# Health-related Quality of Life in Patients with Endocrine Tumours of the Gastrointestinal Tract

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Health-related quality of life (HRQOL) (EORTC QLQ-C30) and levels of anxiety and depression (HADS) were investigated in patients with endocrine tumours of the gastrointestinal tract treated with interferon and/or a somatostatin analogue. In addition, patient perceptions of the importance of and satisfaction with some HRQOL aspects were studied. QOL was perceived as quite good, but more than half of the patients reported diarrhoea. The levels of anxiety and depression were low. Patients perceived physical HRQOL aspects as most important for a good QOL and stated the highest satisfaction with some social aspects. Patients who reported high levels of anxiety or depression were less satisfied with several HRQOL aspects, had more health problems, and a lower level of functioning on several of the EORTC QLQ-C30 scales and single items. Neither demographic nor medical background variables seemed to have an influence on the results. The relatively high QOL could be explained by the fact that most patients had had their treatment for a long period and thus had time to adjust to the situation.

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Endocrine tumours of the gastrointestinal (GI) tract are rare and constitute only about 2% of all malignant GI neoplasms. These tumours can be divided into two main groups: carcinoids and endocrine pancreatic tumours (EPT). A majority of patients with malignant metastasizing tumours demonstrate clinical symptoms related to the specific hormone released by the tumour (1). The most common symptoms associated with carcinoid tumours are: flushing, diarrhoea, bronchial constriction and right heart failure (the carcinoid syndrome) (2). Some of the symptoms of EPT are dyspeptic symptoms, gastric ulcer, diarrhoea, steatorrhea, hypoglycaemia, necrolytic migratory erythema, weight loss, anaemia, impaired glucose tolerance and gallstones (3).

Chemotherapy has constituted the basis for medical treatment of malignant endocrine GI tumours for more than two decades. Since the early 1980s, a more active approach has evolved. Surgery has become more aggressive and biotherapies such as interferon (INF) and somatostatin analogues have been introduced. Further increases of survival rates have thereby been made possible (1). INF has been demonstrated to have significant antitumoural effects on endocrine gut and pancreatic tumours, in terms of both biochemical response and a reduction in tumour size (4).

The most common INFs in clinical usage are Introna®, Wellferon® and Finferon®. They are given as subcutaneous injections $3-5$ times a week. In most cases, patients administer the injections themselves. The most common adverse reactions to INF are 'flu-like' symptoms for the initial $3-5$ days of treatment. Later, fatigue, weight loss and depression may occur. Most of the adverse reactions are dose-related and can be handled by individual adjustment of doses (1).

Somatostatin analogues inhibit the release of various peptide hormones, and have a direct antagonistic effect on the growth of tumour cells. Symptom reduction has been demonstrated in patients with endocrine GI tumours. The most common somatostatin analogue used in practice is Sandostatin®, which is taken as a subcutaneous injection $2-4$ times a day, usually administered by the patient. Side effects are limited, the most common being diarrhoea, steatorrhea and gripes, which are due to inhibitory effects on pancreatic exocrine secretion. These problems can be reduced by supplying pancreatic enzymes in the form of tablets (1).

### *Health-related quality of life*

Improved treatments have prolonged life for many patients with endocrine GI tumours. INF and somatostatin

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analogues are not curative but may control the disease for long periods of time (4). However, it is important that life is not just prolonged but also has a good quality.

There is no single or unequivocal definition of the concept 'health-related quality of life' (HRQOL). Research and discussion about the concept has accelerated since the latter part of the 1980s, and today there is international consensus with respect to at least two major issues related to the measurement of HRQOL (5, 6): it is a multidimensional concept and assessment should be based on subjective evaluation by the patient.

An understanding of how patients perceive symptoms may provide useful strategies for symptom management. Faithfull (7) states that the literature often focuses on symptoms in a way that reflects the pathological process rather than on how patients perceive symptoms. A study of patients undergoing pelvic radiotherapy (7) demonstrated that it is fundamental to know how patients perceive symptoms. Thus, it is not sufficient to know what symptoms are present to develop effective symptom management.

It is well known that a person may change his or her perceptions of what is important in life when struck by a life-threatening disease (8). Perceptions of QOL are probably related to life values, and it can be presumed that the more a person experiences that he or she attains values that are judged to be important, the higher is his or her perceived QOL (8). One of the objectives of HRQOL assessment should therefore be to determine how the patient functions in those HRQOL areas that he or she judges to be the most important.

Few reports have been published in which HRQOL issues have been addressed in patients with endocrine gut and pancreatic tumours and most of these address only general issues of patient HRQOL (1, 3, 9, 10). Findings from a recent study of patients with endocrine gut and pancreatic tumours (11) indicated that patients rated their HRQOL as relatively good. That study mainly addressed the agreement between patient and staff ratings of patient HRQOL. In a study of 11 patients with endocrine GI tumours treated with a somatostatin analogue, results revealed that two domains of HRQOL, ability to relate socially and psychosocial distress, were significantly improved (12).

### *The present study*

The aim of this study was to investigate HRQOL, anxiety and depression in patients with endocrine GI tumours treated with INF and/or a somatostatin analogue. The following research questions were posed: a) How do the patients rate their present HRQOL? b) How important do they perceive selected HRQOL aspects to be? c) How satisfied are they with these HRQOL aspects? d) How do the patients rate their levels of anxiety and depression? e) Are there any differences between HAD anxiety/depression 'cases' and 'non-cases' with respect to HRQOL ratings? and f) Are patient background variables related to the outcome variables mentioned in research questions $1-4$?

## METHOD

### *Setting*

The study took place at the Akademiska Hospital in Uppsala in a ward where patients with endocrine GI tumours are treated.

### *Sample*

During the study period, March to July 1996, 212 patients were eligible for the study. To be eligible, patients had to have been informed about their cancer diagnosis, not be in a terminal stage of the disease, and have been treated with INF and/or a somatostatin analogue for at least 4 weeks prior to the data collection. Patients were excluded if they were hard of sight or hearing ($n = 2$); did not speak Swedish ($n = 13$); were considered to be in too bad a mental, physical or emotional condition ($n = 2$), or were currently undergoing chemotherapy ($n = 84$). Eleven patients did not participate because of scheduling problems on the part of the interviewer (GL) and one patient declined to participate. This left 99 patients for the study, 80 of whom had carcinoid tumours and 19 EPT.

Mean time since diagnosis was 63 months (range 2–286. Mean duration of treatment was 43 months (range $1-162$). The mean number of hospitalizations was 17 (range $2-72$). Forty-three patients were treated with interferon, 10 with a somatostatin analogue and 46 with a combination. Sixty patients were men and 39 were women. Their mean age was 59 years (range $20-82$). The majority were married/cohabiting and had children. Fifty-five patients had some sort of employment.

### *Instruments*

*Present HRQOL.* The EORTC QLQ-C30 (13) and a few additional disease- and treatment-related questions were used to study patient judgement of HRQOL. The EORTC QLQ-C30 is designed to cover a range of HRQOL issues relevant to a broad spectrum of cancer diagnosis (14). It comprises 30 items and includes 9 multi-item scales: five functional scales (physical, role, emotional, cognitive and social functioning); one global health and QOL scale and three symptom scales (pain, fatigue, nausea and vomiting). Single items are included to assess symptoms (dyspnoea, insomnia, appetite loss, constipation and diarrhoea) as well as the perceived economic impact of the disease and treatment. In accordance with the scoring instructions given by the EORTC Quality-of-Life Study Group, (13) the scale scores are linearly transformed to $0-100$ scores. For the functional and global health and QOL scales, a higher score means a better level of functioning. For the

symptom oriented scales and items, a higher score corresponds to a higher level of symptoms.

The EORTC QLQ-C30 has been found to exhibit adequate levels of reliability and validity (construct and discriminant) and the psychometric properties are consistent across languages and countries (13). The questionnaire can be completed without assistance in a relatively short time by most patients.

A few additional disease- and treatment-related questions were designed to assess the three most common problems experienced by this group of patients according to our clinical experience. Patients were asked to report whether they had experienced diarrhoea and/or flush the previous week and, if so, the extent to which it had influenced their family and/or social life, using the following response format: 'not at all'; 'some'; 'quite a bit' and 'very much'. Also, they were asked how often they received help to take their injections: 'never', 'sometimes', 'often' and 'always'. Finally, one question concerned the extent to which taking injections had influenced their social and/or family life: 'not at all', 'some', 'quite a bit' and 'very much'.

*Importance of selected HRQOL aspects*. To investigate the importance of selected HRQOL aspects as judged by patients, 12 questions were formulated using a visual analogue scale (VAS) (100 mm, anchors: 'Very important—Not at all important'). Patients were asked: 'To experience a good QOL, how important is it to...?'. Six questions concerned physical HRQOL aspects: 'Wash yourself, dress, eat, etc.'; 'Do physical exercise'; 'Have good health'; 'Not have pain'; 'Not have diarrhoea'; and 'Not have flush'. Six questions dealt with social HRQOL aspects: 'Associate with the family'; 'Associate with friends'; 'Go to a movie, theatre, exhibition, etc.'; 'Watch TV, listen to the radio, read books, etc.'; 'Work' and 'Do everyday household jobs'.

Patients were asked to put a mark on the 100 mm scale to indicate his/her opinion. The score used in the data analysis was obtained by measuring the number of millimetres from the 'Not at all important' end.

*Satisfaction with selected HRQOL aspects*. VAS (100 mm, anchors: 'Very satisfied'—'Not at all satisfied') were used to investigate patients' satisfaction with selected HRQOL aspects. Patients were asked 'How satisfied are you with...?'. They were asked to put a mark at that position on the VAS which best described their opinion. The selected HRQOL aspects and the VAS scoring procedure were the same as those employed to study the importance of HRQOL aspects.

*Anxiety and depression*. The Hospital Anxiety and Depression Scale (HADS) was used to investigate patient experiences of anxiety and depression. The HADS is a self-assessment scale and comprises two subscales, one measuring anxiety (seven items) and the other depression (seven). Each item has four possible answers, with scores from zero, indicating no problem, to three, indicating a high level of problems (lowest possible total score = 0, highest possible total score = 21). A 'cut-off-point' of = 8 has been recommended for identifying potential clinical cases (15). The HADS has been found to possess sufficient reliability and validity for detecting anxiety and depression in somatically ill patients (16, 17).

*Background data*. Patients were asked to report age, sex, civil status, whether they had children or not, occupational status, type of treatment, diagnosis, time of diagnosis and the number of hospitalizations for the present illness.

### *Procedure*

In accordance with requirements from the Ethics Committee of the Faculty of Medicine, informed consent was obtained from all subjects. When a patient had accepted to participate, he/she was instructed on how to use the instruments by the first author (GL), who was present when the patient completed them.

### *Data analysis*

Paired t-tests were used to compare patients' perceptions of the importance of and satisfaction with some HRQOL aspects. Unpaired t-tests were used to investigate whether background variables had any relation to the ratings of HRQOL, anxiety and depression, and if HADS 'cases' and 'non-cases' differed on the EORTC QLQ-C30 scales. $\chi^2$ -analyses were employed for assessment of associations between dichotomized variables. Since a large number of comparisons were performed on the same data, a p-level of 0.01 was chosen in order to decrease the risk of significant results arising by chance.

## RESULTS

### *Present HRQOL*

The EORTC QLQ-C30 data indicate that patients assigned high scores to the functional scales (Table 1). The role function scale was given the lowest score and the cognitive scale the highest. The score for global QOL was a little lower than for the functional scales.

The results for the symptom scales and single items demonstrate that patients reported most problems with fatigue, dyspnoea and diarrhoea. Least problems were reported for nausea/vomiting and constipation.

Few significant differences were obtained in the EORTC QLQ-C30 ratings between subgroups formed on the basis of demographic background variables (age $\geq 50$ or $> 50$ years, living with someone or living alone, having children or not, working or not), and there was no systematic pattern.

With one exception, medical background variables (treatment, INF and/or a somatostatin analogue, diagno-

**Table 1**

*Patient (n = 99) mean scores on EORTC QLQ-C30 scales and single items*

| | M | SD |
|---|---|---|
| Functional scales[a] | | |
| Physical | 76.6 | 23.7 |
| Role | 71.2 | 29.1 |
| Emotional | 77.3 | 21.6 |
| Cognitive | 79.8 | 20.4 |
| Social | 78.6 | 26.3 |
| Global quality of life[a] | | |
| Global health-status/quality of life | 66.7 | 21.8 |
| Symptom scales[b] | | |
| Fatigue | 39.2 | 25.8 |
| Nausea/vomiting | 8.4 | 14.5 |
| Pain | 25.9 | 31.0 |
| Single items[b] | | |
| Dyspnoea | 34.7 | 29.0 |
| Insomnia | 22.2 | 30.5 |
| Appetite loss | 15.5 | 28.7 |
| Constipation | 8.1 | 20.8 |
| Diarrhoea | 32.3 | 32.8 |
| Economical impact | 19.9 | 31.9 |

[a] Scores range from 0 to 100, with a higher score representing a higher level of function.
[b] Scores range from 0 to 100, with a higher score representing a greater degree of symptoms.

sis, time of diagnosis less than versus more than one year earlier, number of hospitalizations, $\leq 10$ or $> 10$ times) were unrelated to the EORTC QLQ-C30 ratings. Patients with carcinoids had more problems with diarrhoea ($M = 8.3$, $SD = 22.2$) than did patients with EPT ($M = 7.0$, $SD = 13.9$) ($t = 2.8$, $df = 97$, $p < 0.001$).

To sum up, patients rated their HRQOL as relatively high according to functional and symptom scales. However, global QOL was given a lower rating. These results correspond well with those of a previous study (11).

In response to the specific disease-related questions, 61 patients (62%) reported that they had at least some problems with diarrhoea during the last week (Table 2). Nineteen stated that diarrhoea had affected their social life and 24 reported that it had affected family life during the previous week. These results correspond well to the relatively high value given to the EORTC item about diarrhoea as well as to earlier findings (11).

Thirty-nine patients (39%) stated that they had at least some flush during the last week (Table 2). Nine persons reported that it had affected social life and six that it had affected family life during the previous week. Thirty-three patients (33%) stated that they at least sometimes during the last week needed help with their injections. Thirteen persons reported that taking injections had affected social life and 14 stated that it, at least to some extent, affected family life the previous week.

Twenty-seven patients reported both diarrhoea and flush. Relatively few patients considered their family and/or social life to be affected by diarrhoea, flush and/or taking injections. Diarrhoea affected the family life of more persons than flush did.

### *Importance of and satisfaction with selected HRQOL aspects*

Table 3 presents mean values and ranks for perceived importance of and satisfaction with 12 HRQOL aspects. Ten of the 12 aspects were given importance ratings of $> 7$ and were thus rated as, at least 'rather important'. The two aspects given the highest ranks according to importance were of a physical nature: 'Wash yourself, dress, eat, etc.' and 'Have good health'. These results correspond well with those from an earlier study of the same patient population (11). Demographic background variables did not show any consistent pattern of relationships with the ratings of perceived importance of the HRQOL aspects.

Seven out of the 12 QOL aspects were given satisfaction ratings of $> 7$ (see Table 3). Two of the three items with the highest satisfaction ratings were of a social nature: 'Associate with the family' and 'Watch TV, listen to the radio, read books, etc.'

Patients who were diagnosed less than a year ago stated less satisfaction with flush ($M = 8.2$, $SD = 2.5$) than did patients who were diagnosed earlier ($M = 9.6$, $SD = 0.8$) ($t = 2.8$, $df = 92$, $p < 0.01$).

Importance ratings for 'Have good health'; 'Not have pain'; 'Not have diarrhoea'; and 'Do physical exercise' were given significantly higher mean values than corre-

**Table 2**

*Patient (n = 99) ratings of the occurrence of diarrhoea and flush and their influence and that of injections on social and family life*

| During the previous week | Not at all | Some | Quite a bit | Very much |
|---|---|---|---|---|
| Did you have diarrhoea? | 38 | 30 | 22 | 9 |
| Has diarrhoea interfered with your social life? | 80 | 12 | 4 | 3 |
| Has diarrhoea interfered with your family life? | 75 | 19 | 3 | 2 |
| Did you have flush? | 60 | 31 | 5 | 3 |
| Has flush interfered with your social life? | 90 | 7 | 2 | – |
| Has flush interfered with your family life? | 93 | 6 | – | – |
| Have your injections interfered with your social life? | 86 | 10 | 3 | – |
| Have your injections interfered with your family life? | 85 | 13 | – | 1 |

**Table 3**

*Patient (n = 99) mean values and rankings for perceived importance of and satisfaction with 12 HRQOL aspects*

| Quality of life aspect | Importance | | | Satisfaction | | | |
|---|---|---|---|---|---|---|---|
| | Rank | M[a] | SD | Rank | M[a] | SD | t[b] |
| Wash yourself, dress, eat, etc. | 1 | 9.5 | 1.2 | 1 | 9.5 | 1.0 | 0.0 |
| Have good health | 2 | 9.3 | 1.1 | 9 | 6.4 | 3.4 | 8.7*** |
| Associate with the family | 3 | 9.1 | 1.6 | 2 | 8.9 | 1.7 | 0.4 |
| Not have pain | 4 | 8.9 | 2.0 | 8 | 6.8 | 3.7 | 4.6*** |
| Do everyday household jobs | 5 | 8.5 | 2.3 | 6 | 8.1 | 2.9 | 1.4 |
| Not have diarrhoea | 6 | 8.3 | 2.6 | 10 | 6.4 | 3.8 | 4.0*** |
| Watch TV, listen to the radio, read books, etc. | 7 | 8.1 | 2.4 | 3 | 8.8 | 1.5 | 2.8** |
| Associate with friends | 8 | 7.9 | 2.5 | 5 | 8.3 | 2.5 | 1.3 |
| Do physical exercise | 9 | 7.7 | 2.7 | 12 | 6.1 | 3.8 | 4.2*** |
| Not have flush | 10 | 7.4 | 3.1 | 4 | 8.7 | 2.2 | 2.8** |
| Go to a movie, theatre, exhibition, etc. | 11 | 5.8 | 3.5 | 11 | 6.3 | 3.7 | 0.9 |
| Work | 12 | 5.7 | 4.3 | 7 | 7.2 | 3.7 | 2.3 |

[a] Highest possible value = 10, lowest possible value = 0.
[b] df = 90 − 98.
**p < 0.01, ***p < 0.001 for Importance − Satisfaction difference.

sponding satisfaction ratings. It was judged to be of interest to explore the relations between these satisfaction − importance discrepancies and corresponding ratings in the EORTC QLQ-C30 (global health, pain, diarrhoea, physical function). To this end, patients were classified in two groups: those who had higher importance than satisfaction ratings (Global health n = 65; Pain n = 44; Diarrhoea n = 51; Physical function n = 60) and those who had equal ratings or higher satisfaction than importance ratings (Global health n = 34; Pain n = 55; Diarrhoea n = 48; Physical function n = 38) for each of these four HRQOL dimensions. The subgroup with higher importance ratings had significantly higher ratings on two of the EORTC QLQ-C30 symptom scales (Pain $t = 8.3$, $df = 97$, $p < 0.001$; Diarrhoea $t = 7.2$, $df = 97$, $p < 0.001$, $df = 96$, $p < 0.01$) than did the subgroup with equal or higher satisfaction ratings. For physical function and global health, the subgroup with equal or higher satisfaction had higher ratings (Global health $t = 6.3$, $df = 97$, $p < 0.001$ and Physical function $t = 3.1$) than did those with higher importance rating.

In summary, patients stated that they were quite satisfied with the selected HRQOL aspects. However, for some aspects, patient satisfaction did not match the perceptions of importance of these aspects. Satisfaction − importance discrepancies were related to HRQOL dimensions.

*Anxiety and depression*

Levels of anxiety ($M = 4.6$, $SD = 3.9$) and depression ($M = 3.6$, $SD = 3.1$) were low. Nineteen patients (19%) scored at or above the anxiety 'cut-off point' and 13 (13%) above the depression 'cut-off point' (15). These values correspond well with results from other studies of comparable populations (11, 18). Demographic background variables did not show any relationship with patient ratings of anxiety and depression.

Relatively more patients in the group with EPT (8 out of 19) scored as potential anxiety 'cases' than did patients in the carcinoid group (11 out of 80) ($\chi^2 = 8.0$, $df = 1$, $p < 0.01$). More patients who had been on treatment for more than a year scored as potential depression 'cases' than among those who had their treatment less than a year ($\chi^2 = 4.3$, $df = 1$, $p < 0.05$).

Unpaired t-tests were performed to investigate whether HRQOL ratings differed between potential clinical anxiety and depression 'cases' and 'non-cases'.

Significant differences (Table 4) were found between potential anxiety 'cases' and 'non-cases' for nine EORTC QLQ-C30 scales/items: 'role function'; 'emotional function'; 'cognitive function'; 'social function'; 'global health-status'; 'fatigue'; 'pain'; 'insomnia'; and 'economical impact', and between potential depression 'cases' and 'non-cases' for 10 scales/items: 'physical function'; 'role function'; 'emotional function'; 'cognitive function'; 'social function'; 'global health-status'; 'fatigue'; 'nausea/vomiting'; 'pain' and 'dyspnoea'. Throughout, 'non-cases' had higher functions and fewer symptoms than 'cases'.

Potential anxiety 'cases' rated the following four HRQOL aspects as significantly less satisfactory than did 'non-cases': 'Have good health', 'Not have pain', 'Associate with the family' and 'Associate with friends' (Table 5). Potential depression 'cases' were significantly less satisfied than 'non-cases' with 'Wash yourself, dress, eat, etc.'.; 'Do physical exercise'; 'Have good health'; 'Not have pain'; 'Not have flush'; 'Associate with the family'; 'Associate with friends' and 'Do everyday household jobs' (Table 5).

The data indicate that patients who scored at or above the 'cut-off point' for anxiety and depression also reported a higher level of problems and a lower level of function on several of the EORTC QLQ-C30 scales and single items than those who scored below the 'cut-off point'. Furthermore, potential anxiety and depression 'cases' were significantly less satisfied with several of the 12 HRQOL aspects.

## DISCUSSION

### *QOL*

The EORTC QLQ-C30 ratings suggest that patients perceive their HRQOL as relatively good as measured by the function and symptom scales. However, the global QOL score was at a somewhat lower level. One reason for this

**Table 4**

*Mean scores on EORTC QLQ-C30 scales and single items for HADS anxiety 'cases' (n = 19) and 'non-cases' (n = 80) and for depression 'cases' (n = 13) and 'non-cases' (n = 86)*

| EORTC QLQ-C30 scales/items | 'Cases' | 'Non cases' | t[a] |
|---|---|---|---|
| Functional scales[b] | Anxiety | | |
| Physical | 68.4 | 78.5 | 1.7 |
| Role | 54.4 | 75.2 | 2.9** |
| Emotional | 50.0 | 83.8 | 7.7** |
| Cognitive | 64.0 | 83.5 | 4.0*** |
| Social | 63.2 | 82.3 | 3.0** |
| Global quality of life[b] | | | |
| Global health-status/quality of life | 46.0 | 71.6 | 3.7*** |
| Symptom scales[c] | | | |
| Fatigue | 57.9 | 34.7 | 3.7*** |
| Nausea/vomiting | 14.9 | 6.8 | 2.2 |
| Pain | 48.2 | 20.6 | 3.7*** |
| Single items[c] | | | |
| Dyspnoea | 42.1 | 32.9 | 1.2 |
| Insomnia | 38.6 | 18.3 | 2.7** |
| Appetite | 22.8 | 13.8 | 1.2 |
| Constipation | 17.5 | 5.8 | 2.2 |
| Diarrhoea | 40.4 | 30.4 | 1.2 |
| Economical impact | 42.2 | 14.6 | 3.6*** |
| Functional scales[b] | Depression | | |
| Physical | 55.4 | 79.8 | 3.7*** |
| Role | 48.7 | 74.6 | 3.1** |
| Emotional | 50.6 | 81.3 | 5.4*** |
| Cognitive | 56.4 | 83.3 | 5.0*** |
| Social | 55.1 | 82.2 | 3.7*** |
| Global quality of life[b] | | | |
| Global health-status/quality of life | 43.0 | 70.2 | 4.6*** |
| Symptom scales[c] | | | |
| Fatigue | 63.2 | 35.5 | 3.8*** |
| Nausea/vomoting | 18.0 | 6.9 | 2.6** |
| Pain | 57.7 | 21.1 | 3.0*** |
| Single items[c] | | | |
| Dyspnoea | 56.4 | 31.4 | 3.0** |
| Insomnia | 35.9 | 20.1 | 1.7 |
| Appetite loss | 15.4 | 15.5 | 0.0 |
| Constipation | 12.8 | 7.4 | 0.9 |
| Diarrhoea | 48.7 | 29.8 | 2.0 |
| Economical impact | 28.2 | 18.6 | 1.0 |

[a] $df = 93 - 97$.
[b] Scores range from 0 to 100, with a higher score representing a higher level of function.
[c] Scores range from 0 to 100, with a higher score representing a higher degree of symptoms.
**$p < 0.01$, ***$p < 0.001$.

**Table 5**

*Mean scores for satisfaction with 12 HRQOL aspects for HADS anxiety 'cases' (n = 19) and 'non-cases' (n = 80), and for depression 'cases' (n = 13) and 'non-cases' (n = 86)*

| Quality of life aspect | Anxiety | | | Depression | | |
|---|---|---|---|---|---|---|
| | Cases M[a] | Non-cases M[a] | t[b] | Cases M[a] | Non-cases M[a] | t[b] |
| Wash yourself, dress, eat, etc. | 9.2 | 9.6 | 1.8 | 8.5 | 9.7 | 4.3*** |
| Have good health | 4.2 | 6.9 | 3.4*** | 3.1 | 6.9 | 4.0*** |
| Associate with the family | 8.0 | 8.2 | 3.1** | 7.5 | 9.2 | 3.7*** |
| Not have pain | 4.8 | 7.3 | 2.8** | 3.8 | 7.3 | 3.3** |
| Do everyday household jobs | 7.3 | 8.3 | 1.3 | 6.2 | 8.4 | 2.7** |
| Not have diarrhoea | 6.0 | 6.4 | 0.4 | 5.2 | 6.5 | 1.2 |
| Watch TV, listen to the radio, read books, etc. | 8.4 | 8.9 | 1.2 | 8.0 | 9.0 | 2.2 |
| Associate with friends | 6.5 | 8.8 | 3.8*** | 6.0 | 8.7 | 3.7*** |
| Do physical exercise | 5.0 | 6.3 | 1.4 | 3.4 | 6.5 | 2.8** |
| Not have flush | 7.6 | 9.0 | 2.5 | 6.8 | 9.0 | 3.7*** |
| Go to a movie, theatre, exhibition, etc. | 5.0 | 6.5 | 1.6 | 4.9 | 6.5 | 1.5 |
| Work | 6.4 | 7.4 | 1.1 | 6.7 | 7.3 | 0.5 |

[a] Highest possible value = 10, lowest possible value = 0.
[b] df = 89-97.
**p < 0.01, ***p < 0.001.

could be that there are aspects of life not included in the instrument that have a negative influence on patient ratings of overall QOL. Another possibility is that patients weigh the importance of some symptoms in a manner that is not evident from the present data. However, the findings of lower scores on the global than on functional scores corresponds well with results from other studies among patients with a variety of cancer diagnoses (19–23). A similar finding was also reported in a population-based study on 608 women completing the EORTC QLQ-C30 (24).

Since there are few other reports concerning HRQOL ratings in this specific patient group, comparisons were made with results from patients with other diagnoses. With the exception of disease-related symptoms, the present data are roughly comparable with results from a study among patients with newly diagnosed multiple myeloma (25). In comparison to patients with breast cancer in all stages (19) and those with head and neck cancer 6 years after treatment (20), patients in the present study reported a lower HRQOL. Compared to patients with oesophageal cancer (21), those with pancreatic or biliary adenocarcinoma (22) and with lung cancer (13), the present patients rated their HRQOL as better with regard to most of the scales. Thus, it seems that HRQOL ratings of patients with endocrine GI tumours are more comparable with those of patients with diagnoses or stages less likely to have had heavy chemotherapy/radiotherapy than to patients treated with heavy chemotherapy/radiotherapy.

A majority reported that they had at least some diarrhoea, and a little more than a third stated that they had at least some flush during the last week. One-third of the patients stated that they needed help with their injections. Diarrhoea, flush, or taking injections did not seem to have affected family and/or social life for more than a minority of the patients. A reason for this could be that they had had their diagnosis and treatment for a long period and had thus had time to adjust to and accept the situation. This may also have contributed to the relatively high HRQOL ratings.

The present study utilized a single point of assessment and gives no information about the specific phase of the disease of these patients. The duration of the period since diagnosis was quite long as was the mean time on treatment. Since INF/somatostatin analogues are mostly the first-line medical treatment, at least for the patients with carcinoids (4), it can be assumed that at the time of the data collection disease control was quite good for these patients. A possible implication would be that INF/somatostatin analogues do not have a strong negative influence on the HRQOL in this patient population.

The large variation in mean time since diagnosis may be assumed to be accompanied by a parallel variation in QOL. However, the lack of differences between patients diagnosed less versus more than one year before the study did not support that assumption. This should not be taken to suggest that these patients' perception of their QOL does not change much over time. To draw any further conclusions, assessment of QOL among patients with endocrine GI tumours should be performed also at the time of diagnosis. The lack of variability in the QOL responses may also reflect the fact that the natural course of endocrine GI tumours often has a slow progression and spans a long period of time. This gives the patient a chance to adjust to changes due to tumour growth (e.g. more symptoms) and thereby not perceive a deterioration of QOL due to an increased level of symptoms.

*Importance of and satisfaction with selected HRQOL aspects*

All HRQOL aspects were perceived as at least relatively important, and the highest importance was assigned to aspects of a physical nature. This may be expected since the aspects asked for were derived from clinical experience concerning reactions to disease and treatment in this patient group.

It may be argued that the relatively high importance ratings assigned to most HRQOL aspects could be a result of the free response format of the VAS. When 'good things in life' are rated using a free response format, it seems that some individuals tend to give consistently high values (26). However, in a study (27) where breast cancer patients were asked to rate the importance of various QOL aspects with two different techniques, (Q-sort with a forced response format and linear analogue scales with a free response format), similar findings were obtained with both methods. Thus, it can be assumed that the response format has not contributed to the high importance ratings.

Patients reported that they were at least relatively satisfied with the selected HRQOL aspects. However, it may be misleading to draw conclusions on the basis of satisfaction ratings alone without consideration of the importance ratings of each aspect. It seems reasonable that high satisfaction with an important aspect should be weighted differently from high satisfaction with an unimportant aspect.

For two aspects, mean values for satisfaction were significantly higher than those for importance: 'Watch TV, listen to the radio, read books, etc.' and 'Not have flush', and both were rated as quite important as well as satisfactory.

For four of the selected HRQOL aspects, mean importance ratings were higher than satisfaction ratings ('Not have pain', 'Not have diarrhoea', 'Have good health' and 'Do physical exercise'). These aspects are all of a physical nature and related to the disease. The group of patients who gave higher importance than satisfaction values to these four QOL aspects gave lower ratings to corresponding EORTC QLQ-C30 items than patients with equal ratings or higher satisfaction than importance ratings. This suggests that importance – satisfaction discrepancies are valid indicators of patient distress. Although this analysis represents merely an exploratory effort, the data suggest that further analysis is warranted.

*Anxiety and depression*

Anxiety and depression ratings were low and anxiety ratings were higher than depression ratings which accords with previous results (18, 28). Nineteen percent of the patients scored at or above the recommended 'cut-off point' (15) for anxiety and 13% did so for depression. Anxiety and depression 'non-cases' reported a higher HRQOL than 'cases' as assessed by the EORTC QLQ-C30 and the satisfaction scales. Similar results have been reported in a study of 269 cancer patients receiving radiotherapy. Patients who had high levels of anxiety and depression scored high on symptom scales and low on EORTC QLQ-C30 functional scales (23). In a study of 214 breast cancer patients (29) in which 9% scored as anxiety cases and 9% as depression cases, relationships were found between anxiety and functional status and between depression and pain, shortness of breath and functional status measured by the HADS and the Rotterdam Symptom Checklist (30). The direction of influence, if any, between anxiety/depression and HRQOL cannot be determined from the present data. However, the demonstrated relationships imply that determination of HAD 'caseness' yields information about which patients run a risk of a low overall QOL.

A number of studies have reported that cancer patients' coping with various aspects of their disease and treatment is important for their psychological well-being (31–33). The low ratings of anxiety and depression and the relatively high QOL in the present study could be interpreted as signs of adjustment. Since the mean time since diagnosis is as much as five years, the patients have had a good chance of adjusting to their situation. It is known that the majority of cancer patients succeed in adapting to the stressful, adverse effects of the disease and its treatment (34). The fact that more patients who had been on treatment for a longer period of time scored as potential depression 'cases' compared to those with a shorter treatment duration may reflect a side effect (4) of the INF.

Since this study uses a single point of HRQOL assessment and since patients were not randomized between treatments, the data on how different therapies (INF and somatostatin analogues) are related to HRQOL are admittedly weak. Thus the comparisons between, INF, a somatostatin analogue or the combination should be interpreted with caution. The fact that no significant between-group differences were found with regard to HRQOL ratings should also be interpreted in view of the fact that the group treated with a somatostatin analogue was very small ($n = 10$).

*Methodological considerations*

The group of patients in the present study is heterogeneous with regard to diagnosis, treatment and time since diagnosis. This limits the value of a single point of HRQOL assessment. However, the QOL data revealed very few differences related to these background variables as there was no consistent pattern in the QOL, anxiety or depression ratings. Comparisons with patients with other diagnoses in earlier studies indicate that the results were as could be expected in this patient group in view of the characteristics of the disease (diarrhoea, flushing, fatigue) and treatments (INF and/or a somatostatin analogue).

The EORTC QLQ-C30 and HADS questionnaires have not been used in this patient group earlier and psychometric evaluation is therefore of interest. However, it is unlikely that values for internal consistency, test – retest reliability, construct validity and sensitivity to change differ greatly between this patient group and other groups of cancer patients (35–37).

*Implications*

The patients of the present study seem to perceive their HRQOL as relatively good, which is in accordance with earlier findings (10). It is important to analyse further the clinical significance of the small mean score differences in this heterogeneous material. In particular, patient subgroups with an increased risk of QOL deterioration should be focused. In future studies, HRQOL should be assessed repeatedly over time in order to investigate to what extent patient perceptions of their HRQOL change from the time of diagnosis to later phases. This is particularly important as INF/somatostatin analogues are not a curative treatment but may control the cancer disease for long periods of time (4). If caregivers achieve a better understanding of patient perceptions of their QOL they can presumably provide better care for the patient.

## REFERENCES


1. Öberg K. Endocrine tumors of the gastrointestinal tract: systemic treatment. Anti-Cancer Drugs 1994; 5: 503–19.
2. Wilander E, Lundqvist ML, Öberg K. Gastrointestinal carcinoid tumors. In: Graumann W, Lojda Z, Pearse AGE, Schiebler TH, eds. Progress in histochemistry and cytochemistry. Stuttgart: Gustav Fischer Verlag, 1989: 2–19.
3. Öberg K, Eriksson B. Medical treatment of neuroendocrine gut and pancreatic tumours. Acta Oncol 1989; 28: 425–31.
4. Öberg K. Interferon therapy of neuroendocrine tumours. In: Aul C, Schneider W, eds. Interferons: Biological activities and clinical efficacy. Berlin: Springer, 1997: 36–46.
5. Aaronson NK, Cull A, Kaasa S, Sprangers M. The EORTC modular aproach to quality of life assessment in oncology. Int J Mental Health 1994; 23: 75–96.
6. Shumaker SA, Naughton MJ. The international assessment of health-related quality of life: a theoretical perspective. In: Shumaker SA, Bernzon R, eds. The International Assessment of Health-related quality of life: theory, translation, measurement and analysis. Oxford: Rapid Communications of Oxford, 1995: 3–10.
7. Faithfull S. Just grin and bear it and hope that it will go away': coping with urinary symptoms from pelvic radio therapy. Eur J Cancer Care 1996; 4: 158–65.
8. Montgomery H, Johansson US. Life values: their structure and relation to life situation. In: Maital S, ed. Applied behavioral economics. Brighton: Wheatsheaf, 1988: 420–37.
9. Öberg K. Chemotherapy and biotherapy in neuroendocrine tumors. Curr Opin Oncol 1993; 5: 110–20.
10. Öberg K, Eriksson B, Tiensuu JE. Interferons alone or in combination with chemotherapy or other biologicals in the treatment of neuroendocrine gut and pancreatic tumors. Digestion 1994; 55: 64–9.
11. Larsson G, von Essen L, Sjödén PO. Quality of life in patients with endocrine tumours of the gastrointestinal tract: patient and staff perceptions. Accepted for publication in Cancer Nurs 1998; 21: 6.
12. Jacobsen MB, Hanssen LE. Clinical effects of octreotide compared to placebo in patients with gastrointestinal neuroendocrine tumours. Report on a double-blind, randomized trial. J Int Med 1995; 237: 269–75.
13. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ–C30: a quality-of-life instrument for use in international clinical trials in oncology. J Nat Cancer Inst 1993; 85: 365–76.
14. Sprangers MAG, Cull A, Bjordal K, Groenvold M, Aaronson NK. The European Organization for Research and Treatment of Cancer approach to quality of life assessment: guidelines for developing questionnaire modules. Quality of Life Res 1993; 2: 287–95.
15. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983; 67: 361–70.
16. Ibbotson T, Maguire P, Selby P, Priestman T, Wallace L. Screening for anxiety and depression in cancer patients: the effects of disease and treatment. Eur J Cancer 1994; 1: 37–40.
17. Moorey S, Greer S, Watson M, et al. The factor structure and factor stability of the Hospital Anxiety and Depression Scale in patients with cancer. Br J Psychiatry 1991; 158: 255–9.
18. Lampic C, von Essen L, Widmark-Peterson V, Larsson G, Sjödén PO. Anxiety and depression in hospitalized patients with cancer: agreement in patient–staff dyads. Cancer Nurs 1996; 19: 419–28.
19. Carlsson M, Hamrin E. Measurement of quality of life in women with breast cancer. Development of a Life Satisfaction Questionnaire (LSQ–32) and comparison with the EORTC QLQ–C30. Quality of Life Res 1996; 5: 265–74.
20. Bjordal K, Freng A, Thorvik J, Kaasa S. Patients' self-reported and clinician-rated quality of life in head and neck cancer patients: a cross-sectional study. Oral Oncol Eur J Cancer 1995; 4: 235–41.
21. Blazeby JM, Williams MH, Brookes ST, Alderson D, Farndon JR. Quality of life measurement in patients with oesophageal cancer. Gut 1995; 37: 505–8.
22. Glimelius B, Hoffman K, Sjödén PO, et al. Chemotherapy improves survival and quality of life in advanced pancreatic and biliary cancer. Ann Oncol 1996; 7: 593–600.
23. Maher EJ, Mackenzie C, Young T, Marks D. The use of the Hospital Anxiety and Depression Scale (HADS) and the EORTC QLQ–C30 questionnaires to screen for treatable unmet needs in patients attending routinely for radiotherapy. Cancer Treat Rev 1996; 22: 123–9.
24. Klee M, Groenvold M, Machin D. Quality of life of Danish women: population-based norms for the EORTC QLQ–C30. Quality of Life Res 1997; 6: 27–34.
25. Wisloff F, Hjort M, Kaasa S, Westin J. Effect of interferon on the health-related quality of life of multiple myeloma patients: results of a Nordic randomized trial comparing melpheran–prednisone to melpheran–prednisone + α-interferon. Br J Haematology 1996; 94: 324–32.
26. Batey MV. Acquiescent response set: a source of measurement error. Western J Nurs Res 1979; 1: 247–9.
27. Sutherland HJ, Lockwood GA, Boyd NF. Ratings of the importance of quality of life variables: therapeutic implications for patients with metastatic breast cancer. J Clin Epidemiol 1990; 43: 661–6.
28. von Essen L, Burström L, Sjödén PO. Perceptions of caring behaviors and patient anxiety and depression in cancer patient–staff dyads. Scand J Car Sci 1994; 8: 205–12.

29. Hopwood P, Howell A, Maguire P. Psychiatric morbidity in patients with advanced cancer of the breast: prevalence measured by two self-rating questionnaires. Br J Cancer 1991; 64: 349–52.
30. de Haes JCJM, van Knippenberg FCE, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. Br J Cancer 1990; 62: 1034.
31. Morris T. Psychosocial aspects of breast cancer: a review. J Clin Oncol 1983; 19: 1725–33.
32. Morris T, Greer S, White P. Psychological and social adjustment to mastectomy: a two-year follow-up study. Cancer 1977; 40: 2381–8.
33. Rodriguez JR, Behen JM, Tumlin T. Multidimensional determinants of psychological adjustment to cancer. Psycho-Oncol 1994; 3: 205–14.
34. Sprangers M. Response-shift bias: a challenge to the assessement of patients' quality of life in cancer clinical trials. Cancer Treat Rev 1996; 22: 55–62.
35. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale—a review of validation data and clinical results. J Psychosom Res 1997; 42: 17–41.
36. Osoba D, Zee B, Pater J, Warr D, Kalzer L, Latreille J. Psychometric properties and responsiveness of the EORTC Quality of Life Questionnaire (QLQ–C30) in patients with breast, ovarian and lung cancer. Qual Life Res 1994; 3: 353–64.
37. Ringdal GI, Ringdal K. Testing the EORTC Quality of Life Questionnaire on cancer patients with heterogeneous diagnoses. Qual Life Res 1993; 2: 129–40.