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ARTICLE

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The Stockholm Spinal Cord Uro Study: 2. Urinary tract infections in a regional prevalence group: frequency, symptoms and treatment strategies

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ABSTRACT

Objective: To examine symptomatic urinary tract infections (UTI) in a regional prevalence group of patients with traumatic spinal cord injury (SCI), to assess risk factors for recurring infections and to identify a high-risk sub-population for frequently recurring and severe febrile UTIs.

Materials and Methods: Four hundred and twelve patients who attended a yearly check-up at the Spinalis SCI clinic were included. A regional programme for neurogenic bladder dysfunction was applied, including S-creatinine and S-cystatin-C, urine culture, residual urine, ultrasound of kidneys, urodynamic studies and a questionnaire regarding complications during the preceding year. Descriptive statistics and regression analysis were used to estimate risk factors.

Results: Nearly half of all patients reported ≥1 UTI during the preceding year with a mean number of 3.6. Persons who use normal voiding had the lowest frequency, while those with catheter-assisted voiding reported the highest numbers. A sub-group of patients had more frequent and severe UTIs. They were characterized by a cervical or thoracic neurological level lesion and a more severe injury and the presence of SCI-related complications such as spasticity, neuropathic pain and autonomic dysreflexia. The most common signs and symptoms of UTI were smelly and cloudy urine, feelings of malaise and increased spasticity.

Conclusions: Risk profiles for recurring and severe UTIs were catheter-assisted voiding, cervical or thoracic levels and more complete neurological lesions and the co-existence of other SCI-related complications. There is a need for an increased understanding of the special symptoms of UTI in this patient group and a strategy to avoid unspecific antibiotic treatment.

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Introduction

Urinary tract infection (UTI) is the most prevalent complication in patients with chronic SCI and a cause of significant morbidity [1–3]. It may cause or aggravate autonomic symptoms such as spasticity, autonomic dysreflexia and neuropathic pain [4], lead to a need of increased personal assistance, time away from work and social activities, as well as loss of financial income.

Risk factors for symptomatic UTIs in SCI patients have been described by several authors. In two tertiary referral centre databases the evacuation method was the main predictor for symptomatic UTIs [5,6], while others have described higher neurological level and more severe injuries as the main risk factors [7,8].

Through the years, many programmes have been proposed for the treatment and prevention of UTIs in neurogenic bladder dysfunction, ranging from long-term oral antibiotics to intermittent intravesical antibiotics and combinations of antiseptics, vitamins and probiotics.

Some authors have recognized the problem of recurring UTIs during care in the rehabilitation ward and recommended a regimen of continuous antibiotics, based on local patterns of microorganisms and resistance [9]. Others have found that continuous oral antibiotic prophylaxis seems to result in fewer instances of asymptomatic bacteriuria (ABU), but not fewer symptomatic infections and a risk of increased antimicrobial resistance [10].

Intermittent antibiotic prophylaxis is perhaps more promising. In SCI patients followed at an infectious disease outpatient clinic, a weekly oral cyclic antibiotic programme (WOCA) resulted in fewer symptomatic infections during a 2-year follow-up [11].

Intravesical treatment with gentamicin has been proposed in selected patients practicing clean intermittent catheterization (CIC) who suffer recurrent UTIs with highly resistant microorganisms [12].

A recent literature review on UTI in patients with neurogenic bladder dysfunction [13] summarized current

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knowledge on prophylactic effects of several medical measures and interventions. It was concluded that methenamine or cranberry products had no significant preventive effect, while a combination of cranberry and propolis may provide wa prophylactic action as propolis is believed to counteract bacterial adherence. Intravesical instillation of non-pathogenic E. coli has also been shown to reduce the number of symptomatic UTIs per patient-year.

Hopes have been put to improvement of catheter materials and coating, but studies of catheters for intermittent as well as indwelling use have produced varying results [14,15].

Risk factors for UTI in SCI patients are multifaceted, including the method of voiding, neurological level and severity of injury, the need for assistance from others in bladder evacuation, other SCI-related complications and concurrent illnesses. Treatment strategies have to take these many factors into account, along with knowledge of the local bacterial environment and resistance patterns.

The definition of recurrent UTI in biomedical literature is highly variable. One commonly used definition in clinical practice is two or more UTIs during 6 months or three or more UTIs during 12 months [16]. In neurogenic bladder dysfunction and catheter-assisted voiding the frequency of UTI may be even higher [17]. Based on this background and the data collected in this study, we found that the occurrence of 0–3 UTIs/year can be termed low frequency and >3 UTIs/year high frequency.

This article is the second report from the Stockholm Spinal Cord Uro Study, a comprehensive survey of urinary tract function in a regional prevalence population of patients with chronic traumatic spinal cord injury (SCI). In our first article [1] we presented the basic characteristics of the patient group including complications in the urinary tract, as found in a cross-sectional study based on a yearly check-up visit at the Spinalis out-patient clinic in Stockholm.

On sampling at the Spinalis yearly check-up visit, bacteriuria was common, but symptomatic UTIs were rare. However, UTIs were reported by the patients as the most common complication, experienced by 44% during the preceding year. Two sub-groups of patients with further problems were identified: those who had many infections and those who had severe, febrile infections requiring treatment in hospital. In comparison, other urogenital complications were reported at low frequencies, 3–5% [1].

In this article we define the risk profiles for frequent and/or severe febrile UTIs requiring hospital treatment in our regional prevalence population and formulate a basic strategy for treatment of symptomatic infections.

Materials and methods

Participants

Participants in this study were men and women aged 18 years or older with a post-traumatic SCI for at least 1 year.

All individuals were living in the greater Stockholm area and registered at the regional SCI outpatient centre (Spinalis clinic), which oversees follow-up for ~90% of the regional SCI population. Four hundred and fifty-three patients were offered participation in the study as they consecutively attended annual check-up visits.

Four hundred and twelve patients consented to participate, constituting 91% of patients who attended the yearly check-up and 75% of the total prevalence group. Characteristics of the study participants are displayed in Table 1.

Fifteen patients declined participation and 26 were excluded. Reasons for exclusion were old age with frailty and multiple other illnesses ($n = 10$), language difficulties ($n = 1$), non-traumatic SCI and no residual symptoms ($n = 15$).

Methods

In this study, we attempted to fully apply two programmes for follow-up of chronic spinal cord injury: a national Swedish programme for follow-up of medical SCI complications [18] and a regional programme for neurogenic bladder dysfunction (Supplement 1), complemented with a study-specific questionnaire regarding urinary tract complications during the preceding year (Supplement 2). In the questionnaire, participants reported UTIs as infection related symptoms which had been treated with a course of antibiotics.

Table 1. Characteristics of study participants.

Age, years, mean, (SD), range				49.1 (14.7), 18–88
Male/female, *n* (%)				320 (78%) / 92 (22%)
Injury duration, years, mean, (SD), range				16.4 (11.8), 1–51
Neurological level of injury and AIS grades A–D				
	A	B	C	Total (%)
C1–C4	23	7	7	37 (9)
C5–C8	47	24	12	83 (20)
T1–S3	112	17	20	149 (36)
AIS D at any level				143 (35)
				412 (100)

American Spinal Injury Association (ASIA) Impairment Scale (AIS) grades:
A Complete. No motor or sensory function is preserved in the sacral segments S4–S5.
B Incomplete. Sensory function preserved but motor function is not preserved below the neurological level and includes the sacral segments S4–S5.
C Incomplete. Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.
D Incomplete. Motor function is preserved below the neurological level and at least half of key muscles below the neurological level have a muscle grade of 3 or more.

Table 2. Data collection at yearly check-up visits.

Types of data	Method of data collection	References
Information on past illnesses, concurrent medical conditions, current medication, bowel function, pain, spasticity, history of pressure ulcers, circulatory complications related to spinal cord injury	Individual structured interviews, medical file reviews	
Complications of the urinary tract during the preceding year, prophylactic measures to avoid urinary tract infection, bladder management	Study-specific questionnaire completed by patient, medical file reviews	[Supplement 2]
Blood chemistry	S-creatinine and S-cystatin-C. Blood samples taken at check-up visit	[19]
Residual urine	Measured by ultrasound or catheter immediately after patient-preferred method of voiding	[20]
Urine culture	Collected at check-up visit. Notes made on current symptoms	[19]
48-hour voiding diary	Completed by patient at home, sent back in pre-stamped envelope	
Physical and neuro-urological examination	Complete physical examination done by neuro-urology specialist	
Examination of neurological level of injury and severity of lesion	Performed by neurologist according to International standards for neurological classification of spinal cord injury	[21]
Ultrasound of urinary tracts	Performed by radiologist	
Urodynamic testing	Performed by urotherapist/nurse specialist according to Good Urodynamic Practice. Evaluation of graphs by specialists in neuro-urology	[22]

Objective measurements and patient-reported data were collected for each individual, as previously reported [1], see Table 2.

ABU was characterized by a positive urine culture but no concomitant symptoms. A current UTI was understood as the co-existence of a positive urine culture and infection-related symptoms, such as dysuria, increased frequency and urgency, pain in the lower abdomen or urogenital area, foul smelling urine, an increase in neurogenic pain and spasticity, rise in body temperature and/or an increase in urinary leakage.

Data analyses

Data were analysed using SPSS for Windows 25 software (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Descriptive statistics were calculated. Age, neurological level and severity of injury grouping (C1–4 AIS grades A, B and C; C5–8 AIS grades A, B and C; T1–S3 AIS grades A, B and C; and AIS D at any level) [21], and duration of injury were used as independent variables, as well as types of bladder management and amount of residual urine. Regression analysis was used to estimate risk profiles for more than three UTIs during the preceding year. Variables included were age, gender, severity of injury and duration of injury. Data on types of bladder management, residual urine and other SCI-specific complications were not normally distributed and were therefore evaluated by descriptive statistics only.

Results

All patients ($n = 412$) completed the study-specific questionnaire and 395 patients (96%) had a urine specimen taken for bacterial culture.

Objective data

The number of positive/negative urine cultures at the time of the check-up visit were 220 (56%)/175 (44%). Two hundred and seven positive urine cultures were classified as ABU and 13 as a current UTI.

Table 3. Types of bacteria in asymptomatic bacteriuria (ABU) and in current symptomatic urinary tract infection (UTI) at the yearly check-up visit.

Type of bacteria	ABU at yearly check-up visit, *n* (% of patients with ABU)	Symptomatic UTI at yearly check-up visit, *n*
E. coli	81 (39)	6
Mixed flora	60 (29)	1
Klebsiella	16 (8)	2
Enterococcus	15 (7)	1
Pseudomonas	9 (4)	1
Enterobacter	6 (3)	1
Staphylococcus	6 (3)	
Citrobacter	4 (2)	
Streptococcus	4 (2)	
Proteus	3 (1.5)	
Serratia	2 (1)	1
Corynebacterium	1 (0.5)	

Types of bacteria in positive urine cultures are displayed in Table 3. E. coli was the most frequently diagnosed agent in ABU as well as in current UTIs, occurring in ~40% of ABU and 50% of symptomatic infections.

Residual urine was measured in 75% of all study patients [1]. Those who practice normal micturition or reflex stimulation had the highest frequency of residual volume >100 mL (17% and 67%, respectively), while users of CIC or indwelling catheter had the lowest rates (6% and 0%, respectively). We found no co-variation between the presence or volume of residual urine and the number of UTIs or the number of antibiotic prescriptions for UTI.

Patient-reported data

Two hundred and seventeen patients (53%) reported no urinary tract complications during the past year. One hundred and ninety-five patients (47%) had experienced at least one episode of urogenital complications. UTI was the most common one, experienced by 183 patients (44%).

Patients who had a current UTI at the time of the check-up visit were distributed in groups who reported 0–8 UTIs during the preceding year.

The number of patient-reported UTIs is displayed in Table 4. Among those who had UTIs during the preceding year, two-thirds reported 1–3 infections, with three the most

Table 4. Patient-reported number of urinary tract infections (UTI) during the preceding year.

Number of UTIs during the preceding year	Number of patients, *n* (% of entire study group)	Men/women	Percentage of patients in UTI group (*n* = 183)	Total number of UTIs	UTI at yearly check-up visit
0	229 (56)	177/52			3
1	34 (8)	27/7	19	34	2
2	35 (8.5)	27/8	19	70	2
3	51 (12)	37/12	28	153	2
4	16 (4)	9/6	8.5	64	1
5	15 (3.6)	14/2	8	75	1
6	15 (3.6)	12/2	8	90	0
7	2 (0.5)	2/1	1	14	1
8	8 (2)	6/1	4	64	1
10	5 (1.2)	6/1	3	50	0
12	1 (0.2)	2/0	1	12	0
15	1 (0.2)	1/0	0.5	15	0
Sum total	412 (100)	320/92	100.0	661	0
Median/Mean number of UTIs			3/3.6		

Urinary tract infection (UTI) was reported by patients as infection related symptoms which had been treated with a course of antibiotics. Infection-related symptoms included dysuria, increased frequency and urgency, foul smell of urine, pain in the lower abdomen or urogenital area, increased neurogenic pain, rise in body temperature, increased urinary leakage and increased spasticity.
UTI group: 183 patients who reported that they had >1 UTI during the preceding year.

Table 5. Bladder management and patient-reported number of urinary tract infections (UTI) during the preceding year.

Bladder management	*n* (%)	Mean number of UTIs per type of bladder management	Number of patients per number of UTIs and type of bladder management				Total number of UTIs per type of bladder management
			0 UTIs	1–3 UTIs	4–6 UTIs	>6 UTIs	
CIC	157 (38)	2.5	58	57	26	16	397
Normal voiding	120 (29)	0.2	107	11	2	0	28
Indwelling suprapubic catheter	45 (11)	2.5	12	23	8	2	113
Reflex stimulation	33 (8)	1.1	18	12	3	0	36
Indwelling urethral catheter	15 (4)	1.6	5	8	2	0	24
Continent urinary diversion	15 (4)	1.3	7	7	1	0	20
Abdominal pressure	10	2.2	5	2	2	1	22
Incontinent urinary diversion	9	1.6	6	2	0	1	14
Other	5	0.6	4	1	0	0	3
External compression	2	1.5	1	1	0	0	3
SARS	1	0	1	0	0	0	0
All study patients	412	1.6	221	126	47	18	661

CIC: Clean Intermittent Catheterization; SARS: Sacral anterior root stimulation.

prevalent number. The male/female distribution was on average 78%/22%, equal to the gender proportions in the total study group.

Bladder management and the number of patient-reported UTIs is shown in Table 5.

Among patients who voided by CIC, 95% used hydrophilic catheters and 5% used plastic catheters with or without the addition of lubricant gel.

Patients who practiced normal voiding all had AIS grades C or D. Half of them had injuries at cervical neurological levels, one third at thoracic levels and one sixth at lumbar neurological levels.

The study patients reported a total of 661 symptomatic UTIs during the preceding year, with a median of 3 and mean number of 3.6 UTIs in the group that had infections. According to notations in medical files, which were collected from primary care facilities and from the Spinalis clinic, ~690 antibiotic courses were prescribed due to urinary symptoms. We were able to verify 450 actual prescriptions in available medical files.

Table 6. Antibiotics courses prescribed for UTI, verified in patient files.

Type of antibiotic	*n*
Ciprofloxacin	119
Trimethoprim and trimethoprim-sulfonamide	113
Nitrofurantoin	109
Pivmecillinam	41
Norfloxacin	39
Cefalosporines	21
Amoxicillin	8
Sum total	450

Ciprofloxacin, trimethoprim and nitrofurantoin were prescribed in approximately equal proportions, well in accordance with the current regional antibiotics programme (Table 6). On suspicion of UTI, a urine culture and prescriptions were carried out through the Spinalis clinic or through primary care facilities in approximately equal proportions. The Spinalis clinic had a strict policy of collecting a urine sample for bacterial culture prior to treatment with antibiotics. This was not always true in primary care, but there were

Table 7. Patient-reported signs and symptoms of urinary tract infection (UTI).

Sign/symptom	*n* (% of patients who reported UTI during past year)
Foul smell and cloudiness of urine	161 (88)
General feeling of malaise/illness	113 (62)
Rise in body temperature $\leq$ 38 °C	111 (61)
Rise in body temperature $>$ 38 °C and shivering	95 (52)
Increased spasticity	88 (48)

Rise in body temperature $\leq$38 °C: in clinical practice/primary care routinely understood as a sign of a lower UTI and patients were advised to start antibiotics at home.
Rise in body temperature $>$38 °C and shivering: in clinical practice/primary care routinely understood as a sign of a possible upper UTI and patients were advised to attend an emergency room or other hospital clinic for evaluation before antibiotics were started.

no significant differences in choices of antibiotics or in adherence to regional recommendations.

Forty-nine patients reported that they had 1–2 antibiotic courses prescribed without prior urine culture.

Patients who reported >3 UTIs ($n = 63$, 15.5%) were mostly found in the CIC group ($n = 40$) and suprapubic group ($n = 13$) and were characterized by a cervical ($n = 30$) or thoracic ($n = 20$) neurological level injury with AIS grades A–C. Regression analysis verified the main risk profiles as cervical lesions with AIS grades A–C (odds ratio, OR = 2.3 versus all AIS grade D) and duration of injury (OR = 1.6). There was no risk difference with age or gender. Other SCI-related complications such as spasticity ($n = 31$), neurogenic pain ($n = 32$), autonomic dysreflexia ($n = 17$) and pressure ulcers ($n = 16$) were frequent, whereas other specific complications of the urinary tract were not more common than in the study group as a whole. The mean age was 42.8 years (range = 19–68) and mean duration of injury was 13.4 years (range = 1–44).

Twenty-one patients (5%) reported treatment in hospital due to a febrile UTI. They were all found in groups who practice catheter-assisted micturition such as CIC ($n = 10$), indwelling suprapubic or urethral catheter ($n = 8$) or had a urinary diversion ($n = 3$). Nearly all had a cervical or thoracic neurological level lesion and two-thirds had AIS grades A or B. Due to the limited number of patients, this sub-group was evaluated by descriptive statistics only. Fifty per cent had other SCI-related complications such as spasticity, neurogenic pain, autonomic dysreflexia and pressure ulcers. One fourth had other complications of the urinary tract, such as bladder stones, orchitis and prostatitis. Thirteen patients overlapped with the group who had >3 UTIs. The mean age was 49.8 years (range = 24–83) and mean duration of injury was 26 years (range = 1–51).

Signs and symptoms of UTI were reported by the patients according to Table 7.

For prevention of UTI, one fourth of all study patients used antiseptics and/or low-dose antibiotics and a few participants had a regular intake of health foods and vitamins. There was no difference in the frequency of UTIs between these patients and the entire study group.

Discussion

In a previous report from the Stockholm Spinal Cord Uro Study, we presented the basic characteristics and a problem inventory regarding urinary tract function of this regional prevalence group with a traumatic spinal cord injury [1]. UTI was the most prevalent complication. We have now further explored the frequency, symptoms, treatment and risk factors for UTI.

Our results indicate that risk profiles for more frequent and/or more severe, febrile UTIs are multifaceted and include higher neurological levels and more severe SCI (AIS A and B), long duration of injury, higher age, catheter-assisted voiding and a co-variation with other SCI-related complications, particularly spasticity and neurogenic pain. AIS grade of injury A–B had a greater impact than neurological level of injury. The use of catheter-assisted voiding co-varied with a higher frequency of UTIs and febrile infections. No co-variation was found with other urinary tract complications, but these numbers were very low. We found no gender differences, although this has previously been reported by other authors [23].

There was an obvious difference in the patient-reported numbers of UTI between those who use normal voiding versus catheter-assisted voiding. In catheter-assisted voiding, the numbers of UTI were lowest for urethral indwelling catheter, higher for CIC and highest for suprapubic indwelling catheter. There was no co-variation with the presence of residual urine, which in clinical practice has traditionally been regarded a risk factor for UTI.

Our findings indicate that prevention of UTI with antiseptics or low dose antibiotics is of limited value and these results are in accordance with other reports [13]. A WOCA regimen could provide better control, as it has been shown to decrease the incidence of symptomatic UTI, reduce the overall consumption of antibiotics and reduce the risk for development of multiresistant bacteria. Non-antibiotic prophylactic and therapeutic strategies must be further developed as we recognize the complexity of the urinary microbiome and of infections in SCI patients [24].

UTIs in this patient group have a direct impact on quality-of-life [4]. The patient-reported symptoms of increased spasticity, fever and shivering and a general feeling of illness all indicate that a UTI may significantly add to the difficulties already caused by the physical disability. The ability to work and move outside of home may be compromised and the need for personal assistance increased. Foul smelling urine may lead to severe hygiene and social complications. Long-term complications may include stone formation in the urinary tract and a decline in kidney function.

Symptomatic bacterial infections should be promptly treated in order to reduce the risk of complications. However, it is also well known that symptoms of infection and pain are often misunderstood in SCI patients and may lead to over-treatment with antibiotics [25].

Most patients in our prevalence group have easy access to care facilities for testing of urine and acquiring treatment of symptomatic infections. This is reflected in a high number of urine cultures per infection and few instances of antibiotic courses without previous urine testing. Our results seem to demonstrate a lower incidence of symptomatic UTIs and a lower rate of prophylactic antibiotics than some previous

studies from Scandinavian areas [2,26]. We believe that these improvements over time are related to the structured follow-up programme and continuity of care in a specialized SCI outpatient centre.

An urgent issue is the presence of multiresistant bacteria, which calls for restrictive use of antibiotics. The medical professions have to promote acceptable methods for patients to live with asymptomatic bacteriuria, while treating promptly when infection related symptoms occur [27]. To establish common prevention and treatment programmes for UTIs among the different medical specialists involved in SCI care is an important challenge.

Based on our findings we would like to propose that a treatment strategy for symptomatic UTIs should include a basic check list of adequate infection-related and other SCI-related symptoms, a checklist of other possible causes of autonomic dysfunction such as increased spasticity, neuropathic pain or autonomic dysreflexia and a urine culture including resistance pattern before antibiotic treatment is started.

Treatment should be carried out in accordance with local antibiotics programmes and based on updated information on resistance patterns. Bladder management should be monitored and adjusted when necessary to achieve optimal voiding routines. Any indwelling catheters should be exchanged during ongoing antibiotic treatment [28]. A holistic approach should ideally include evaluation of other current SCI-related complications or concurrent illnesses, which may influence the risk for recurrent infections. The patient-reported outcome of antibiotic treatment should be followed up, but repeated urine cultures are not indicated if symptoms have diminished or ceased. In individual patients with recurring symptoms, the history of previous bacterial cultures, resistance patterns and antibiotic treatments may be informative [29].

Further research on neurogenic bladder dysfunction post-SCI is warranted to develop methods for efficient bladder emptying without the use of catheters. Neuromodulation is a possible future improvement in this regard. Urodynamics could play an important role as a guide to optimize voiding methods on an individual basis and hopefully reduce the number of UTIs. Our data on urodynamics from the Stockholm Spinal Cord Uro Study will explore this subject in a separate report.

Conclusions

In a regional prevalence population of patients with chronic traumatic spinal cord injury:

- Nearly half of all patients reported at least one UTI during the past year with a mean number of 3.6.
- Patients who practice normal voiding had a low number of UTIs, comparable to that of the general population.
- Risk profiles for frequent and severe, febrile UTIs include catheter-assisted voiding, cervical and thoracic neurological levels of SCI with AIS grades A and B and the presence of other SCI-related complications.
- There is a need for an increased understanding of UTI related symptoms in this patient group and a treatment strategy to avoid unspecific antibiotic treatment and development of bacterial resistance.

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Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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