of the theoretical model and the analysis of the international data (19) and from previous research (3–6). The association between the QOLIBRI and the amount of help needed has also been reported previously (19), whereas age at injury and education level were novel predictors of the QOLIBRI, which had a small, but significant, impact on reported HRQoL in this study. Both are recognized as factors contributing to outcome after TBI in the literature (29). Truelle et al. (2010) also found that patients with a lower level of education experienced lower quality of life in several domains measured by the QOLIBRI, which is consistent with our finding. Compared with the large international sample, the variance in education level was greater and the follow-up time after injury was longer in the Finnish sample, which could have made these phenomena more visible. Younger age is also consistently associated with better functional outcome after TBI (29, 30), but the literature concerning age and cognitive outcome after TBI is still rather limited. It has been shown in one longitudinal study, however, that most patients with TBI experience mild cognitive decline during follow-up, but this decline is influenced by gender and age at injury (31). Our finding, that age at TBI is related to the patient's subjective satisfaction with their cognitive functioning, complements these results nicely.

Time since TBI was not associated with quality of life in our sample. On the contrary, HRQoL remained relatively stable in the long-term in this rehabilitation group. Studies concerning life satisfaction several years after TBI are rare (32), and studies of long-term quality of life after rehabilitation are even rarer. Cicerone et al. (33) found that patients less than one year after TBI demonstrate significantly higher quality of life, whereas no significant differences were found later after injury; this can be interpreted as a result of early anosognosia. Jacobson et al. (32), on the other hand, found that life satisfaction improved over time many years after injury. They concluded that perceived self-efficacy may mediate the relation between the individual expectations and achievements, and thereby contribute to overall subjective well-being. In our study, all of the participants had undergone an intensive multidisciplinary rehabilitation period, which could affect both their perceived self-efficacy and self-awareness.

The psychometric properties of the Finnish QOLIBRI proved to be good. Consistency of the measure was excellent for the total score (alpha = 0.954) and good or excellent for the separate scales (alpha = 0.79 to 0.92). Consistency was even slightly higher than in the multi-centre study, in which alpha varied between 0.75 and 0.89. Test-retest reliability of the QOLIBRI was considered acceptable. The overall structure of the measure was reproduced quite well by the principal component analysis, although one of the scales (Daily life and autonomy) loaded on several factors. This could have been due to the relatively small sample size for this type of analysis. Despite small differences, the results concerning the reliability of the Finnish QOLIBRI are well in line with previous QOLIBRI studies (19–21).

The validity of the QOLIBRI was examined by comparing it with other measures known to relate to the HRQoL. Significant correlations were found between the QOLIBRI and the SF-36, a general HRQoL-measure. The mental summary scale of the SF-36 was particularly associated with the Emotions-scale of the QOLIBRI and the physical summary scale of the SF-36 correlated most strongly with the Physical problems-scale of the QOLIBRI, which shows that the sub-scales of the QOLIBRI measure different concepts in a consistent manner. In addition, the measure of depression and anxiety (HADS) was strongly associated with the QOLIBRI, as noted previously. These findings confirm the construct validity of the QOLIBRI. Functional outcome measured by GOSE was moderately related to the QOLIBRI. It is noteworthy, however, that HRQoL is not strongly determined by functional outcome in this sample. A similar finding has been reported in some previous research (1, 21, 34) and suggests adjustment to disability caused by TBI.

A negative correlation was found between the QOLIBRI and injury severity measured by the GCS, which indicates lower HRQoL in the patients with milder TBI compared with more severe injuries. This was unexpected, since such an association was not found in the analysis of the international data. However, previous research has revealed that relationship between injury severity and HRQoL after brain injury is not straightforward; some studies have found no connection between injury severity and HRQoL or life satisfaction (34, 35, 20) and a few have revealed a similar relationship between these variables that we found (32, 36, 37), although this phenomenon has not been widely reported. One possible explanation for this finding in our study is that it is at least partially due to the selection of the sample. Patients classified as having mild traumatic brain injury, are in fact a heterogeneous group. There is, for example, discussion about whether GCS 13 should be considered as indicating mild TBI as the risk of intracranial lesions is considerably higher in this group than in patients with GCS 14–15 (38). Outcome after mild TBI is usually good, but this does not

apply to all cases; outcome is moderated by various pre-injury, injury related and post-injury factors (38). In our sample the vast majority (98.7%) had moderate or severe disabilities and only a few (1.3%) displayed good recovery assessed by the GOSE. It is therefore reasonable to conclude that patients who are referred to residential rehabilitation after TBI primarily classified as "mild", are usually in need of special help and do not represent typical cases of mild TBI. These patients could also have had more difficulties in getting the help they need, and they may have had to struggle more with the consequences of their TBI.

It is likely, however, that selection is not the only factor affecting these results, since some similar findings have been reported previously. Jones et al. (37) present the interesting idea that a positive relationship between injury severity and life satisfaction is mediated by personal and social changes, in that severely injured patients have a greater sense of "survivorship" along with greater levels of social support. Such personal and social variables may play a part in our sample too, although they were not specifically measured. In addition, patients with low self-awareness might estimate their HRQoL higher (39), although divergent results have also been reported (34). Lower self-awareness has also been found to associate with more severe injuries (39, 40), and therefore lack of self-awareness could also be a mediating factor in our findings.

These results have important implications for clinicians working with brain injury patients in clinical settings: Sufficient follow-up after mild TBI is recommended in order to target patients in need of support and to prevent secondary consequences of TBI, such as depression. Furthermore, examination of the underlying causes of poor HRQoL is an essential part of the rehabilitation process after mild TBI as well as after more severe injuries.

The main limitations of the present study are the selectiveness of the sample and the moderate sample size. Since the sample was limited to patients who have received residential rehabilitation, the results concerning HRQoL cannot be generalized to other TBI populations. For the purpose of validating the Finnish QOLIBRI, the sample was considered to be sufficiently heterogeneous, however. The cross-sectional study design also creates limitations for the study. The participants span different generations, and it can therefore be hypothesized that their concepts and expectations of good quality of life may differ from each other on a group level, as well as on individual level. This factor could, in theory, influence the age- and time-related results.

It is concluded that the Finnish version of the QOLIBRI is reliable, and that it can be used both for scientific and clinical purposes. In addition, the investigation of HRQoL in a patient group referred to residential rehabilitation reveals a unique and interesting pattern of HRQoL, which could be explored further by comparison with other patient groups. Our study, somewhat surprisingly, suggests lower life satisfaction after milder injuries in certain populations. Selection of the sample is probably an explanatory factor in our study, but there might be other factors involved (37, 39). Further investigation into this relationship between injury severity and HRQoL is recommended in order to enhance our understanding of the mediating factors. In future, the use of the QOLIBRI could also be studied in longitudinal settings to examine the potential usefulness of the instrument in setting and measuring attainment of goals in rehabilitation. The QOLIBRI has been in regular clinical use in the Käpylä Rehabilitation Centre since the translation of the questionnaire, and experiences of its use in rehabilitation setting have been positive. As pointed out earlier, HRQoL is not strictly determined by injury severity or the functional status of the patients. Therefore it is important to identify the goals that matter to the patient. The QOLIBRI adds important information to the standard clinical procedure, as it brings out the subjective experience and values of the patient in a structured, comprehensive and practical manner.

REFERENCES

1. Dijkers M. Quality of life after traumatic brain injury: a review of research approaches and findings. Arch Phys Med Rehab 2004; 85: S21–S35.
2. von Steinbüchel N, Richter S, Morawetz C, Riemsma R. (2005b). Assessment of subjective health and health-related quality of life in persons with acquired or degenerative brain injury. Curr Opin Neurol 2005; 18: 681–691.
3. Corrigan JD, Bogner JA, Mysiw WJ, Clinchot D, Fugate L. Life satisfaction after traumatic brain injury. J Head Trauma Rehabil 2001; 16: 543–555.
4. Hibbard MR, Ashman TA, Spielman A, Chun D, Charatz HJ, Melvin S. Relationship between depression and psychosocial functioning after traumatic brain injury. Arch Phys Med Rehabil 2004; 85: S43–S53.
5. Kalpakjian CZ, Lam CS, Toussaint LL, Hansen Merbitz NK. Describing quality of life and psychosocial outcomes after traumatic brain injury. Am J Phys Med Rehabil 2004, 83: 255–265.
6. Underhill AT, Lobello SG, Stroud TP, Terry KS, Devivo MJ, Fine PR. Depression and life satisfaction in patients with traumatic brain injury: a longitudinal study. Brain Inj 2003, 17: 973–982.
7. Koskinen S. Quality of life 10 years after a very severe traumatic brain injury (TBI): the perspective of the injured and the closest relative. Brain Inj 1998, 12: 631–648.
8. Ergh TC, Hanks RA, Rapport LJ, Coleman RD. Social support moderates caregiver life satisfaction following traumatic brain injury. J Clin Exp Neuropsychol 2003; 25: 1090–1101.
9. Kozlowski O, Pollez B, Thevenon A, Dhellemmes P, Rousseaux M. Outcome and quality of life after three years in a cohort of patients with severe traumatic brain injury. Ann Readapt Med Phys 2002; 45: 466–473.
10. Baumann CR, Werth E, Stocker R, Ludwig S, Bassetti CL. Sleep-wake disturbances 6 months after traumatic brain injury: a prospective study. Brain 2007; 130: 1873–1883.
11. Emanuelson I, Andersson Holmkvist E, Björklund R, Stålhammar D. Quality of life and post-concussion symptoms in adults after mild traumatic brain injury: a population-based study in western Sweden. Acta Neurol Scand 2003; 108: 332–338.
12. Branca B, Lake AE. Psychological and neuropsychological integration in multidisciplinary pain management after TBI. J Head Trauma Rehabil 2004; 19: 40–57.
13. Dahlberg C, Hawley L, Morey C, Newman J, Cusick CP, Harrison-Felix C. Social communication skills in persons with post-acute traumatic brain injury: three perspectives. Brain Inj 2006; 20: 425–435.
14. Pierce CA, Hanks RA. Life satisfaction after traumatic brain injury and the World Health Organization model of disability. Am J Phys Med Rehabil 2006; 85: 889–898.

15. Bullinger M. Assessing health related quality of life in medicine. An overview over concepts, methods and applications in international research. Rest Neurol Neurosci 2002; 20: 93–101.
16. Corrigan JD, Bogner J. Latent factors in measures of rehabilitation outcomes after traumatic brain injury. J Head Trauma Rehabil 2004; 19: 445–458.
17. Neugebauer E, Bouillon B, Bullinger M, Wood-Dauphinee S. Quality of life after multiple trauma-summary and recommendations of the consensus conference. Rest Neuro Neurosci 2002; 20: 161–167.
18. von Steinbüchel N, Petersen C, Bullinger M, and the QOLIBRI group. Assessment of health-related quality of life in persons after traumatic brain injury – development of the Qolibri, a specific measure. Acta Neurochir Suppl 2005; 93: 43–49.
19. von Steinbüchel N, Wilson L, Gibbons H, Hawthorne G, Hofer S, Schmidt S, et al. Quality of Life after Brain Injury (QOLIBRI) – Scale validity and correlates of quality of life. J Neurotrauma 2009; 27: 1157–1165.
20. von Steinbüchel N, Wilson L, Gibbons H, Hawthorne G, Höfer S, Schmidt S, et al. Quality of Life after Brain Injury (QOLIBRI) – Scale development and metric properties. J Neurotrauma 2010; 27: 1157–1165.
21. Truelle JL, Koskinen S, Hawthorne G, Sarajuuri J, Formisano R, Von Wildt K, et al. Quality of life after traumatic brain injury: the clinical use of the QOLIBRI, a novel disease-specific instrument. Brain Inj 2010; 24: 1272–1291.
22. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. J Neurotrauma 1998; 15: 573–585.
23. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67: 361–370.
24. Ware JE, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36). 1. Conceptual framework and item selection. Med Care 1992; 30: 473–483.
25. Anagnostopoulos F, Niakas D, Tountas Y. Comparison between exploratory factor-analytic and SEM-based approaches to constructing SF-36 summary scores. Qual Life Res 2009; 18: 53–63.
26. Conover WJ, Iman RL. Rank transformation as a bridge between parametric and nonparametric analysis. Am Stat 1981; 35: 124–133.
27. WHOQOL group. (1998). The World Health Organization Quality of Life Assessment (WHOQOL): development and general psychometric properties. Soc Sci Med 46: 1569–1585.
28. Power M, Quinn K, Schmidt S. Development of the WHOQOL-Old module. Qual Life Res 2005; 14: 2197–2214.
29. Kim Y-J. A systematic review of factors contributing to outcomes in patients with traumatic brain injury. J Clin Nurs 2011; 20: 1518–1532.
30. Hukkelhoven C, Steyerberg E, Rampen A, Farase E, Habbema J, Marshall L, et al. J Neurosurg 2003; 99: 666–673.
31. Himanen L, Portin R, Isoniemi H, Helenius H, Kurki T, Tenovuo O. Longitudinal cognitive changes in traumatic brain injury. Neurology 2006; 66: 187–192.
32. Jacobsson LJ, Westerberg M, Malec JF, Lexell J. Sense of coherence and disability and their relationship with life satisfaction 6–15 years after traumatic brain injury in Northern Sweden. Neuropsychol Rehabil 2011; 21: 383–400.
33. Cicerone KD, Azulay J. Perceived self-efficacy and life satisfaction after traumatic brain injury. J Head Trauma Rehabil 2007; 22: 257–266.
34. Mailhan L, Azouvi P, Dazord A. Life satisfaction and disability after severe traumatic brain injury. Brain Inj 2005; 19: 227–238.
35. Colantonio A, Dawson D, McLellan B. Head injury in young adults: long-term outcome. Arch Phys Med Rehabil 1998; 79: 550–558.
36. Findler M, Cantor J, Haddad L, Gordon W, Ashman T. The reliability and validity of the SF 36 health survey questionnaire for use with individuals with traumatic brain injury. Brain Inj 2001; 15: 715–723.
37. Jones JM, Haslam SA, Jetten J, Williams WH, Morris R, Saroyan S. That which doesn't kill us can make us stronger (and more satisfied with life): the contribution of personal and social changes to well-being after acquired brain injury. Psychol Health 2011; 26: 353–369.
38. Shukla D, Devi B. Mild traumatic brain injuries in adults. J Neurosci Rural Pract 2010; 1: 82–88.
39. Sasse N, Gibbons H, Wilson L, Martinez-Olivera R, Schmidt H, Hasselhorn M, et al. Self-awareness and health-related quality of life after traumatic brain injury. J Head Trauma Rehabil 2012 Aug 29 [Epub ahead of print].
40. Prigatano P. Disturbances of self-awareness and rehabilitation of patients with traumatic brain injury: a 20-year perspective. J Head Trauma Rehabil 2005; 20: 19–29.