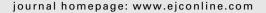


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# Quality of life and persisting symptoms after oesophageal cancer surgery

### Pernilla Viklund<sup>a,\*</sup>, Yvonne Wengström<sup>b</sup>, Ioannis Rouvelas<sup>a</sup>, Mats Lindblad<sup>a</sup>, Jesper Lagergren<sup>a</sup>

<sup>a</sup>Unit of Esophageal and Gastric Research, Department of Molecular Medicine and Surgery P9:03, Karolinska Institutet, Karolinska University Hospital, SE-171 76 Stockholm, Sweden

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#### ABSTRACT

To assess quality of life (QoL) and symptoms after oesophageal cancer surgery, a prospective nationwide population-based study was conducted in 2001–2005, including most surgically treated oesophageal cancer patients in Sweden. Six months postoperatively patients responded to an EORTC quality of life core questionnaire (QLQ C-30) with an oesophageal-specific module (OES-18). Mean scores were calculated. Mann-Whitney test was used for group comparisons. Among 282 patients, QoL was considerably reduced compared to a reference general population (P < 0.001), and functioning scales were similarly negatively affected; particularly role (P < 0.001) and social (P < 0.001) functions. Younger patients scored worse than older. No gender differences were found. Dominating general symptoms included fatigue, appetite loss, diarrhoea, and dyspnoea, each significantly more pronounced than the general population (P < 0.001). Eating problems, cough, reflux, and oesophageal pain were common oesophageal-specific symptoms. Thus, patients who undergo oesophageal cancer resection suffer greatly from reduced QoL and several general and oesophageal-specific symptoms six months postoperatively.

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#### 1. Introduction

Oesophageal resection alone is the most established treatment that can offer a cure for patients with oesophageal cancer. The outcome measure used in most research on oesophageal cancer surgery has been survival, on account of its obvious relevance and its ease of interpretation and calculation. A second relevant outcome measure is the occurrence of postoperative complications, which has been less well studied even though oesophageal cancer surgery is burdened with a substantial risk of severe complications. Gomplications have recently been shown to impair the patients' long-term quality of life (QoL) postoperatively.

is, in turn, a third relevant outcome measure, and this is addressed in the current study. QoL after oesophageal cancer surgery has only been reported in studies of small or selected samples, and no population-based investigations are available.<sup>8–10</sup> Recent advances in the development of self-administered structured and validated tools for the assessment of QoL and general symptoms, designed for cancer patients, as well as of organ-specific symptoms, including an oesophageal-specific module, have developed QoL research.<sup>11,12</sup> Assessment of the QoL would seem particularly important after oesophageal cancer surgery.<sup>13</sup> Even though this surgery is especially extensive, the majority of the surgically treated patients die from spread of their oesophageal cancer within

<sup>&</sup>lt;sup>b</sup>Department of Oncology and Pathology, Karolinska Institutet, SE-171 76 Stockholm, Sweden

<sup>\*</sup> Corresponding author: Tel.: +46 8 5177 5984; fax: +46 8 33 15 87. E-mail address: pernilla.viklund@karolinska.se (P. Viklund). 0959-8049/\$ - see front matter © 2006 Elsevier Ltd. All rights reserved. doi:10.1016/j.ejca.2006.02.005

three years. <sup>1,14</sup> Thus, most oesophageal cancer resections can only offer palliation. The high prevalence of morbidity, which can reduce the QoL, is recognized among oesophageal surgeons. To our knowledge however, there have been no population-based studies in which systematic attempts have been made to estimate the QoL or morbidity among surgically treated oesophageal cancer patients. We therefore conducted a nationwide, prospective, population-based study in Sweden with the principle aim of obtaining valid measures of the QoL and information on general and oesophageal-specific symptoms six months after oesophageal cancer surgery, and to compare the results with the general population.

#### 2. Patients and methods

#### 2.1. Study design

A prospective, population-based study was performed in Sweden during the four-year period April 2, 2001 through June 30, 2005. Eligible for the study were all Swedish residents newly diagnosed with an oesophageal or cardia cancer who were treated by oesophageal resection during the period April 2, 2001 through December 31, 2004. The data were collected from the Swedish Esophageal and Cardia Cancer (SECC) register, an almost complete nationwide surgical register. The principles of the comprehensive organization of this register and the prospective registration have been presented in detail elsewhere. 6,15 In brief, the register is based on a collaborative Swedish nationwide network of hospital departments and physicians involved in the diagnosis or treatment of oesophageal or gastric cardia cancer, as well as all six Swedish regional tumour registers. 15 This network enabled us to identify all patients throughout the country shortly after the diagnosis. Details about the patient, the tumour, the surgical procedures, complications, and length of hospital stay were collected through our own manual scrutiny of each case record. The classification of the location of the adenocarcinomas was based on the Siewert definitions.<sup>16</sup> Tumour stage was classified in accordance with the definitions proposed by the Union Internationale Contre le Cancer. 17 Measures of QoL were assessed through self-administered questionnaires, described in more detail below, which were sent out to the patients six months after surgery within the framework of the SECC register. The timing of the assessment was based on previous research that has identified a stable time window with regard to QoL six months postoperatively. 8,9,18,19 In total, up to three letters to remind the candidate participants about the questionnaires were sent out.

#### 2.2. The questionnaires

The assessment of QoL was based on a previously validated cancer-specific core questionnaire, the QLQ-C30 (version 3.0), <sup>11</sup> and an oesophageal cancer-specific module QLQ-OES 18, <sup>12</sup> both developed by the European Organisation for Research and Treatment of Cancer (EORTC). The QLQ-C30 includes one global QoL scale, five functional scales (role, social, emotional, physical, and cognitive), three general symptom scales (fatigue, pain, and nausea and vomiting), and finally, six single-item general symptom measures or

problems (appetite loss, diarrhoea, dyspnoea, insomnia, financial difficulties, and constipation). Each item has four response alternatives: 1) "Not at all", 2) "A little", 3) "Quite a bit", and 4) "Very much", except for the global QoL scale which has a range from: 1) "Very poor" to 7) "Excellent". The QLQ-OES 18 <sup>12</sup> assesses symptoms specific to oesophageal cancer and comprises four symptom scales (eating, reflux, oesophageal pain, and dysphagia) and six single items (cough, dry mouth, taste, choking, speech, and trouble swallowing saliva). This questionnaire has the same four response alternatives as the core questionnaire.

#### 2.3. Statistical methods and data analyses

Scores, derived from the questionnaires were linearly transformed into a 0 to 100 scale according to the EORTC Scoring Manual,<sup>20</sup> where a high score in the functional and global QoL scales represented a higher level of function and better global QoL whereas a high symptom score represented more symptoms. All data analyses were performed by using the statistical software SAS 9.1. for Windows. Mean scores and standard deviations (SDs) were calculated using the proc means procedure of SAS. Based on previous research, 21 we considered a difference in mean scores of 10 or more on the 0 to 100 scale as being of clinical relevance. This interpretation of clinical relevance has also been adopted in other studies.<sup>22–25</sup> When mean scores differed by at least 10 between groups of patients in our study, the Mann-Whitney test was used to examine for statistical significance at the 5% level. Results of comparisons with a reference general Swedish population<sup>22</sup> were also tested with the two sample t-test whenever sample size, mean scores and standard deviations were available for both groups and when the mean scores differed by at least 10.

#### 2.4. Ethical considerations

Informed consent was obtained from each patient before inclusion in the study. The ethics committee at Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden, approved the study.

#### 3. Results

#### 3.1. Patients

During the four-year study period, 458 patients treated with surgery with a curative intent for oesophageal or gastric cardia cancer were recorded in the SECC register. Of these, 96 (21%) died before the six-month follow-up, 31 (7%) did not respond to the questionnaire, and 49 (11%) did not receive the questionnaire in time for the follow-up because of delayed registration. Thus, 282 (62%) patients who had undergone oesophageal resection remained for final analysis. Some characteristics of the study patients are presented in Table 1. Their median age was 67 years and the majority (68%) of the patients were within the age range 60–79 years. There was a 5:1 male predominance. The resected tumours were located more frequently in the oesophagus (56%) than in the cardia. The most frequent tumour stage was stage III (40%). The standard surgical procedure was a combined transabdominal and

Table 1 – Characteristics of 282 oesophageal cancer patients treated with surgery

	Number	Percentage (%)
Age, years		
<60	71	25
60–69	91	32
70–79	100	35
>79	20	7
Gender		
Male	224	79
Female	58	21
Diagnosis		
Esophageal squamous cell carcinoma	66	23
Esophageal adenocarcinoma	92	33
Cardia cancer	124	44
Tumour stage		
0–I	59	21
II	89	32
III	114	40
IV	20	7
Surgical approach		
Transthoracic	233	83
Transhiatal	49	17
Esophageal substitute		
Stomach	216	77
Jejunum	59	21
Colon	7	2
At least one complication within 30 days after surgery		
No	154	55
Yes	128	45
Macroscopic radicality		
Yes	266	94
No	16	6

transthoracic approach (through a separate right-sided incision), with a gastric tube reconstruction pulled up as oesophageal substitute. Nearly half (45%) of the patients had at least one complication within 30 days after surgery. Few tumours (n = 16; 6%) were not radically removed macroscopically.

## 3.2. Quality of life and general symptoms among oesophageal cancer resection patients compared to the general population

Patients treated with oesophageal cancer surgery six months earlier reported worse mean scores for QoL, functional performance and general symptoms, compared to a random reference sample of the Swedish general population (Table 2). Compared to a sample of this reference population without chronic health problems, the mean scores for the QoL and functioning scales among the study patients were even lower, and those for general symptoms even higher. The QoL scores were also generally worse among our study patients when compared to a sample of the reference population that had a cancer diagnosis. The mean score of the global QoL scale among the study patients was 59, which was lower than that of both the total reference population (mean score differences

of 15 and 19 among women and men, respectively; P < 0.001) and the reference persons with cancer (mean score difference 14). In the functioning scales, the role function was most severely affected, followed by the scales for social, emotional, physical, and cognitive functioning. Compared to the total reference population, all differences regarding functioning scales, except for the cognitive scale, were statistically significant and of clinical relevance. Among the general symptom scales, problems with fatigue were particularly observed in the study group, with mean scores for women and men that were higher (i.e. worse) by 20 and 25 than those in women and men of the reference population (P < 0.001), respectively, and a mean score (total for women and men) that was higher by 17 than that of the reference cancer patients. General pain was reported to a similar extent by the study patients and the reference cancer group. Nausea and vomiting were more common than in the general reference population. Among the general symptom items, appetite loss, diarrhoea, and dyspnoea were dominating problems that were considerably more prevalent than in the general population, particularly appetite loss (mean score differences 30-34, P < 0.001) and diarrhoea (mean score difference 28, P < 0.001). Insomnia, financial difficulties and constipation were comparatively less troublesome for the study patients (Table 2).

## 3.3. Relation of gender, age, and macroscopic radicality to quality of life and general symptoms after oesophageal cancer surgery

The mean scores in all scales and items were similar between genders (Table 2). Table 3 shows mean scores categorized by age groups and macroscopically radical resection (yes or no). The emotional function was more negatively affected in the youngest age group (<60 years) than in older patients (P < 0.01). Similarly, insomnia (P < 0.05) and financial difficulties (P < 0.001) were more commonly reported by younger patients, while the role function was clinically but not statistically significantly worse in the youngest age group. The mean scores in other scales or items did not differ clinically or with statistical significance between age groups. Patients whose tumours were not radically resected macroscopically experienced poorer global QoL and worse scores in all functioning scales and all general symptom scales, compared to patients with radical resection. The role function was particularly affected in the former patients (mean score difference 35, P < 0.001). Regarding the general symptom items, dyspnoea was more common in the non-radical resection group compared to the group with a radical resection (mean score difference 32, P < 0.001).

### 3.4. Oesophageal-specific symptoms after oesophageal cancer surgery

The mean scores for oesophageal-specific symptoms six months after oesophageal cancer surgery are presented in Table 4. No comparison population was available, but most people in the population at large have no oesophageal symptoms, and therefore our general reference population would have a mean symptom score close to 0, except for reflux which is common in the population. Each evaluated

Table 2 – Quality of life and general symptoms, presented as mean scores with standard deviations (SDs), in 282 oesophageal cancer patients treated with surgery who responded to the EORTC QLQ-C 30 questionnaire compared with a general Swedish population

	Male reference n = 1450 <sup>c</sup>	Male study patients n = 224	Female reference n = 1619 <sup>c</sup>	Female study patients n = 58	No chronic health problem reference n = 721 <sup>c,d</sup>	Cancer reference n = 134 <sup>c,d</sup>	Total mean scores for study patients n = 282
Global quality of life scale <sup>a</sup>	78 (21)	59 (24)***	75 (22)	60 (21)***	85	73	59 (23)
Functioning scales <sup>a</sup>							
Role	87 (24)	62 (35)***	87 (24)	64 (31)***	94	82	63 (34)
Social	91 (19)	71 (29)***	90 (20)	73 (28)***	97	88	71 (29)
Emotional	84 (20)	73 (24)***	78 (22)	69 (28)	86	82	72 (25)
Physical	92 (16)	77 (23)***	88 (18)	75 (21) <sup>***</sup>	97	82	76 (23)
Cognitive	88 (17)	81 (21)	89 (18)	82 (22)	93	87	81 (21)
General symptom scales <sup>b</sup>							
Fatigue scale	19 (21)	44 (28)***	23 (22)	43 (25)***	13	27	44 (28)
Pain scale	16 (23)	26 (29)***	21 (27)	25 (28)	9	26	26 (28)
Nausea and vomiting scale	3 (10)	18 (21)***	4 (11)	26 (28)***			19 (23)
General symptom items	b						
Appetite loss	4 (14)	34 (36)***	5 (15)	39 (33)***			35 (35)
Diarrhoea	5 (15)	33 (32)***	5 (16)	33 (33)***			33 (32)
Dyspnoea	20 (28)	32 (31)***	16 (24)	33 (33)***	13	25	33 (32)
Insomnia	14 (25)	23 (30)	20 (28)	31 (32)**	11	25	24 (30)
Financial difficulties	6 (19)	15 (27)	7 (21)	18 (29)**	1	8	16 (27)
Constipation	3 (12)	12 (25)	7 (18)	14 (27)			13 (25)

Mean score differences of at least 10 were tested for statistical significance.

- a Score range 0 to 100. Higher score represents a better quality of life or a higher level of functioning.
- b Score range 0 to 100. Higher score represents more severe symptoms.
- c Mean scores of a large Swedish population used as reference groups.<sup>22</sup> When testing for P values, males and females in the population were used as reference groups.
- d Where mean scores are missing the mean scores were not presented in the large Swedish population study; no SD available.<sup>22</sup>
- \* P value < 0.05.
- \*\* P value < 0.01.
- \*\*\* P value < 0.001

oesophageal-specific symptom was negatively affected after surgery. Eating problems (mean score 35) were the single worst oesophageal-specific symptom. Thereafter, problems with cough, reflux, oesophageal pain, dry mouth, dysphagia, and taste were reported very frequently by the study patients (mean scores in the range of 24 to 28). There were no clinically relevant differences in oesophageal-specific symptoms between males and females. Similarly, the mean scores were in general, evenly distributed between age groups. Regarding the radicality of the resection, patients whose resection was not macroscopically radical had higher mean scores regarding reflux, cough, dry mouth, choking, and speech (Table 4).

#### 4. Discussion

This population-based study indicates that the QoL is greatly reduced and that various general and oesophageal-specific symptoms still constitute major problems six months after oesophageal cancer surgery. Compared to a reference population and to other cancer patients, the global QoL, functional scales, and general symptoms, particularly fatigue, appetite loss, and diarrhoea, were considerably worsened among the

study patients. Eating problems were the single worst persisting oesophageal-specific symptom, followed closely by problems with cough, reflux, oesophageal pain, dry mouth, dysphagia, and taste. No appreciable differences were found between genders or age groups.

The most likely explanation for the low scores in the study patients is the magnitude of the surgical procedure, entailed by considerable morbidity. Another potential explanation would be recurrent disease, which is demonstrated in the group of patients without macroscopically signs of remaining cancer in the surgical specimen, but our choice of time window for the assessment of these scores should act against such influence. Previous studies that have compared measures of QoL in patients after oesophageal cancer resection and the general population are lacking. The differences were striking. Interestingly, the study patients had a considerably poorer global QoL and suffered more from general symptoms than patients with a known cancer in the general reference cohort. The latter difference might not be explained by psychological factors, since both groups had cancer. Thus, much of the reduction in QoL might have been caused by persistence of symptoms resulting from the operation per se. The

Table 3 – Quality of life and general symptoms presented as mean scores with standard deviations (SDs) of 282 oesophageal cancer patients who responded to the EORTC QLQ-C 30 six months after surgery

		Age groups	s, years (SD)		Macroscopic	ally radical (SD)
	<60	60–69 <sup>c</sup>	70–79	>79	Yes <sup>c</sup>	No
	n = 71	n = 91	n = 100	n = 20	n = 266	n = 16
Global quality of life scale <sup>a</sup>	56 (21)	64 (23)	57 (24)	57 (23)	60 (23)	42 (23)**
Functioning scales <sup>a</sup>						
Role	56 (33) <sup>ns</sup>	66 (35)	66 (33)	63 (36)	65 (33)	30 (31)***
Social	65 (30)	72 (28)	74 (29)	81 (21)	73 (28)	50 (33)**
Emotional	65 (26) <sup>**</sup>	76 (22)	72 (27)	80 (17)	73 (25)	59 (28) <sup>*</sup>
Physical	79 (20)	79 (23)	73 (24)	73 (22)	77 (22)	57 (28)**
Cognitive	80 (23)	83 (19)	81 (21)	82 (22)	82 (21)	70 (25) <sup>*</sup>
General symptom scales <sup>b</sup>						
Fatigue scale	43 (27)	41 (28)	45 (28)	50 (32)	42 (27)	64 (30)**
Pain scale	29 (28)	21 (23)	30 (33)	15 (22)	25 (28)	41 (27)**
Nausea and vomiting scale	21 (25)	18 (23)	21 (33)	13 (13)	19 (23)	29 (25) <sup>ns</sup>
General symptom items <sup>b</sup>						
Appetite loss	29 (32)	33 (35)	39 (37)	45 (35) <sup>ns</sup>	34 (35)	42 (38)
Diarrhoea	36 (32)	34 (35)	31 (30)	26 (29)	33 (32)	31 (33)
Dyspnoea	34 (30)	31 (31)	33 (34)	32 (31)	31 (31)	63 (36)***
Insomnia	31 (33)*	17 (22)	29 (33)	17 (30)	24 (31)	31 (26)
Financial difficulties	33 (35)***	13 (25)	9 (18)	5 (12)	15 (27)	25 (33) <sup>ns</sup>
Constipation	14 (25)	6 (19)	17 (29)	17 (30)	13 (25)	15 (27)

Mean score differences of at least 10 were tested for statistical significance.

ns = non-significant.

Table 4 – Oesophageal-specific symptoms presented as mean scores with standard deviations (SDs) in 282 oesophageal cancer patients who responded to the EORTC oesophageal-specific module QLQ-OES 18 six months after surgery

	Gender (SD)		Age groups, years (SD)			Macroscopically radical (SD)		Total (SD)	
	Male n = 224	Female n = 58	<60 n = 71	60–69 <sup>b</sup> n = 91	70–79 n = 100	>79 n = 20	Yes <sup>b</sup> n = 266	No n = 16	n = 282
Symptom scales <sup>a</sup>									
Eating	34 (26)	36 (24)	35 (27)	32 (24)	37 (28)	35 (24)	34 (26)	41 (25)	35 (26)
Reflux	24 (28)	32 (31)	26 (29)	23 (28)	30 (24)	18 (23)	25 (29)	43 (34)*	26 (29)
Oesophageal pain	26 (23)	27 (26)	29 (25)	23 (20)	29 (26)	15 (18)	26 (24)	31 (21)	26 (24)
Dysphagia	25 (27)	25 (26)	23 (25)	23 (26)	26 (29)	32 (29)	25 (27)	24 (27)	25 (27)
Symptom items <sup>a</sup>									
Cough	28 (31)	25 (25)	28 (32)	27 (31)	28 (33)	23 (27)	26 (31)	48 (40)*	28 (32)
Dry mouth	27 (32)	26 (30)	16 (26)	25 (32)	33 (34)	33 (26)	25 (31)	46 (38)*	26 (32)
Taste	24 (32)	24 (33)	20 (30)	21 (28)	27 (36)	35 (37) <sup>ns</sup>	24 (32)	29 (36)	24 (32)
Choking	20 (26)	19 (27)	18 (25)	24 (30)	20 (25)	12 (20) <sup>ns</sup>	19 (26)	40 (31)**	20 (27)
Speech	12 (25)	14 (29)	13 (28)	11 (25)	15 (27)	7 (17)	12 (25)	29 (36) <sup>**</sup>	13 (26)
Trouble swallowing saliva	14 (26)	9 (23)	10 (25)	17 (28)	13 (25)	7 (14) <sup>ns</sup>	12 (24)	25 (37) <sup>ns</sup>	13 (25)

Mean score differences of at least 10 were tested for statistical significance.

ns = non-significant.

a Score range 0 to 100. Higher score represents a better quality of life or a higher level of functioning.

b Score range 0–100. Higher score represents more severe symptoms.

c Reference group in test for P value.

<sup>\*</sup> P value < 0.05.

<sup>\*\*</sup> P value < 0.01.

<sup>\*\*\*</sup> P value < 0.001.

a Score range 0–100. Higher score represents more severe symptoms.

b Reference group in test for P value.

<sup>\*</sup> P value < 0.05.

<sup>\*\*</sup> P value < 0.01.

mean score in the global QoL scale in our study group was as low as that reported by incurable oesophageal cancer patients scheduled for palliative treatment.<sup>26</sup> Another study found that patients treated with surgery had a better QoL then palliative treated patients.<sup>27</sup> Nevertheless, the low scores in our study patients stress the need to further evaluate the QoL after surgery. Among the functioning scales, scales assessing role and social functions were particularly affected among the study patients. The poor scores of these functioning scales are also likely to be closely linked with persistence of postoperative symptoms, i.e. problems with fatigue, appetite loss, diarrhoea, eating, and cough.

Among the general symptoms, the greater degree of fatigue among the study patients compared to the reference groups might be explained by a long recovery time after the extensive surgical procedure and the patients' disappointment with persisting symptoms. Appetite loss severely affected the patients, and is probably explained by the surgical reconstruction of the upper gastrointestinal tract. Problems with diarrhoea are likely to be due to the mandatory division of the vagal nerve during surgery. Dyspnoea and cough can be explained by residual pulmonary dysfunction after single lung ventilation during surgery, by the voluminous oesophageal substitute, or by pulmonary aspiration followed by gastro-oesophageal reflux. Among oesophagealspecific symptoms, the eating scale scores were particularly high, possibly due to the need for changes of the distribution, frequency, and size of their meals. Reflux is a well-known problem in this group of patients, and is due to changes in the anatomy of the gastro-oesophageal junction, including the loss of function of the lower oesophageal sphincter. Oesophageal pain might be due to gastric retention or postoperative dumping. Dysphagia was not an unexpected symptom, since the oesophageal substitute is not comparable with the normal oesophagus. Moreover, some patients may suffer from postoperative anastomotic strictures. Taste problems and dry mouth might be due to reflux.

The finding of more financial difficulties in younger patients is probably explained simply by them being of working age. One reason for the lower scores in most functioning scales in younger patients might be that it can be harder to accept the cancer diagnosis or long-standing symptoms in younger persons, who in general might live more active lives. The few patients who were not radically resected macroscopically had low scores in the functioning scales, especially for role functioning, and their speech problems might be explained by paresis of the laryngeal recurrent nerve due to tumour overgrowth. These data argue against palliative oesophagectomy, and stress the need for selection of patients to surgery who are of a chance of cure.

To facilitate preventive actions and early interventions, it might be important to provide thorough information about problems that may occur. Well-informed patients may cope with their postoperative problems more readily. For example, it can be difficult for a patient to understand that diarrhoea can be connected with the oesophageal resection. For support and to facilitate early interventions, the patients might benefit from contact with a specialist nurse during the care pathway. Furthermore, regular contact with an experienced dietician would seem of particular relevance to reduce

eating and dysphagia problems. Use of percutaneous endoscopic gastrostomy or nutritional jejunal catheter could further improve the nutritional status. Postoperative dysphagia, which is often feared by the patients to be due to a recurrent cancer, is most likely caused by anastomotic stricture, and is usually readily treated by endoscopic dilatation. Reflux and its entailing respiratory problems might be prevented by a modified fundoplication during surgery,<sup>28</sup> or by using acidreducing medications. Pre- and postoperative respiratory training by a physiotherapist should also be beneficial. Patients with postoperative diarrhoea can be improved by symptomatic medication. Any measures that can prevent the occurrence of postoperative complications can reduce the negative impact on QoL after oesophageal cancer surgery, and concentration of the surgical procedures to highvolume units might prevent a reduction in the postoperative QoL. 6,29 Patients should be informed of postoperative problems that often occur also since this might influence their approval to accept the surgical treatment. It is, however, encouraging that the QoL among patients who are long-term survivors seems to approach preoperative levels, 8,30 but these patients might not be representative of the entire group of surgically treated patients, in view of possible selection. Finally, minimally invasive surgery might be entailed by less postoperative problems.31

Some methodological aspects of our study deserve attention. The population-based design reduces the risk of selection bias and facilitates generalization. The number of registered patients corresponded well with the approximately 25% resection rates recently reported in Sweden, 14 indicating a good nationwide coverage. The use of questionnaires with documented good reliability and validity 11,12 is a strength of the study. Moreover, the large sample size diminished the risk of chance errors. To reduce the risk of chance findings due to multiple testing, we only tested the statistical significance when the differences in mean scores between comparison groups were at least 10, i.e., of clinical relevance. 21-25 The choice of one "stable" time window for the assessment of QoL, i.e., six months after surgery, was based on the findings in previous studies that the QoL has generally returned to a stable preoperative baseline value about six months after oesophageal surgery, indicating that acute problems after surgery have subsided.<sup>8,9,18,19</sup> Moreover, among patients who have undergone radical surgery tumour recurrence is unlikely to cause symptoms so rapidly after the operation.<sup>9,18</sup> Tumour recurrence is probably the single strongest factor that negatively influences QoL,9 a notion that is further supported by our finding of much worse problems among patients in whom the resection was not radical. Hence, assessment of QoL at later time points after surgery would be greatly influenced by tumour recurrences, and other potentially relevant factors would be impossible to evaluate.

In conclusion, most surgically treated oesophageal cancer patients still suffer severely from reduced QoL and various symptoms six months after the operation. Among functioning scales, role- and social functions were particularly reduced. The dominating general symptoms were fatigue, appetite loss, diarrhoea and dyspnoea and the most prevalent oesophageal-specific symptoms were eating problems, cough, reflux, oesophageal pain, dry mouth and dysphagia.

These findings highlight the need for preventive measures, early interventions and thorough patient selection for surgery, and future research on this topic is warranted.

#### Conflict of interest statement

There are no conflicts of interest.

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