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Associations in health-related quality of life between patients and family caregivers 1 year after oesophageal cancer surgery

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ABSTRACT

Purpose: Whether patients' health-related quality of life (HRQL) influences the HRQL of their family caregivers remains to be clarified. Therefore, the aim of this study was to investigate the association in HRQL between patients and family caregivers one year after oesophageal cancer surgery.**Methods:** The study was based on a prospective, nationwide, and population-based cohort including patients treated by surgery for oesophageal cancer in Sweden from 2013 to 2021 and their family caregivers. Data were collected one year after surgery, using the summary score of the EORTC QLQ-C30 and the RAND-36 questionnaire. Univariate and multivariate linear regression models providing regression coefficients with confidence intervals (CI) were used to estimate the association between the HRQL among patients and family caregivers. The analyses were adjusted for potential covariates.**Results:** In total, 275 patients and paired family caregivers were included in the study. Patients reported a mean HRQL summary score of 81.4, indicating reductions in functions as well as many burdensome symptoms. Among family caregivers, lowest HRQL scores were reported for pain (69.2 ± 26.0) and energy/fatigue (65.1 ± 20.4). A 10-point change in the patients' summary score corresponded to a 7-point change for family caregivers' emotional role function ($\beta = 7.0$; 95% CI: 3.6–10.3). For other HRQL dimensions among the family caregivers, no clinically relevant associations with patients HRQL were found.**Conclusion:** The current study indicates that family caregivers' emotional role function is influenced by patients' overall HRQL one year after surgery. The finding suggests that follow-up interventions should include not only patients but also their family caregivers.

1. Introduction

Oesophageal cancer has a poor prognosis with a 5-year survival rate of 30–55% for patients treated with curative intention (neoadjuvant chemoradiotherapy and surgery) (Lagergren et al., 2017). The surgery is extensive and often entails several side effects that have a negative impact on a patient's health-related quality of life (HRQL). Earlier studies indicate a reduced HRQL in a short-term (Schandl et al., 2020) and a long-term perspective (Parameswaran et al., 2010) and also when compared to a matched background population (Derogar and Lagergren, 2012; Viklund et al., 2005). Furthermore, a cancer diagnosis impacts not only the patient but also the family in different ways and they are considered a part of the cancer survivorship experience (National

Cancer Institute, 2022). A family caregiver has been defined as "any relative, partner, friend or neighbour who has a significant personal relationship with, and provides a broad range of assistance for, an older person or an adult with a chronic or disabling condition" (Family Caregiver Alliance, 2022).

There is a general agreement on that receiving a cancer diagnosis induces stress for the patients as well as for their families since they are involved in each other's coping and support processes. Cancer seems to influence the couple as a unit, rather than as isolated individuals (Hagedoorn et al., 2008; Hodges et al., 2005). Caring for a person who has undergone the extremely extensive surgery for oesophageal cancer, is burdensome and may induce psychological distress symptoms for the patient (Hellstadius et al., 2017) as well as for the family caregiver

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(Schandl et al., 2022; Graham et al., 2016), which in turn, may entail consequences on their daily living and work capacity.

Follow-up of HRQL in patients during the years after oesophageal cancer surgery is common, but data on family caregivers' HRQL are rare. To be able to help the dyadic couple, it would be value to know if patients' HRQL measurements could be used to predict the HRQL of family caregivers. Therefore, the aim of this study was to clarify whether overall HRQL among oesophageal cancer survivors is associated with different aspects of HRQL in family caregivers.

2. Material and methods

2.1. Study design

This study was based on a prospective, nationwide, and population-based cohort entitled "Oesophageal Surgery on Cancer patients – Adaptation and Recovery (OSCAR) study", which previously has been described in detail for patients (Schandl et al., 2020) and for family caregivers (Schandl et al., 2022).

2.2. Data source

In brief, all patients surgically treated for oesophageal cancer in Sweden from 2013 to 2021 and their closest family caregivers were included in the OSCAR study one year after surgery. Eligible patients were identified through an ongoing collaboration with all pathology departments in Sweden (Schandl et al., 2020).

Eligible patients were first contacted by a letter followed by a telephone call by the project coordinator. During this call, the patients were asked to identify their closest (and most suitable to participate in the study) family caregiver. A time and place, suitable for the patients (usually in their home), for a personal appointment was agreed upon. The project coordinator sent written study information together with two separate questionnaire kits to be filled in before the appointment, one by the patients and one by the family caregiver.

Patients' medical information was collected from hospitals and registries: 1) Tumour stage, histology and sub-site (histopathology reports), 2) treatment (medical records/charts, oncology records and dieticians' and nurses' documentation), 3) postoperative complications and length of hospital stay (hospital discharge notes), and 4) hospital of surgery, hospitalizations, outpatient visits and co-morbidities (from the nationwide Swedish Patient Registry).

Background data regarding the family caregivers such as marital status and occupational status were self-reported in the questionnaires. In addition, information about education level was collected from the national register Longitudinal Integrated Database for Health Insurance and labour market studies – LISA (Schandl et al., 2020).

2.3. Exposure

Patients' HRQL was assessed by using the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire. It contains 30 items incorporating 9 scales: 5 functional scales (physical, role, cognitive, emotional, and social); 3 symptom scales (fatigue, pain, and nausea and vomiting); and a global health and quality-of-life scale. Several single-item symptom measures such as diarrhoea, pain and nausea are also included. For the analysis of this study, the summary score of the QLQ-C30 was used as exposure measure. The summary score was calculated from 13 of the 15 subscales, excluding the global quality of life scale and the item about financial difficulties (Fayers et al., 2001). The summary score was transformed into a 0–100 scale. A higher score indicates a higher level of HRQL (Aaronson et al., 1993). The summary score was used as a continuous variable in the analysis.

2.4. Outcome

The outcome was family caregivers' HRQL measured using the RAND-36 questionnaire. The RAND-36 is a questionnaire intended for a generic measure of HRQL. It contains 36 items incorporating eight subscales (physical functioning, social functioning, role functioning/physical, role functioning/emotional, pain, general health, energy/fatigue, and emotional well-being). In addition, two component scores (mental and physical) were included in the analysis (Ware and Kosinski, 2001). The overall and subscale scores are transformed into a 0–100 scale. The higher scores, the higher the level of HRQL (Orwelius et al., 2018). All subscales were used as continuous variables in the analyses.

2.5. Covariates

To minimize multicollinearity in the regression model, correlations between potential confounder pairs (for patient and family) were individually tested before the main analysis. Only independent covariate pairs were considered in the final model. The considered covariates were patients' comorbidities (0, 1 or >1), tumour stage (TNM I-II or TNM III-IV) and postoperative complications (no or yes). In addition, family caregiver's disabilities (0, 1 or >1), age (continuous variable), gender (male or female) and education level (≤ 9 years or > 9 years) were included in the models.

2.6. Data analysis

Descriptive analyses were used for demographic and disease characteristics among patients and family caregivers, and presented as counts, percentages and mean scores (MS) with standard deviations (SD) where appropriate (MS \pm SD). In addition, patients' and family caregivers' HRQL scores are presented (MS \pm SD).

Univariate and multivariable linear regression were used to estimate the association between the QLQ-C30 summary score and the different RAND-36 subscale scores with adjustment for the covariates listed above and presented as regression coefficients (β) with 95% confidence intervals (CI). The unit of QLQ-C30 summary score was divided by 10 (one unit change = summary score changes by 10), and β shows the corresponding change in the RAND-36 subscale score when QLQ-C30 summary score is changed by one unit. Stratified analyses were also performed for age (< 65 or ≥ 65), gender (female or male), and educational level (≤ 9 years or > 9 years) by adding an interaction between the stratified variable and QLQ-C30 summary score. Clinical relevance was set to a difference of > 10 for the QLQ-C30 summary score and ≥ 5 for the RAND-36 (Samsa et al., 1999).

Two-sided tests with a 0.05 level of significance were used for statistical testing. Complete case analyses were carried out regarding missing data. An experienced biostatistician was responsible for the statistical analyses, and SAS® 9.4 (SAS Institute, Cary, NC, USA) software was used for all analyses.

3. Results

In total, 275 individual patients with family caregivers were included in the study. The mean age of the patients was 67 years (SD = 8.6). Most patients were male (88.7%), with a higher education level (> 9 years) (79.1%), a tumour stage of 0-II (34.6%) and at least one comorbidity (54.1%) (Table 1). (Table 2).

Among family caregivers, the mean age was 63 years (SD = 12.6), females were overrepresented (84.7%), and the majority had a higher education level (> 9 years) (85.1%) (Table 1).

3.1. Patients' and family caregivers' HRQL

The mean HRQL scores for patients and family caregivers are presented in Tables 2 and 3. The mean score of the patients' HRQL from the

Table 1

Characteristics of patients surgically treated for oesophageal cancer and their family caregivers. In total, there were 275 paired patients and family caregivers.

	Patients Number (%)	Family caregivers Number (%)
Age, years		
Mean (standard deviation)	67.2 (8.6)	62.8 (12.6)
Gender		
Female	31 (11.3)	233 (84.7)
Male	244 (88.7)	42 (15.3)
Educational level		
≤9 years	73 (26.6)	41 (14.9)
>9 years	201 (73.1)	234 (85.1)
Missing	1 (0.5)	–
Comorbidity/Number of disabilities		
0	117 (42.6)	126 (45.8)
1	94 (34.2)	83 (30.1)
≥2	64 (23.3)	66 (24.0)
Tumour stage		
0-I	95 (34.6)	–
II	81 (29.5)	–
III-IV	99 (36.0)	–
Complications		
No	95 (34.6)	–
Yes	180 (65.5)	–

Table 2

Health-related quality of life using data from QLQ-C30 among 275 patients treated for oesophageal cancer.

Outcome QLQ-C30	Mean	Standard Deviation
Summary score	81.4	13.0
Physical function	84.8	17.3
Role function	78.8	28.6
Emotional function	84.1	18.6
Cognitive function	86.1	17.5
Social function	83.3	22.6
Fatigue	30.3	22.4
Pain	17.5	23.1
Nausea	13.9	18.5
Dyspnea	28.3	28.4
Insomnia	23.1	30.5
Appetite loss	18.2	27.0
Constipation	7.5	19.3
Diarrhoea	19.8	27.7
Financial difficulties	8.7	21.6

Table 3

Health-related quality of life data using RAND-36 among 275 family caregivers of patients treated for oesophageal cancer.

Outcome RAND-36	Mean	Standard Deviation
Physical function	81.1	21.0
Social function	81.3	22.3
Physical role	73.3	37.3
Emotional role	77.5	35.9
Pain	69.2	26.0
General health	70.6	20.0
Energy/fatigue	65.1	20.4
Emotional wellbeing	75.8	18.4
Mental component scale	50.9	11.4
Physical component scale	47.8	10.3

QLQ-C30 summary score was 81.4 (SD = 13.0). In function scores, patients reported the lowest score in role function (78.8 ± 28.6). Regarding symptoms, patients reported symptom burden in almost all symptoms where fatigue (30.3 ± 24.4), dyspnea (28.3 ± 28.4) and insomnia (23.1 ± 30.5) were the most troublesome.

For family caregivers, physical function (81.1 ± 21.0) and social function (81.3 ± 22.3) were the highest scored functions, while pain

(69.2 ± 26.0) and energy/fatigue (65.1 ± 20.4) were the lowest scored subscale.

3.2. Patients' HRQL in relation to family caregivers' HRQL

Table 4 shows the association between patients' QLQ-C30 summary score and family caregivers' different HRQL aspects. A clinically relevant and statistically significant association was found only for family caregivers' RAND-36 emotional role function. A 10-point change in patients' QLQ-C30 summary score corresponded to a 7-point change for family caregivers' emotional role function score ($\beta = 7.0$; 95% CI: 3.6–10.3) (Table 4; Fig. 1). However, social function ($\beta = 4.6$; 95% CI: 2.5–6.6) and physical role ($\beta = 3.7$; 95% CI: 0.5–6.8) were on the borderline of reaching a level of clinical relevance. The other RAND-dimensions were not associated with patients' QLQ-C30 summary score.

3.3. Stratified analysis

A 10-point change in patients' QLQ-C30 summary score was clinically relevant and statistically significantly associated with a change in emotional role function especially among women ($\beta = 6.8$; CI 95%: 3.2–10.5) and highly educated individuals ($\beta = 7.4$; CI 95%: 3.9–11.0). Further, a QLQ-C30 summary score among patients of 10 points change was associated with a clinically relevant change in physical function among male family caregivers with clinical relevance ($\beta = 5.8$; CI 95%: 1.6–10.0).

4. Discussion

This population-based nationwide study of patients treated for oesophageal cancer and their family caregivers showed that the overall HRQL among patients was associated with reduced emotional role function for family caregivers.

The main strength of the current study is the population-based and nationwide study design which reduces the risk of selection bias. The inclusion of patients treated for oesophageal cancer and their family caregivers covers the whole of Sweden. The inclusion rate in the OSCAR study is considerable high, 69% among patients (Schandl et al., 2020) and of these patients, 81% included a family caregiver of which 86% participated. The nationwide design and the considerably high inclusion rate decrease the risk of selection bias and at the same time increase the generalizability of the results. In addition, the use of well-validated questionnaires in the current study counteracts misclassification bias. The QLQ-C30 is a cancer generic instrument that is widely used

Table 4

Results of the association of the exposure (oesophageal cancer patients QLQ-C30 summary score) and the outcome (family caregivers' RAND-36 scores).

Outcome RAND-36	Univariate	Multivariate**
	β (CI 95%)	β (CI 95%)
Physical function	0.4 (–1.6–2.3)	2.0 (0.3–3.6)
Social function	3.9 (1.9–6.0)	4.6 (2.5–6.6)
Physical role	1.8 (–1.6–5.3)	3.7 (0.5–6.8)
Emotional role	7.0 [#] (3.7–10.2)	7.0 [#] (3.6–10.3)
Pain	–0.2 (–2.6–2.2)	0.8 (–1.4–3.0)
General health	0.9 (–1.0–2.8)	1.6 (–0.1–3.2)
Energy/fatigue	3.5 (1.7–5.4)	3.2 (1.3–5.1)
Emotional wellbeing	2.9 (1.2–4.6)	2.9 (1.1–4.6)
Mental component scale	2.5 (1.5–3.5)	2.2 (1.2–3.3)
Physical component scale	–0.5 (–1.5–0.5)	0.2 (–0.6–1.0)

*Statistically significant: $p < 0.05$. # = clinically relevant. CI=Confidence Interval **The model is adjusted for: patient's and family caregiver's comorbidity number: 0, 1 or >1; family caregiver's age: continuous variable; family caregiver's sex: male or female; family caregiver's education level: ≤ 9 years and >9 years; the patient's tumour stage: TNM I-II and III-IV and postoperative complications: no or yes.

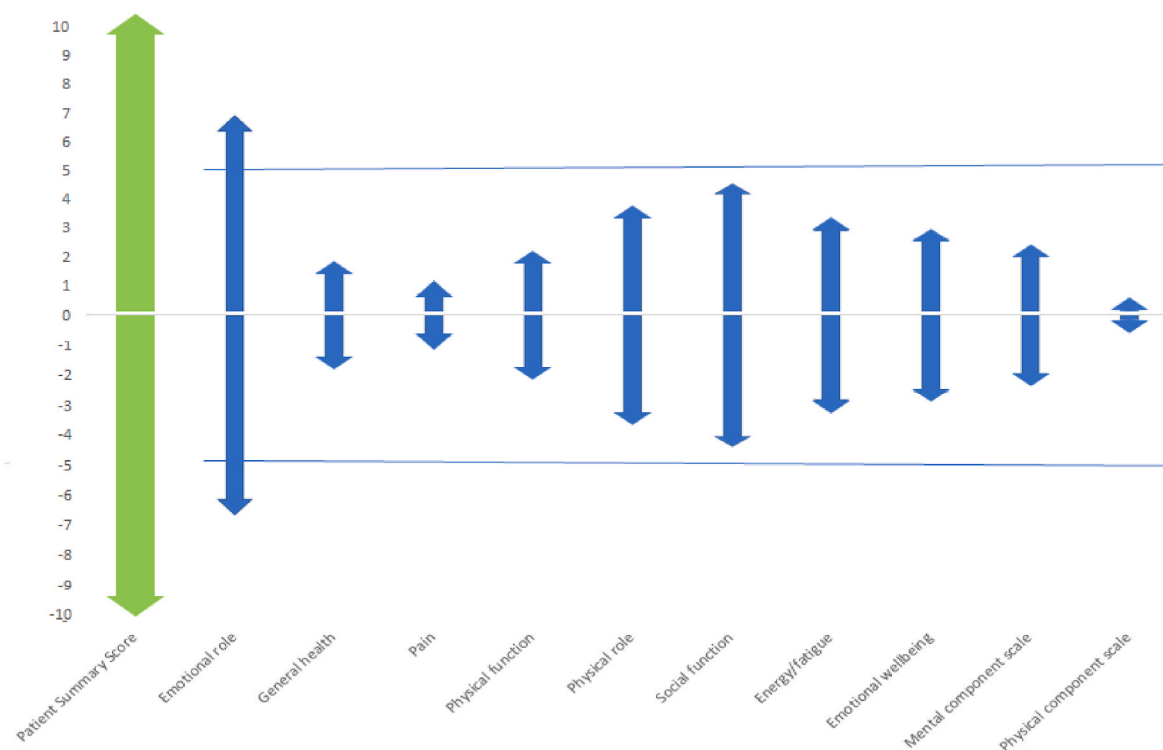


Fig. 1. Association between health-related quality of life (HRQL) in patients surgically treated for oesophageal cancer and their family caregivers. The green bar represents patients' HRQL summary score of 10. The blue bars represent the change in family caregivers' HRQL when the patients' HRQL summary score changes by 10. The horizontal line represents the clinical relevance cut off for RAND-36, changed score by ≥ 5 . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

(Aronson et al., 1993). As well as the RAND-36 questionnaire, which is one of the most used generic instruments for measuring HRQL in the world (Orwelius et al., 2018). Both QLQ-C30 and the RAND-36 have been validated in Swedish (Orwelius et al., 2018). The extensiveness of the two instruments measuring HRQL ensures the results of the current study with detailed information about associations of patients' and family caregivers' HRQL.

Even though the inclusion rate is high, the risk of selection bias still exists (Tripepi et al., 2010). There is a risk that the healthier survivors are the ones who choose to participate in a study since they are in better condition. This may contribute to an underestimation of the problem and the information about the patients with worse HRQL may be missing. In addition, when using questionnaires, the risk of response bias is present. However, the risk can be considered relatively small since the researchers who conducted the current study did not have contact with the patients or the family caregivers, so it is not likely that they have influenced their responses. In addition, the use of well-validated questionnaires also reduces the risk of response bias.

The most prominent finding of the current study is the association between patients' HRQL summary score and the family caregivers' HRQL regarding the subscale emotional role function. The association was found to be both clinically relevant and statistically significant. The mean HRQL summary score of 81.4 in patients may not seem to be alarming. However, it corresponds to a substantial reduction in almost all subscales of the QLQ-C30 compared with an age-matched normal population (Nolte et al., 2019). A similar pattern was seen for the family caregivers of the present study, in which our cohort reported lower scores in the majority of the subscales of RAND-36, in particular for emotional role (-4.9 in mean score) and social function (-4.4 in mean score) compared with scores of a normal population in similar age (Ohlsson-Nevo et al., 2021).

Emotional role function in the RAND-36 is measured by using three items in the questionnaire (Hays and Morales, 2001). The three items

assess whether a person has role limitations due to personal or emotional problems in their daily work or activities (RAND, 2022). No previous study has, to the best of our knowledge, studied the association between oesophageal cancer patients' and their family caregivers' HRQL. However, a study investigating HRQL among family caregivers to advanced cancer patients also found the highest impairments for the emotional role function (Ullrich et al., 2017). Caring for a patient treated for oesophageal cancer can inhibit family caregivers in their daily activities. In a previous study, the family caregivers of oesophageal cancer survivors experienced that they were fully in charge of the patients' care at home (Ringborg et al., 2021) and had to give up on other activities which may limit their emotional role function.

Based on the knowledge that the family caregivers' age, education level and gender are closely associated with HRQL after the patients' surgery, we choose to stratify the analyses according to these parameters (Ringborg et al., 2022). Because of the small number of family caregivers included that have a lower education level and are men, the result from stratified analysis in the current study regarding education level and gender should be interpreted cautiously.

In this study, we used a RAND-36 cut-off for clinical relevance of < 5 points (Samsa et al., 1999), to have a high cut off for our findings. However, a minimal clinical important difference between 3 and 5 points has been suggested (Samsa et al., 1999) and has also been used in studies including other diagnoses than cancer (Badhiwala et al., 2018). If we had used the lower cut-off in this study, not only emotional role function would have been clinically relevant associated with patients' HRQL, but also social function, physical role and energy/fatigue. Therefore, we suggest future studies including larger samples to be able to determine whether these are true clinically relevant associations or not.

Several studies have indicated that patients treated for oesophageal cancer have a decreased HRQL (Derogar and Lagergren, 2012; Kauppila et al., 2018; Lagergren et al., 2007; Schandl et al., 2016), however little

is known about how this is related to the HRQL of their family caregivers. There is a need to expand the research field within the HRQL perspective for family caregivers to better understand their need for support. Such data may be useful for developing a prediction tool for identifying family caregivers who are at an increased risk of a reduced HRQL. The results from the current study can contribute to the development of such a tool. Because of the QLQ-C30 being widely used and most often filled in by patients with cancer, we believe that by using the summary score we could be able to identify dimensions among family caregivers' HRQL that could be impacted.

In conclusion, the current study indicates that emotional role function in family caregivers is influenced by the overall HRQL in patients one year after surgery. The finding suggests that follow-up interventions should include not only patients but also their family caregivers. Future studies investigating HRQL among family caregivers is needed to be able to predict the risk of poor HRQL and to better understand their needs.

Data availability

The data that support the findings of this study are available from the corresponding author, [PL], upon reasonable request.

CRediT authorship contribution statement

Cecilia H Ringborg: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Project administration. **Zhao Cheng:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Asif Johar:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Supervision. **Anna Schandl:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing, Supervision. **Pernilla Lagergren:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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