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THE PERSPECTIVE OF BEING A FAMILY CAREGIVER OF A PATIENT TREATED FOR OESOPHAGEAL CANCER – PROBLEMS AND NEEDS

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THE PERSPECTIVE OF BEING A FAMILY CAREGIVER
OF A PATIENT TREATED FOR OESOPHAGEAL
CANCER – PROBLEMS AND NEEDS
THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

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POPULÄRVETENSKAPLIG SAMMANFATTNING

Matstrupscancer är en cancersjukdom med dålig prognos. Av de patienter som får matstrupscancer överlever endast 20 procent vilket gör den till den sjätte mest dödliga cancersjukdomen i världen. Det finns möjligheter till behandling med syfte att patienten ska botas. På grund av att tumören ofta upptäcks sent, är dock endast 25 procent av patienterna lämpliga för sådan behandling. Behandlingen är komplex och innefattar medicinsk behandling med cytostatika, strålterapi och avancerad kirurgi. Patienter som behandlas i botande syfte drabbas av många sidoeffekter av behandlingen. Dessa sidoeffekter gör att patienterna ofta lever med en försämrad livskvalitet både kort och lång tid efter behandling.

En cancersjukdom drabbar även närstående till patienten. Hur det är att vara närstående till patienter behandlade för matstrupscancer har vi begränsad kunskap om. Dock indikerar ett fåtal studier en ökad risk för psykisk ohälsa i form av depression och ångest hos närstående till patienter med matstrupscancer.

För att bättre förstå situationen för närstående till patienter som behandlats för matstrupscancer avhandlades två huvudsyften i fyra delstudier. Det första syftet var att undersöka närståendes erfarenheter av att vara närstående till en patient behandlad för matstrupscancer. Det andra syftet i avhandlingen var att urskilja faktorer som kan påverka närståendes livskvalitet. För att få den information som behövdes användes en svensk nationell kohort av patienter och närstående. Data som samlats in är omfattande och berör såväl medicinska som psykosociala aspekter avseende patienter och närstående.

Det framkom i studierna att närstående fortfarande två år efter patientens behandling, upplever psykosociala konsekvenser på grund av patientens diagnos och behandling. Närstående upplever sig som ansvariga för patientens vård i hemmet och upplever otillräckligt stöd från vården. De lever i en förändrad livssituation som de inte kunde förutse. Vidare har närstående mindre social samvaro med andra människor och upplever sig som ensamma.

Avseende syftet att undersöka faktorer som påverkar närståendes livskvalitet fann avhandlingen att närståendes ålder och utbildningsnivå är associerad med deras livskvalitet. Närstående med en ålder över 65 år rapporterade lägre fysisk funktion, men en högre nivå av energi jämfört med närstående under 65 år. De närstående med en högre utbildningsnivå rapporterade bättre fysisk funktion och mindre smärta. Patientens komplikationer på grund av behandling visade sig ha den absolut största påverkan på närståendes livskvalitet. Om en patient hade komplikationer rapporterade närstående bland annat lägre fysisk funktion och mer smärta. Vidare rapporteras i den sista delstudien att patienternas livskvalitet var associerad med närståendes emotionella rollfunktion, dvs om patienten sjönk i sin nivå av livskvalitet, så försämrades närståendes emotionella rollfunktion.

Sammanfattningsvis indikerar denna avhandling att närstående till patienter behandlade för matstrupscancer upplever konsekvenser av patientens diagnos och behandling. Dessa

konsekvenser påverkar närstående på ett psykosocialt plan varpå deras livskvalitet är påverkad. Fortsättningsvis behövs information om hur närstående kan få individanpassat stöd för att underlätta deras förändrade livssituation.

ABSTRACT

There is a need to put family caregivers on the cancer survivorship research agenda. Research among family caregivers of patients treated for oesophageal cancer is sparse. However, it has been indicated that they are at an increased risk of emotional distress in terms of anxiety and depression. To better understand the family caregivers' situation there were two main aims of this thesis; 1) to explore the family caregivers' experiences at one and two years after the patients' surgery (study I-II) and 2) to investigate which factors impact the family caregivers' health-related quality of life (HRQL) (study III-IV).

Study I

This qualitative study used material from a Swedish nationwide and prospective cohort including patients surgically treated for oesophageal cancer and their closest family caregivers. Family caregivers received a questionnaire-kit one year after the patients' surgical treatment. For this study, the responses to one open-ended question "Is there anything else you would like to share?" were analysed by using thematic analysis.

In total, 112 responses from family caregivers to the open-ended question were included. The analysis rendered three themes:

Discontinued support from healthcare – family caregivers had a positive experience during treatment, however, after the patients' discharge from hospital, the family caregivers felt fully responsible for the patients' care.

A changed life – this was experienced as an unprepared situation that changed life by the time of the patients' diagnosis. Family caregivers felt that they lost their identity and that nothing will ever be the same again.

Psychological distress – this was experienced as a feeling of being alone. Now, the patient was the one that mattered and the family caregivers expressed a feeling of being invisible.

Study II

This qualitative study was conducted among family caregivers of patients surgically treated for oesophageal cancer in Sweden in 2018. Thirteen telephone interviews were held in 2020, two years after the patients' surgery. An abductive approach was used for the analysis, starting with an inductive approach using thematic analysis, and thereafter, a deductive approach to interpret the findings in relation to the conceptual model "The Cancer Family Caregiving Experience".

The study found that the family caregivers suffered from many stress factors. The most prominent stress factors were distress regarding fear of tumour recurrence, worry about the future and the patients' nutritional status. Family caregivers also experienced a transition from family member to caregiver. Many psychosocial aspects in this transition were highlighted during the disease trajectory.

Study III and IV

Study III and IV used data on HRQL (RAND-36 and QLQ-C30) from a Swedish nationwide and prospective cohort of patients surgically treated for oesophageal cancer and their closest family caregivers. Factors being investigated in study III were family caregivers' characteristics (age, gender, education level) and patients related factors (tumour stage, complications, weight loss and comorbidities). In study IV, patients overall HRQL was used to find out whether it affected family caregivers' HRQL. Linear regression models were used for measuring mean score differences (MSD) in study III and the regression coefficients (β) in study IV.

In study III, 257 family caregivers were included. Family caregivers ≥ 65 years reported a lower physical function (MSD=-8.4; $p=0.001$) but a higher level of energy (MSD=9.2; $p=0.002$). Those with a higher education level had less pain (MSD=11.2; $p=0.01$) and better physical function (MSD=9.1; $p=0.006$). Regarding patient-related factors, postoperative complications were negatively associated with family caregivers' physical function (MSD=-6.0; $p=0.01$) and pain (MSD=-7.9; $p=0.01$). No associations were found for patients' tumour stage and comorbidities.

In study IV, 275 patients and paired family caregivers were included. Patients reported a mean HRQL summary score of 81.4, which indicates reductions in functions and burdensome symptoms. Lowest HRQL scores were reported among family caregivers 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). No clinically relevant associations were found for patients' HRQL and the other subscales of RAND-36.

In conclusion, these studies suggest that family caregivers of patients treated for oesophageal cancer may struggle with the psychosocial consequences of a changed situation in life which, in turn, has an impact on their psychological health and social context. Moreover, their HRQL is affected by the patient's cancer diagnosis and its treatments. It is of great importance to further investigate aspects of HRQL among family caregivers in order to predict the risk of poor HRQL. In addition, improved supportive interventions are needed for family caregivers during the whole disease trajectory of the patient.

LIST OF SCIENTIFIC PAPERS

- I. **Ringborg C, Schandl A, Wengström Y & Lagergren P. Experiences of being a family caregiver to a patient treated for oesophageal cancer – one year after surgery.**
Supportive Care in Cancer. 2021. Aug; 30:915–921.
- II. **Ringborg C, Wengström Y, Schandl A & Lagergren, P. The long-term experience of being a family caregiver of patients surgically treated for oesophageal cancer.**
Manuscript
- III. **Ringborg C, Johar A & Lagergren P. Health-related quality of life among family caregivers of oesophageal cancer survivors one year after curative intended treatment – a nationwide population-based study.**
Acta Oncologica. 2022. Jan; 61(3): 378-384.
- IV. **Ringborg C, Cheng Z, Johar A, Schandl A & Lagergren P. Associations in health-related quality of life between patients and family caregivers 1 year after oesophageal cancer surgery.**
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LIST OF ABBREVIATIONS

CI	Confidence Interval
EORTC	European Organization for Research and Treatment of Cancer
HADS	The Hospital Anxiety and Depression Scale
HRQL	Health-Related Quality of Life
MOS	Medical Outcome Study
MS	Mean Score
MSD	Mean Score Difference
OAC	Oesophageal Adenocarcinoma
OSCC	Oesophageal Squamous Cell Carcinoma
OSCAR	Oesophageal Surgery on Cancer patients – Adaptation and Recovery
SF-36	The Short Form-36 Item Survey
SD	Standard Deviation
TNM	Tumour-Nodes-Metastatic classification
QLQ-C30	Quality of Life-Core 30

1 INTRODUCTION

Oesophageal cancer has a poor prognosis and is the sixth most common cancer-related cause of death in the world. Patients with curatively intended treatment have a 5-year survival rate of 30-55%. The treatment is extensive with several side-effects that negatively impact patients' HRQL.

A cancer diagnosis also influences the patients' family caregivers. 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 caregivers of oesophageal cancer patients have been neglected in previous research and little is known about their life situation. A small number of studies indicates that family caregivers of oesophageal cancer patients have a high caregiver burden and are at increased risk of psychological distress.

To better understand the family caregivers' situation and to learn how they can be helped, this thesis aimed to evaluate perspectives and consequences of being family caregivers of patients treated for oesophageal cancer.

2 LITERATURE REVIEW

2.1 CANCER AND CANCER SURVIVORSHIP

Worldwide, cancer is one of the most increasing health issues today and continues to be a challenge for the healthcare systems (1-4). Cancer can affect individuals regardless of personal characteristics, ethnicities or sociocultural perspectives. The economic consequences are both a human and a socioeconomic challenge (5, 6). The number of cancer cases is constantly increasing worldwide. It is predicted that in Europe 4.3 million new patients will receive a cancer diagnosis by 2035 (3) and 29 million new cases are predicted by 2040 worldwide (3). However, because of improvements in early detection of the tumours and better treatment strategies, about 50% of these patients are predicted to survive (7).

The cancer issues are many and multiple actions are needed. Prevention to decrease incidence and mortality, improved diagnostics and treatments to increase cure and survival are examples of actions. Another important aspect is the increased number of survivors. Cancer survivorship starts at the time of the patients' initial cancer diagnosis and follows through their whole lifespan (8). Research is needed to identify and counteract the consequences of a cancer diagnosis and treatment regarding health-related quality of life (HRQL) and psychosocial well-being. The increasing number of survivors will affect healthcare with a higher economic burden and challenges to improve the survivorship. There is a gap between how we cure patients with cancer and how we support them to live after the treatment is completed.

2.2 OESOPHAGEAL CANCER

Oesophageal cancer is ranked the seventh most common cancer disease and is the sixth most common cancer-related cause of death worldwide (when excluding non-melanoma skin cancer and considering colon cancer and rectal cancer as one group) (9) and has been for the last couple of years (10, 11). The prognosis is poor with an overall survival of about 20% and a 5-year survival rate of 30-55% for curative intended treated patients (12).

There are two histological main types of oesophageal cancer: oesophageal squamous cell carcinoma (OSCC) and oesophageal adenocarcinoma (OAC) (13). OSCC represents almost 90% of all the oesophageal cancer cases worldwide and is most prevalent in the East. OSCC is related to lifestyle factors such as tobacco smoking and overconsumption of alcohol. OAC is more common in western countries and is related to background pathological conditions such as gastric reflux and obesity (13).

The initial symptoms of oesophageal cancer are usually dysphagia, weight loss and cough. However, when these symptoms are noticeable the progress of the tumour growth is usually in a later stage (13). The staging of oesophageal cancer is based on the Tumour-Nodes-Metastatic classification (TNM) (14). Due to the advanced tumour stage at diagnosis and poor health condition, only about 25% of patients are eligible for curative intended treatment with surgery (12).

Patients treated with a curative intention receive extensive treatment often with combined neoadjuvant chemo- and radiotherapy and advanced surgery. The most common surgical procedure is removing a large part of the oesophagus together with a part of the stomach. The remaining part of the stomach is formed as a tube and connected to the remaining part of the oesophagus. Instead of a normal stomach, the patient has a formed feeding tube, which is lacking a cardiac orifice. In addition, sometimes, the patients also receive adjuvant treatment of chemo- and radiotherapy after the surgery (12).

2.3 HRQL AMONG PATIENTS TREATED FOR OESOPHAGEAL CANCER

Due to the complex and extensive treatment, the patients treated for oesophageal cancer often suffer from several side-effects most often related to food intake. The side-effects have been shown to have an impact on patients' HRQL. It has been observed that the side-effects reduce the patients' HRQL both in a short- and a long-term perspective (15-17). Moreover, the surgical complications have been shown to have a negative impact on patients' HRQL up to 5 years after surgical treatment while the impact of medical complications on the HRQL seems to last for 10-years after surgery (18). The most common late side-effects for 10-year survivors are related to food intake and problems with gaining weight (17).

2.4 FAMILY CAREGIVERS OF PATIENTS WITH CANCER

A cancer diagnosis does not only affect the patient but also the people close to the patient and family caregivers are a part of the survivorship experience (8). Being a family caregiver is 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." (19). It has been requested to "care for the caregivers" since they are a part of the care team and deserve attention (20). Family caregivers are an important source of care for patients (21), therefore, there is a need to support them and give them the tools they need to care.

Caregiver burden has been observed in previous research regarding the situation of family caregivers of patients with cancer. The burden has been indicated to be associated with the patients' HRQL and the severances of the symptoms (22, 23). In addition, family caregivers of patients with cancer have a high prevalence of depression (24). Studies show that family caregivers often take a lot of the responsibility for the patients' care at home without any kind of education or knowledge about caring for a patient and most often with limited resources (25). However, being a healthcare professional and a family caregiver has been observed to be even more burdensome with fewer abilities to find coping strategies (26). A systematic review of how to help family caregivers of patients with cancer requested more research to be able to characterize family caregivers at high risk of burden and to explicate relationships between patients and family caregivers to be able to develop interventions (27).

Family caregivers sometimes also struggle with their own daily life activities. For family caregivers who were employees at work, it has been observed that they usually restricted their working time by arriving later and leaving earlier. Beyond that, some of the caregivers go

from working full-time to part-time or take a leave of absence while many family caregivers give up their work entirely (28). The average time for an employee caring for the cancer patient was 23.4 hours of care per week, which was significantly lower than for a family caregiver who was not an employee and had an average caring time of 42.5 hours per week. In addition, it was found that more than one-third of the employed family caregivers indicated a high financial strain (28).

Although a lower level of HRQL among family caregivers is associated more with recently diagnosed patients (29, 30), it is indicated that if they are still caring for the patient five years after the initial diagnosis they continue to experience a decreased quality of life (29).

2.5 FAMILY CAREGIVERS OF PATIENTS WITH OESOPHAGEAL CANCER

Little is known about the perspective of being a family caregiver of a patient with oesophageal cancer. Because of the lack of research, there is a substantial gap in evidence-based knowledge, in general, addressing family caregivers of patients with oesophageal cancer.

A few studies have assessed psychosocial aspects among family caregivers. Previous research on family caregivers of oesophageal cancer patients used different kinds of questionnaires that are most commonly self-assessed. One of the most commonly used measurement is The Hospital Anxiety and Depression Scale (HADS) (31-33). Also, some additional questionnaires have been used to identify different psychosocial aspects among family caregivers.

One of the most common findings from these previous studies is that family caregivers of patients with oesophageal cancer have a higher proportion of symptoms of psychological distress in terms of anxiety and depression (31, 32, 34). The level of distress and strain has shown to be comparable to the same level as for family caregivers of palliative patients (34). In addition, they have a significantly higher level of depression when measuring depression and anxiety over time (12 months from surgery) (32). A coping strategy by trying to have a positive focus was found to reduce the levels of both anxiety and depression. However, for family caregivers who had a more diversionary and relaxation strategy the level of anxiety seemed to increase (17).

A previous study found that family caregivers who experienced strain had a significant relation to a higher level of psychological distress. Also, a correlation between a high level of strain and poor mental health status was indicated (34). The proportion of family caregivers with poor mental health was considered high. Family caregivers of newly diagnosed patients had higher scores of strain and psychological distress, which indicates poor mental health, compared to family caregivers of patients diagnosed more than six months ago (34).

In the cohort study of Graham et al. (2016), they also found that fear of tumour recurrence among family caregivers was shown to be stable over time (32). However, a significant

predictor was family caregivers using interpersonal coping over time. This was associated with increased fear of recurrence over time.

In a previous study, it has been reported by more than 33% of the family caregivers of patients with oesophageal cancer that they continued to have a high caregiver burden three years after the patient's curative treatment. Factors associated with the high burden were fatigue of the patient and depression of the family caregiver (33).

There was one qualitative study conducted in Sweden that used semi-structured interviews to find out more about the experiences of family caregivers of oesophageal cancer patients. It was observed that family caregivers were not aware of the severe consequences of the diagnosis and what impact it had on the family. Family caregivers were unprepared to receive the diagnosis and they were faced with uncertainty, which affected their everyday life (35).

Previous studies are asking for further research to find interventions to improve the family caregivers' health and wellbeing, but what kind of interventions is not discussed in detail (31-33). In addition, large sample sized studies are required to have more statistical power to draw sound scientific conclusions (34).

2.6 WHAT IS HRQL?

Quality of life as a concept has different meanings to different people and is dependent on which context it is being applied. To distinguish between a "normal" quality of life and a clinical quality of life used in medical research, the term HRQL is frequently used (36). There is a large number of different instruments used to assess HRQL and many of them are patient-reported outcomes or person-reported outcomes (PROs). These questionnaires are self-assessed (36). In this thesis, one generic and one generic cancer-specific questionnaire were used.

2.7 HRQL MEASURES

2.7.1 RAND-36

One of the most frequent and probably the most used questionnaire worldwide to measure HRQL is the RAND-36 Item Health Survey (37, 38). The RAND-36 is identical to the Short Form-36 Item Survey (SF-36) (39). However, the RAND-36 is a public domain form of questionnaire and SF-36 is a copyrighted and commercially distributed one (40).

The RAND-36 is a generic HRQL instrument. So, unlike a disease-specific instrument, a generic instrument can be used in any context by anyone. The RAND-36's items were originally collected from a large study called the Medical Outcome Study (MOS), which resulted in a large pool of items (37).

The RAND-36 contains eight subscales: physical function, role functioning – physical, role functioning – emotional, social functioning, emotional well-being, energy/fatigue, pain and

general health. The questionnaire takes about 7-10 minutes to fill in. The responses to the items are scored from 0-100. A higher score indicates a better HRQL (24).

The RAND-36 has been translated into Swedish and validated across the general population in Sweden (41). This was a four-year project conducted at the same time in 15 different countries and languages where construct validity was examined. The construct validity aims to examine the theoretical relationship of the items to each other and to the subscale they belong to, in other words, the degree to which an instrument measures the construct that it was designed to measure. Construct validity is one of the most important characteristics of a measurement instrument (36). Sullivan et.al (1995) concluded that the construct validity of the questionnaire was consistently high in subgroups and scales (41).

Reliability is determining that a measurement or instrument is reproducible and gives consistent results. There are two types of reliability: repeatability reliability (correlation between repeated measurements) and internal reliability (item-to-item correlations in multi-item scales (36). Responsiveness is a measure of the instrument's sensitivity to see changes in, for example, patients' improvements or deterioration in their disease (36).

A study testing the repeatability reliability by using test-retest in a patient population in Sweden concluded with evidence supporting the reliability and responsiveness of the translated RAND-36 (40). However, it was considered good in detecting changes except from two subscales, especially general health. Earlier studies have also observed this poor responsiveness in general health. It has been discussed whether three of the items in this scale have difficulties with the sensitivity in determining change during a shorter time period (33).

In conclusion, the RAND-36 is a validated and reliability tested instrument that is used when measuring self-assessed HRQL. It is frequently used worldwide and has been translated and tested on the general population in Sweden.

2.7.2 EORTC QLQ-C30

European Organisation for Research and Treatment of Cancer (EORTC) started in 1986 as a research project to develop a questionnaire to assess the HRQL of patients with a cancer diagnosis. There was a lack of instruments that could be used to analyse if different types of interventions within cancer clinical trials affected the HRQL in different ways (42). The development of the instrument took about a year to be completed. The QLQ-C30 has a total of 30 questions and contains nine multi-item scales. Five of the scales are assessing the patient's functioning (physical, role, emotional, social and cognitive functioning). Three scales are related to the patient's symptoms (fatigue, pain and nausea/vomiting). There is one question assessing health and one quality of life scale. The remaining questions are cancer-specific, measuring different symptoms. They assess, for example, the patient's appetite, dyspnoea and constipation. The questionnaire has been well accepted by patients and takes about 11-12 minutes for completion (42). Today the instrument is available in more than 80 different languages (43).

2.8 RATIONALE

Overall, cancer is a growing problem worldwide that will increasingly affect more people. To be able to help the patients and to improve their survivorship we need to have a holistic perspective of the patients including the people close to them. The extensive treatment of oesophageal cancer has several short- and long-term side-effects that impact patients' HRQL. Since family caregivers are a part of the survivorship experience, it is a need to understand how patients' diagnosis and treatment affect them and explore the family caregivers' perspective of their situation. Such information is of importance in order to improve the situation for family caregivers and potentially thereby the HRQL and survivorship of patients with oesophageal cancer.

3 RESEARCH AIMS

The overarching aim of the thesis was to evaluate perspectives and consequences of being a family caregiver of a patient treated for oesophageal cancer.

The aim of each study within the thesis:

- To explore the experiences of family caregivers of patients treated for oesophageal cancer one year after treatment (study I).
- To explore the experiences of family caregivers of patients treated for oesophageal cancer two years after treatment (study II).
- To investigate factors that might influence the HRQL of the family caregivers of oesophageal cancer patients one year after surgery (study III).
- To investigate the association in HRQL between patients and family caregivers one year after oesophageal cancer surgery (study IV).

4 MATERIALS AND METHODS

4.1 OVERVIEW OF THE STUDIES

Table 1. An overview of the two qualitative studies within the thesis.

	Study I	Study II
Design	Qualitative study using one open-ended question	Qualitative study using telephone interviews
Participants	Family caregivers in the OSCAR study	Family caregivers in the OSCAR study
Time after surgery	1-year after patients' surgery	2-years after patients' surgery
Approach	Inductive approach	Abductive approach
Analysis	Thematic analysis	-Thematic analysis -Conceptual model

Table 2. An overview of the two quantitative studies within the thesis.

	Study III		Study IV	
Design	Cohort study		Cohort study	
Data Source	OSCAR – 1-year after treatment		OSCAR – 1-year after treatment	
Population	Family caregivers of oesophageal cancer		Patients treated for oesophageal cancer and their family caregivers	
Exposure	-Family caregivers' age, sex, education level - Patients' tumour stage, postoperative complications, weight loss and comorbidities		-Patients' HRQL	
Outcome	Family caregivers' HRQL		Family caregivers' HRQL	
Covariates	<i>Family related:</i> -Age -Sex -Education level	<i>Patient related:</i> -Tumour stage -Surgical complications -Weight loss -Comorbidities	<i>Family related:</i> -Age -Sex -Education level -Comorbidities	<i>Patient related:</i> -Comorbidities -Tumour stage -Postoperative complications
Statistical analysis	Multivariable linear regression models		Univariate and multivariable linear regression	

4.2 DATA SOURCE – THE OSCAR STUDY

Data used in the thesis were collected from a prospective, population-based nationwide cohort study entitled Oesophageal Surgery on Cancer patients – Adaptation and Recovery (OSCAR). The data collection started in 2014 and inclusion was closed in June 2020. Patients operated on for oesophageal or gastroesophageal junction cancer in Sweden were included one year postoperatively. The patients were then followed-up up to 12 years after surgery. Eligible patients were identified through collaboration with all pathology departments in Sweden. Patients' data collected were assessing different psychosocial and disease-specific aspects through self-reported questionnaires, medical aspects in medical records as well as sociodemographic data from registries (16). The questionnaire used in this thesis is regarding the patients' HRQL (QLQ-C30).

In addition, one family caregiver per patient was included. The patient decided if to include a family caregiver and suggested which family caregiver he/she thought was most appropriate to be included in the cohort. The project coordinator sent out a written consent to the family caregiver that they could choose to participate or not. In addition, the family caregiver that chose to participate was included in the present study one year after the patient's surgery. Thereafter they were/are followed up at 1.5, 2, 2.5, 3, 4 and 5 years postoperatively.

Details about the data collection can be found in a separate study (44). In brief, all family caregivers participating in OSCAR are required to fill in a self-report questionnaire-kit containing several well-validated measurements together with some study-specific questions (for example marital status, relationship to the patient, working or retired etc.). In addition, the cohort is linked to the Swedish national register; Longitudinal Integrated database for Health Insurance and Labour Market studies – LISA (45) where information about the family caregivers' education level was collected.

The last open-ended question in the questionnaire-kit was used in study I and an additional interview was conducted for study II among family caregivers included in OSCAR. The questionnaire used for assessing HRQL of the family caregivers' was the RAND-36 (study III and IV).

4.3 THE CANCER FAMILY CAREGIVING EXPERIENCE

In 2000 a model for research “*The Family Caregiver of the Older Cancer Patient*” was developed (46). The model was amplified from other models assessing the experience of caregivers and specified for family caregivers of patients with cancer. Further from this model, a more expanded model was launched in 2012: “*The Cancer Family Caregiving Experience*” (47). The model includes three main elements: the stress process, contextual factors and the cancer trajectory. Within the stress process, five different stress factors are included 1) Primary stressors, 2) Secondary stressors, 3) Appraisal and 4) Cognitive-Behavioural responses and 5) Health and Wellbeing. Regarding the contextual factors, the family caregivers' personal, sociocultural, economic and healthcare status is taken into consideration. The disease trajectory starts at the time of the patient's diagnosis and continues

until bereavement or cancer-free survivorship (47). The conceptual model was used in one of the studies (study II) in this thesis.

4.4 STUDY DESIGN

4.4.1 Study I

4.4.1.1 Design

A qualitative study using open-ended questions from the OSCAR questionnaire-kit.

4.4.1.2 Material

For study I, the responses to the last question in the one-year questionnaire-kit was used. The question was: “*Is there anything else you would like to share?*”. All handwritten responses were scanned, transcribed and analysed by conducting thematic analysis (48). By adding a reflective approach to the thematic analysis it was possible to go back to the text, changing codes and themes reflectively during the analysis process (49). The analysis was conducted by two researchers separately. Any disagreement was discussed until the most appropriate consensus was reached. The results were then triangulated and discussed with the Surgical care science patient research partnership group within OSCAR to make sure that the results reflected the family caregivers’ experiences. The patient research partnership group included both patients surgically treated for oesophageal cancer and family caregivers (50).

4.4.2 Study II

4.4.2.1 Design

A qualitative interview study using an abductive analysis approach.

4.4.2.2 Material

For study II, an in-depth telephone interview was conducted among family caregivers in OSCAR. For this study, all family caregivers included in 2019 (patients operated in 2018) were asked to participate in a telephone interview two years after the patients’ initial surgery. In total, 13 out of 38 family caregivers accepted to participate in the study. All interviews were performed by the doctoral candidate (CR). The telephone interviews were recorded and transcribed verbatim.

The text was then, in the first step, analysed using inductive thematic analysis (48). After the first analysis, the second part of the analysis was deductive, and *the Cancer Family Caregiving Experience* model was applied as an interpretative theory (47). The conceptual model was used to give a wide perspective of the experience of the family caregivers.

4.4.3 Study III

4.4.3.1 Design

A cross-sectional study within a prospective, population-based nationwide cohort study including family caregivers of oesophageal cancer patients.

4.4.3.2 Data, exposures and outcome

For study III, all eligible family caregivers in OSCAR 2014-2018 were included. The data from the one-year questionnaire-kit were used. Two groups of exposures were used; 1) family caregiver-related exposures and 2) patient-related exposures. The exposures related to family caregivers were age (<65 and ≥ 65), sex (female and male) and education level (≤ 9 years and >9 years). Exposures related to patients were tumour stage (TNM I-II and TNM III-IV), 24 different postoperative complications (including, for example, pulmonary and coronary complications, infections and anastomotic leakages) (0 and ≥ 1), weight loss (<10% and $\geq 10\%$) and comorbidities included in the Charlson comorbidity index (51).

The outcome was the family caregivers' HRQL by using the responses from the RAND-36. All dimensions were presented as well as two summary scores. One for physical health and one for mental health.

4.4.3.3 Statistical analysis

Multivariable linear regression models were used to assess the associations between exposures and the outcome (HRQL). Mean score difference (MSD) with 95% confidence intervals (CI) were calculated. Adjustments were made for the following covariates: (age: continuous; sex: male and female; education level: ≤ 9 years and >9 years; the patient's tumour stage: TNM I-II and III-IV; surgical complications: (0 or ≥ 1); weight loss: (<10% or $\geq 10\%$); and comorbidities (0 or ≥ 1)). Two summary scores for physical health and mental health were calculated by standardising the RAND-36 scales by a z-score transformation (using means and standard deviations (SD) from the general U.S. population) (52). In addition, a sensitivity analysis was conducted on partners only following the same modelling approach as the main analysis.

Based on previous research, clinical relevance was considered when a mean score difference was ≥ 5 (53).

4.4.4 Study IV

4.4.4.1 Design

A cross-sectional study within a prospective, population-based nationwide cohort study including patients surgically treated for oesophageal cancer and their closest family caregivers.

4.4.4.2 *Data, exposures and outcome*

Data from the one-year follow-up in OSCAR 2014-2020 were used for patients and family caregivers. Patients' HRQL was assessed by using the summary score of the QLQ-C30 questionnaire (54). The outcome was family caregivers' HRQL measured by using the RAND-36 questionnaire. All subscales were used as continuous variables in the analysis, including two summary scores.

4.4.4.3 *Statistical analysis*

Descriptive analyses were used for demographic, disease characteristics and HRQL among patients and family caregivers, and presented as counts, percentages and means with standard deviations where appropriate.

Univariate and multivariable linear regression was used to estimate the association between the QLQ-C30 and the RAND-36. Adjustments were made for potential covariates: patients' tumour stage (TNM I-II or TNM III-IV), patients' comorbidities (0, 1 or >1), and patients' postoperative complications (no or yes). Also, family caregivers' age (continuous variable), sex (male or female), education level (≤ 9 years or >9 years) and diagnosis (0, 1 or >1), were included as covariates.

The QLQ-C30 scores were standardized by dividing the score by 10, and β indicating the change of the RAND-36 scores when the QLQ-C30 score changed by one unit (corresponding to a clinically relevant score change of 10 (55)). For RAND-36, a score change of ≥ 5 was considered clinically relevant (53).

The analyses were also stratified for family caregivers' age (<65 or ≥ 65), sex (female or male), and education level (≤ 9 years or >9 years).

4.4.5 Ethical considerations

All material used within this thesis was from the OSCAR study. OSCAR was ethically approved by the Regional Ethical Review Board in Stockholm before the data collection started. All participants in OSCAR were informed that participation was voluntary and that the research was not connected to their medical treatment. All the participants were provided with oral and written information about the study and have signed written consents. In addition, participants were informed about their right to withdraw participation at any time, without giving a reason.

All participants were given a participation number when approving participation. The number is used to make sure that no personal data are available for unauthorised. Further, all data are stored in a safe server and is only available for a limited number of researchers within the research group, working with OSCAR.

Interviews were used to get a narrative approach of the OSCAR data. When conducting interviews with humans, memories that are brought up that can sometimes be difficult to handle for the person being interviewed. Regarding the interviews in this thesis, it was important to make sure that the person being interviewed was not emotionally affected in a negative way when ending the interview. To make sure that the participants were doing well, the interviewer always ended the conversations with some regular chat, before ending the call. However, the experience of the interviewer (CR) was that the family caregivers wanted to talk and describe their situation.

In OSCAR, information about being a patient with oesophageal cancer or a close family caregiver was reported. The information can contribute to improvements in treatment and the care program for future patients diagnosed with oesophageal cancer. In addition, family caregivers' data can highlight their perspective and can be used for developing support from healthcare for future family caregivers.

5 RESULTS

5.1 STUDY I

From a total of 238 questionnaires, 112 family caregivers had responded to the open-ended question. These 112 answers were included in the analysis. The mean age of the family caregivers who had answered the question was 62 years, 87% of them were women and 75% were partners to the patients. The other family caregivers were children (11%) or friends, siblings or had another relationship with the patient (14%).

The thematic analysis resulted in three themes describing the experiences that the family caregivers had had during the first year of the patients' cancer trajectory. The themes are presented in Table 3. The first theme was "*Discontinued support from healthcare*". The theme was experienced and expressed as having full support from the healthcare during the patients' diagnosis and treatment. However, after the patients discharge from hospital and back at home, the family caregivers felt left alone with their duty to care for the patient. In addition, when they had questions or when the patients were struggling with complications, the family caregivers felt like they had no one to turn to for help.

The second theme was "*A changed life situation*" and reflected upon family caregivers' experiences of their new life living with the aftermaths of the patients' disease and treatment. The family caregivers described that this was a new life situation that they did not expect to have after the patients' treatment. They felt unprepared for the changes in becoming a caregiver. One prominent change for the family caregivers was the loss of social interaction due to the patients' fatigue and problems with food intake. Some family caregivers requested more information from the healthcare professionals before the surgery about the risk of complications and postoperative side-effects. They thought that if they would have been more informed, they could have been better prepared for this change of life situation.

The third theme in the analysis was "*Psychological distress*". Caring for a patient treated for oesophageal cancer was experienced as being stressful for the family caregivers. The most prominent worry regarding the patients' diagnosis was the risk of tumour recurrence. The fear led to anxiety and sometimes resulted in sleeping problems. Also, a feeling of guilt was expressed for not being good enough when caring for the patient. A feeling of loneliness was another psychological straining feeling that the family caregivers had. It was expressed as a feeling that no one could understand how the family caregivers were doing and what they were struggling with. However, thinking positive was one way to handle the situation and be able to continue with life.

Table 3. Results of study I, aiming to explore family caregivers' experiences of caring for a patient surgically treated for oesophageal cancer (themes and a brief description).

<i>Discontinued support from healthcare</i>	<i>A changed life situation</i>	<i>Psychological distress</i>
<ul style="list-style-type: none"> -Good support during the hospital stay -Left alone after hospital discharge -Lack of information and no one to ask for help 	<ul style="list-style-type: none"> -Less social interactions -Food in focus -Transformation to caregiver 	<ul style="list-style-type: none"> -Fear of recurrence -Feeling of guilt -Developing strategies

5.2 STUDY II

In total 13 out of 38 family caregivers accepted to participate in the interview study. Of the 13 participants, 10 were females, the majority were spouses (n=12) and one was a good friend. The mean age was 71 years.

Primary stressors

Family caregivers had *primary stressors* that were connected to *patient-related illness factor, fear of tumour recurrence and treatment symptoms and side-effects*. Being worried that the patient might get the disease back and struggling with worry during the medical examinations in the hospitals was expressed as stressful for the family caregiver. The fear of tumour recurrence was still constant two years after the patients' treatment. Also, symptoms and side-effects due to treatment were something the family caregiver needed to handle in their everyday life. Most prominent for these family caregivers was the patients' malnutrition because of the extensive surgery that the patients had gone through. The family caregivers felt they needed to guard the patients and force them to eat to make sure they would not lose weight. *The care demands from the diagnosis into survivorship* was partly to arrange all the hospital visits for the patients and, additionally, to communicate with different hospital settings. It was demanding for the family caregivers and they wished for a better discussion between healthcare providers and family, especially between the contact nurse and the family caregiver.

Secondary stressors

Secondary stressors among the family caregivers were regarding *schedule and lifestyle impact on roles in our relationship - from family member to caregiver*. The theme described the family caregivers' experiences of going into a phase of shock at the time of diagnosis and the transformation to the new normal life. Other themes within the secondary stressors were *Changing roles and relationships*, *Impact on employment and finances* and *Self-concept – new perspectives*. These themes were experienced by having a hundred per cent focus on the patient through the whole cancer trajectory but having a short amount of time to be able to handle daily activities such as work and taking care of the patient. Further, the family caregivers landed in their new normal, during the time of surveillance.

Considering **appraisal** in the conceptual model, family caregivers experienced both positive and negative aspects of caring for a patient treated for oesophageal cancer. *Burden and distress – uncertainty about the future*, *Rewards and benefits – re-prioritization of what is important in life* and *Needs – letting your guard down* were three themes describing the family caregivers' experiences, their strong fear of uncertainty if the tumour might come back and the fear of losing the patient. However, also experiences of benefits, that the disease made the patient and the family caregiver even closer in their relationship. Support from friends and family was a strongly described need.

Cognitive-behavioural responses included three themes in the analysis. *Planning ahead – the new normal*, *Self-care and caregivers' behaviours – need to focus on own needs* and *Coping – using different strategies*. Even though the family caregivers feared the risk of recurrence, they felt they needed to plan ahead in their "new normal" and they needed to go with the flow. To relieve the worry, talking to others helped the family caregivers. Few of the family caregivers had been offered support from the healthcare. Finding ways to cope when giving up is not an option was another helping factor. To stay positive and be as prepared as possible was two described coping strategies.

The last part of the stress process in the model is **health and wellbeing**. The theme in our analysis was *Worry about the future*. Two major concerns bothered the family caregivers. Firstly, as mentioned previously, the fear of recurrence was always in their mind. The second concern was about the patients' food intake. Patients' malnutrition was expressed as being very stressful for the family caregivers. In addition, worry about patients' physical health was bothering them; however, their own health was not in focus.

The results of the stress process are presented in Figure 1.

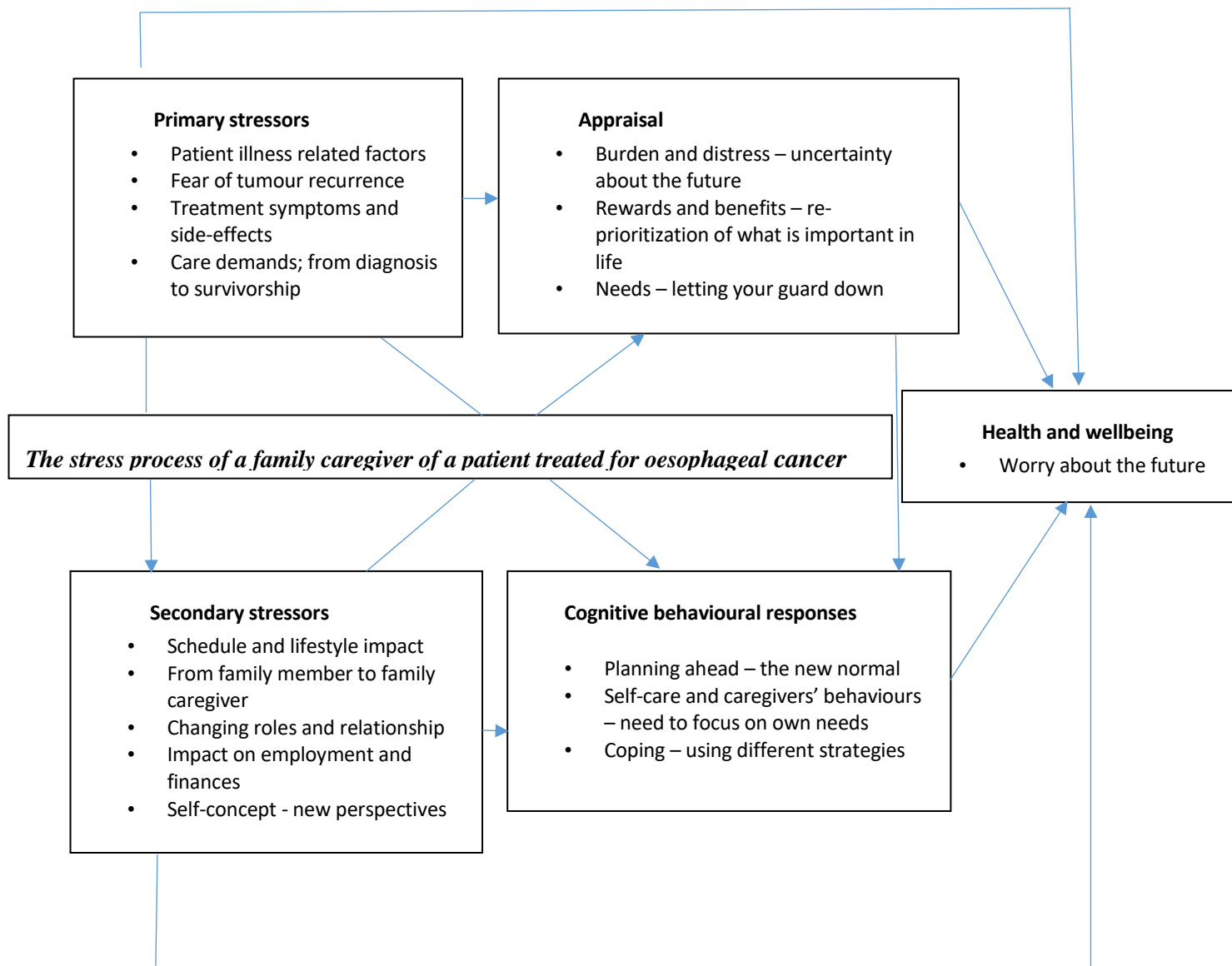


Figure 1. Illustration of the interpretation of the stress process of family caregivers of patients treated for oesophageal cancer by using the stress process in the Cancer Family Caregiving experience by Fletcher et al. (2012).

5.3 STUDY III AND STUDY IV – DESCRIPTIVES

Table 4. Characteristics of patients included in study III and IV.

	Study III		Study IV	
	Family caregivers	Family caregivers	Patients	
Age				
Mean ± Standard deviation	62.6 ± 12.5	62.8 ± 12.6	67.2 ± 8.6	
Sex				
Female	216 (84)	233 (85)	31 (11)	
Male	41 (16)	42 (15)	244 (89)	
Education level				
≤ 9 year	37 (14)	41 (15)	73 (27)	
>9 year	220 (86)	234 (85)	201 (73)	
Relation to patient				
Partner	208 (81)			
Children	22 (9)			
Others	27 (10)			
Tumour stage				
0-I			95 (35)	
II			81 (29)	
III-IV			99 (36)	
Diagnosis/Comorbidity				
0			126 (46)	117 (43)
1			83 (30)	94 (34)
≥2			66 (24)	64 (23)
Complications				
Yes			95 (35)	
No			180 (65)	

All values are numbers (%) unless otherwise stated.

5.4 STUDY III

In total 257 family caregivers were eligible and included in the study. The mean age of the group was 63 years. The majority of the family caregivers were women (84%) and had more than 9 years of education (86%). Most of the family caregivers were partners of the patients (81%), 9% were children and about 10% were either a friend or a neighbour.

Family caregivers' HRQL and demographic factors

Table 5 shows the results of the family caregivers' exposures. Older family caregivers reported a clinically relevant and statistically significant lower physical function (MSD=-8.4; p=0.001) and a higher energy level (MSD=9.2; p=0.002) compared to younger family caregivers. In addition, older family caregivers had a clinically relevant better emotional role functioning (MSD=6.3).

Female caregivers reported a clinically relevant better emotional role functioning compared to men (MSD=5.6).

Family caregivers with a lower education level reported clinically relevant and statistically significantly more pain (MSD=11.2; p=0.01) compared to those with a higher education level. The higher education group reported clinically relevant and statistically significantly better physical function (MSD=9.1; p=0.006) and a clinically relevant better physical role functioning (MSD=5.6) than the family caregivers with lower education.

Table 5. Clinically relevant results of the **family caregivers' exposures** impact on family caregivers' health-related quality of life of patients treated for oesophageal cancer using the RAND-36 questionnaire.

Family caregivers' exposures	Mean Score Difference (95% CI)
Age ≥65	
Physical function	-8.4 [#] (-13.4 to -3.4)*
Role functioning – emotional	6.3 [#] (-4.0 to 16.7)
Energy	9.2 [#] (3.5 to 14.9)*
Sex - Female	
Role functioning – emotional	5.6 [#] (-7.8 to 18.9)
Education level >9 years	
Physical function	9.1 [#] (2.6 to 15.7)*
Role function – physical	5.6 [#] (-7.5 to 18.7)
Pain	11.2 [#] (2.3 to 20.1)*

*Statistically significant: p<0.05. CI: Confidence interval. # = clinically relevant. **The model is adjusted for: age: continuous; sex: male and female; education level: ≤ 9 years and >9 years; the patient's tumour stage: TNM I-II and III-IV; surgical complications: (0 or ≥1); weight loss: (<10% or ≥10%); and comorbidities (0 or ≥1).

Family caregivers' HRQL and patient-related factors

If patients had one or more than one complication, family caregivers' HRQL was clinically relevant and statistically significantly poorer regarding physical function (MSD=-6.0; p=0.01) and pain (MSD=-7.9; p=0.01) compared to family caregivers of patients not experiencing complications. In addition, family caregivers of patients with one or more than one complication had clinically relevant poorer physical role functioning (MSD=-6.0), social function (MSD=-5.9) and more pain (MSD=-5.0).

Table 6. Results of the **patient-related exposures'** impact on family caregivers' health-related quality of life of patients treated for oesophageal cancer using the RAND-36 questionnaire.

Patients' exposures	Mean Score Difference (95% CI)
Complications ≥ 1	
Physical function	-6.0 [#] (-10.7 to -1.4)*
Role functioning – physical	-6.0 [#] (-15.3 to 3.3)
Social function	-5.9 [#] (-12.0 to 0.3)
Pain	-7.9 [#] (-14.2 to -1.6)*
Weight loss $\geq 10\%$	
Pain	-5.0 [#] (-11.6 to 1.6)

*Statistically significant: p<0.05. CI: Confidence interval. # = clinically relevant. **The model is adjusted for: age: continuous; sex: male and female; education level: ≤ 9 years and >9 years; the patient's tumour stage: TNM I-II and III-IV; surgical complications: (0 or ≥ 1); weight loss: (<10% or $\geq 10\%$); and comorbidities (0 or ≥ 1).

Sensitivity analysis

The sensitivity analysis on the subgroups of partners showed similar results to the results from the main analysis, except for education level losing statistical significance for physical function (MSD=9.1, p>0.05) and pain (MSD=8.8, p>0.05) and clinical relevance for role function-physical (MSD=2.7, p>0.05). Complications became more clinically relevant for all previous clinically relevant findings and statistically significant for role functioning-physical (p<0.05).

5.5 STUDY IV

In total, 275 individual patients with family caregivers were included in the study. The mean age of patients was 67 years. Most patients were males (89%), with a higher education (79%), a tumour stage of 0-II (35%) and at least one comorbidity (54%).

Among family caregivers, the mean age was 63 years, females were overrepresented (85%), and the majority had a higher education level (85%).

Patients' and family caregivers' HRQL

The mean score of the patients' HRQL from the QLQ-C30 summary score was 81.4 \pm 13.0. Patients reported the lowest function score in role function (78.8 \pm 28.6). For symptoms

scores, patients reported symptom burden in almost all symptoms. Fatigue (30.3±24.4), dyspnoea (28.3±28.4) and insomnia (23.1±30.5) were the most troublesome symptoms.

Among family caregivers, physical function (81.1±21.0) and social function (81.3±22.3) were the highest scored subscales, while pain (69.2±26.0) and energy/fatigue (65.1±20.4) were the lowest scored subscales.

Patients’ HRQL in relation to family caregivers’ HRQL

A clinically relevant and statistically significant association was found between patients’ HRQL summary score and family caregivers’ emotional role function assessed with the RAND-36 when using a clinically important difference of 5 points (53). A 10-point decrease in patients’ QLQ-C30 summary score corresponded to a 7-point decrease in family caregivers’ emotional role function score ($\beta = 7.0$; 95% CI: 3.6-10.3). No other RAND-36 subscales were found to be associated with patients’ QLQ-C30 summary score. Figure 2 shows an illustration of the results.

Stratified analysis

A 10-point reduction in patients’ QLQ-C30 summary score was associated with reduced emotional role function to a clinically relevant and statistically significant level, 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 change in QLQ-C30 summary score of 10 points was associated with clinically relevant changes in physical function among male family caregivers ($\beta = 5.8$; CI 95%: 1.6-10.0).

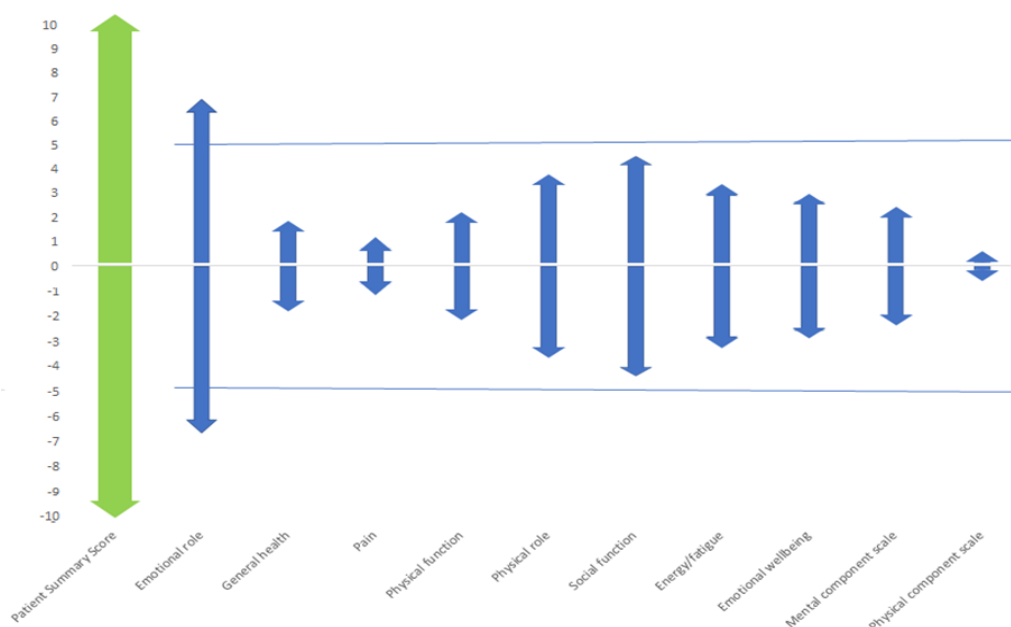


Figure 2. Association between health-related quality of life (HRQL) in patients surgically treated for oesophageal cancer and their family caregivers. The green bar represents patients’ HRQL summary score of 10. The blue bars represent the change in family caregivers’ HRQL when the patients’ HRQL summary score changes by 10. The horizontal line represents the clinical relevance cut off for RAND-36, changed score by ≥ 5 .

6 DISCUSSION

6.1 METHODOLOGICAL CONSIDERATIONS

6.1.1 Study design

Study I and study II were both qualitative studies, using two different approaches. Regarding the quality of qualitative studies, trustworthiness is essential. Trustworthiness includes; *credibility*, *dependability* and *transferability* (56). *Credibility* implicates how well the data and the analysis have been processed. *Dependability* refers to the consistency of the researchers during the data collection and the analysis. The *transferability* means to what extent the findings in a qualitative study can be transferred to other populations. This can be discussed by the researchers, however, it is up to the reader to decide whether it can be transferred or not (56). The contents of trustworthiness will be discussed for the two qualitative studies in the following discussion.

Study III and study IV are cross-sectional studies within a prospective, population-based nationwide cohort (OSCAR). Unlike the qualitative studies, the quantitative studies' quality is dependent on the *internal validity*: the ability to measure what is aimed to be measured (57); and the *external validity*: whether the findings can be applied to other populations (57). When performing research on cohorts, there are several risks of bias that need to be taken into consideration to maintain the best possible quality of the research. Both the internal and external validity will be discussed for the two quantitative studies in the following discussion.

6.1.2 Trustworthiness - the qualitative studies

6.1.2.1 Credibility

The material for study I and II was analysed by at least two researchers which decreases the risk of misinterpretation, but it is also a way to broaden the findings. The concept of having more than one researcher working on the analysis is called investigator triangulation (58). Triangulation in qualitative studies increases the credibility and by that also the trustworthiness of the study. Member-checking is an additional way to investigate the credibility of a study (59). Both studies were member-checked by our patient research partnership group. It can be described as checking if the results of a study reflect the "members" experiences. The member-checking helps to decrease the risk of misinterpretation (59).

6.1.2.2 Dependability

In study I, responses to an open-ended question from the OSCAR questionnaire-kit were used and analysed. The question was the last question in the questionnaire-kit and a response was voluntary. All the responses were transcribed verbatim into a document by one researcher.

In study II, interviews were conducted with family caregivers included in the OSCAR study. These interviews were conducted by the author of the current thesis (by the first author of the

publication). By having one researcher conducting the interviews the possibility of having consistency is facilitated.

All 13 interviews were conducted over a couple of weeks, so the risk that the circumstances would cause data to change over time and would impact the results was minimized. All the interviews were recorded and transcribed verbatim into a document by the interviewer. The interviewer also made notes during the interviews if there was something that needed to be explained or clarified.

For both studies, two researchers were main-responsible for the two analyses. However, the results were discussed and triangulated with another two researchers, which gave the opportunity to discuss the findings, both that they were consistent, but also if there were some differences in the interpretation of findings.

6.1.2.3 Transferability

Study I with 112 responses is built on quite large material (for a qualitative study) with participants across the whole of Sweden. The nationwide design enriches the variation of experiences having family caregivers of patients treated in different hospitals. Some of the findings could be considered as transferable to other family caregivers of patients with a cancer diagnosis. However, the findings regarding disease-specific and treatment side-effects are specific for patients with oesophageal cancer and might not be similar for other patient groups.

Usually, saturation is the term used in qualitative research to make sure that the number of participants is satisfying. When the analysis reaches saturation, the researcher believes that no new information will be revealed by including more participants (60). However, it has been suggested to use “information power” instead (61). Information power indicates that the more adequate information the researcher can receive from the participants, the lower number of participants is needed (61). Study II included 13 participants, however, the analysed material was extensive and covered many aspects of the experiences of family caregivers of patients treated for oesophageal cancer. Therefore, study II can be considered as having good information power. Transferability to family caregivers in the same situation could be considered. However, many aspects in the stress process could probably be similar for other family caregivers representing other tumour diseases.

Overall, the two qualitative studies have a high level of trustworthiness. However, for study I, the researchers could not ask follow-up questions if anything in the responses was unclear. That might, in some cases, lead to misinterpretations.

Regarding study II, it would have been preferable to conduct the interviews face-to-face to be able to visualise the informant so no underlying information would be lost. However, it has been discussed whether telephone interviews should be considered inferior to face-to-face interviews (62). When using a telephone for interviewing, some visual cues might be lost,

however, the participants might be more willing to tell sensitive information because of the distance to the researcher (62).

6.1.3 Internal validity – the quantitative studies

6.1.3.1 Selection bias

Selection bias occurs when there is a risk that the selected participants in a study are not representative of the studied population. The type of selection bias that can be considered in study III and study IV is the non-response bias (63).

For study III and IV with considerably large sample sizes of family caregivers in the Swedish context, the risk of non-response selection bias still exists. For example, there could be a possibility that the patients with a poor health condition declined to participate in OSCAR, which resulted in lost information about these family caregivers that might in fact have other support needs.

Another challenge for reaching generalisation is the skewed characteristics of the family caregivers participating in the study. For example, the majority of patients are men so there is a majority of female family caregivers in the OSCAR that are partners to the patients. To be able to generalise, one could wish for a more heterogenic group of family caregivers regarding sex, age, education level and their relationships to the patients.

In addition, when extracting information from medical records for study III and IV there is a risk that some factors might be underreported or misclassified (64). What has been reported in the medical records cannot be changed and adjusted for when collecting data retrospectively. However, to minimize the risk of misclassification study, a protocol was used for the data collection in the medical records. In addition, more than one researcher reviewed the medical records as a validation.

6.1.3.2 Information bias

Information bias exists when a measurement does not respond to the right value. By using well-validated instruments for measuring HRQL for both patients and family caregivers, the risk of information bias is reduced. It can be discussed whether recall bias could be introduced when using a questionnaire with retrospective questions (57). However, both the RAND-36 and QLQ-C30 have a time span of seven days, which could be considered short and easy to remember. The risk of response bias is present in the two quantitative studies. The extent number of questions that the participants fill in might be tiring and the participants might not respond to the questions accurately.

6.1.3.3 Confounding

A confounder is defined as a factor that can influence both the exposure and outcome (64). By anticipating potential confounders and adjusting for these factors, the risk of confounding is reduced. If the factors are not taken into consideration, the findings can be insufficient (64).

The adjustments for confounders in study III and IV have been rigorously considered to avoid as much confounding as possible. OSCAR includes comprehensive information about patients and family caregivers which helped the process of adjusting for confounders. However, there is a risk of residual confounding due to unmeasured confounders (65) which could have affected the results. For example, coping strategies, if the family caregivers had experience in caring or how stress resistant they are could affect the results.

6.1.4 Random errors and precision – quantitative studies

Random errors and precision are the other equivalents. Random errors refer to the overall errors that can affect the precision of the estimate. So, with larger precision and large power, the random error can be avoided to a greater extent. By hypothesis testing and using 95% CI and p-value 0.05, the risk that the results are only by chance can be rejected. Both study III and IV had good power that increases the precision. In addition, statistical significance testing was conducted for the findings to be clinically relevant. Also, CI of 95% were used to make sure that the findings were, by 95%, not by chance.

6.1.5 External validity – quantitative studies

External validity refers to what extent the findings can be generalised to populations other than the one being studied (65). The internal validity of the two quantitative studies have been discussed and can be considered as good. The sample sizes are considerably large which promotes generalisability. About 76% of all patients who received curative intended treatment during this time survived one year after surgery and 66% of them agreed to participate in OSCAR (16). Of these patients, 86% had family caregivers who were included in the cohort. However, as mentioned earlier, there is a risk that the patients who chose not to participate could be the patients in the worst condition. The prognosis of oesophageal cancer is poor and the surgical procedure is extensive and is only being performed on 25% of the patients that are eligible for curatively intended treatment (12). Therefore, the findings can only be transferred to other family caregivers of oesophageal cancer patients that have been eligible for curative intended treatment. In addition, study III and IV were conducted on data one year after the patients' surgery. Therefore, the timeframe also needs to be considered if generalising the results.

Overall, the two quantitative studies have been conducted trying to reach as exact precision as possible. Study protocol meetings have been organised for each study and study protocols have been established to make sure that the studies are well designed before analysing the data and that the research as a whole is of high quality.

6.2 GENERAL DISCUSSION

To gain more knowledge about the experience of being a family caregiver of a patient treated for oesophageal cancer, the two qualitative studies were included in the thesis. Study I, exploring the experiences one year after surgery, found that the family caregivers were satisfied with the healthcare during the patients' treatment and the care the patient received at the time immediately following surgery in the hospital. Unfortunately, after the patient was discharged from the hospital the family caregivers experienced that they carried a large responsibility for the patients and the patients' care and that they lacked support. Family caregivers felt that they had no one to turn to for information about how to treat and take care of the patient. The feeling of loneliness was expressed and more support from the healthcare to the family caregiver could have been beneficial for both the family caregivers and the patients.

In study II, two years after the patients' treatment, family caregivers still suffer from extent stress mostly connected to the care of the patients. Most of the family caregivers in the two studies stated that they had not been offered the necessary support, including psychosocial support, by healthcare.

The findings from the two studies indicate that family caregivers of patients treated for oesophageal cancer belong to a vulnerable and neglected group. The experience of insufficient support by healthcare was prominently described in the two studies. Family caregivers expressed that they had not been involved in the discussions at medical appointments and that they were on their own after the patients discharge from hospital in charge of treatment and care. The challenges of family-centred and a holistic perspective of caring for patients have been described previously and a more holistic perspective of supportive care is needed (66). Comprehensive supportive care should be patient-centred with good communication, including family members, throughout the patients' disease trajectory (67).

Fear of tumour recurrence seems to be the greatest worry the family caregivers described in both study I and II. The fear of tumour recurrence is related to the poor survival rate of oesophageal cancer. It has been suggested that family caregivers have more fear of recurrence than the patients themselves (68) and a systematic review conducted to investigate fear of tumour recurrence showed that the family caregivers experienced more fear compared to the cancer survivors (69). Fear of uncertainty in the future and that the cancer might come back has also been described in previous qualitative studies among family caregivers of patients with a cancer diagnosis (70, 71). With increasing survival, both in oesophageal cancer, but also other cancer diagnoses, the fear of tumour recurrence will be a prominent issue in the clinical setting (72) both regarding patients and family caregivers. Unmet needs among family caregivers of survivors have been shown to have a negative impact on their quality of life. The most prominent unmet need is their concern of recurrence (73). Also, adjusting to a new normal life when the patient does not need cancer care anymore, the family caregivers felt lost. To develop comprehensive supportive care in the cancer area together with family-

centred care and a more holistic perspective is essential for the development of high-quality survivorship care.

It is well known that oesophageal cancer patients suffer from a reduced HRQL due to treatment side-effects (74-76). However, whether the family caregivers' HRQL is impacted by the patients' disease and treatment has not been in focus in previous research. Results from study III showed that family caregivers' age, sex and education level were associated with their HRQL. In addition, patients' complications and patients' weight loss were associated with their family caregivers' HRQL. Patients' complications were the exposure that had the strongest association with the family caregivers' HRQL. Complications among patients are common after extensive surgery. Complications might increase the worry among family caregivers which could impact the HRQL. The patients' tumour stage and comorbidity were not associated. Having knowledge in tumour histology, one would think that an advanced tumour stage would impact family caregivers. However, all patients included in OSCAR had been selected as eligible for curatively intended treatment. Maybe, that could be seen as the most important factor for family caregivers, and therefore, the tumour stage was irrelevant. Study IV showed that a worse overall HRQL among patients was associated with reduced emotional role function for family caregivers. In addition, some of the HRQL subscales in the RAND-36 were on the border of being clinically relevant (social function, physical role and energy/fatigue).

Stress has been found to be a strong predictor of family caregivers quality of life (77). Male caregivers had a positive experience of being a caregiver, especially husbands, having less psychological distress and better mental health. While females found caregiving more stressful. The traditional role among females being more aimed to care, the men might be satisfied to take over the caring role (77). The results in study III indicated that female caregivers have a higher level of emotional role compared to men. Maybe, this could be because females traditionally have more responsibility for caring at home with daily housework. However, it would be interesting to study the psychological distress among the family caregivers included in the thesis. Females are over representative and if they experience a higher level of distress, it is necessary to find ways to support them.

It has been indicated that the HRQL among family caregivers of patients with a cancer diagnosis varies along the disease trajectory and that there is a knowledge gap on the long-term perspective after treatment (78). An American study investigating family caregivers eight years after the patients' initial diagnosis showed that they still suffer from mental and physical health problems compared to the US general population (79). There is a need to expand the research field within the HRQL perspective for family caregivers to better understand their need for support. In addition, such data can be useful in developing a prediction tool that can identify family caregivers who are at an increased risk of a reduced HRQL. The results from study III and IV can contribute to the development of such a tool. The RAND-36 does not capture caregiver burden and specific caregiver HRQL. It would be preferable with studies of more detailed outcomes regarding such aspects. In addition, due to

the long-term effect of HRQL among patients due to complications, it would be highly advisable to investigate family caregivers' burden and specific HRQL for a longer period than one year to see whether there is an association between complications and family caregivers' HRQL in the long term.

All four studies within the thesis together give a clearer picture of what it is like to be a family caregiver of a patient treated for oesophageal cancer. The stress process is extensive and innovative support by the healthcare is needed to release their burden. Further, they need psychosocial support to be able to control their fear of tumour recurrence. In addition, some factors impacting their HRQL are known.

How the family caregivers' HRQL and psychosocial factors can be improved is an important aspect to consider in the research field of cancer survivorship. One, systematic review of 15 studies from 2020 about interventions among family caregivers of patients with cancer showed that psychoeducation had a positive effect on the burden, quality of life aspects and psychological symptoms. In addition, counselling among family caregivers of advanced cancer patients or family caregivers with a high symptom burden reduced psychological symptoms and benefited their quality of life (80). However, another meta-analysis that investigated interventions among family caregivers of patients with cancer highlighted that many of the 29 studies included did not have the main intention to study the family caregivers. The studies were designed for the patients and the content regarding family caregivers was a secondary focus provided by incident or as an afterthought (81). If research among family caregivers is not conducted as the main aim and with full focus on how they can be helped, the findings might be doubtful. Several of these studies in the review and meta-analysis concluded that the family caregivers were negatively affected in psychosocial aspects which is consistent with what was also observed in the studies of this thesis. There is a need to put more focus on family caregivers' perspectives on the research agenda in order to support them.

Considering the prediction that Europe will have 4.3 million new patients with a cancer diagnosis by 2035 (3), and more than 50% of these patients are predicted to survive (7), this will increase the challenges of cancer survivorship care. To include the people that care for the patients is fundamental to improve the survivorship of these patients. Nevertheless, more research is needed into determining what interventions are effective to support family caregivers. By strengthening supportive care and including family caregivers, the survivorship of patients and the quality of life of family caregivers will increase.

7 CONCLUSIONS

- Family caregivers of long-term survivors after oesophageal cancer treatment are struggling with psychosocial consequences because of the patients' cancer diagnosis and its treatments.
- Family caregivers experience that they are responsible for the patients' care at home. They are lacking support after the patients' hospital discharge and express a need for more information from the healthcare.
- Family caregivers' HRQL is impacted by the patients' diagnosis and treatment.

8 POINTS OF PERSPECTIVE

Family caregivers of oesophageal cancer patients have an impaired life situation as shown in the current thesis. A further step in research and a clinical context is to develop, implement and evaluate supportive care interventions. The interventions should be both for patients and family caregivers aiming at a more family-centred perspective. The interventions could benefit from adaption to the disease trajectory, from diagnosis to survivorship. One suggestion could be to start with an educational program for patients and family caregivers at the time of diagnosis to make sure that all patients and family caregivers receive the correct and the same information. Another suggestion to help the family caregivers to reduce their feeling of loneliness could be an intervention with a digital forum. An application with information about the disease, treatment and how to handle side-effects but also the function to interact with others. This could be used to help the family caregivers to meet with other family caregivers. In this way, they could exchange experiences and information, but also feel an affinity in a context. Such interventions could relieve burden and stress and positively affect family caregivers' HRQL.

Additionally, it is of utmost importance to identify family caregivers at risk of psychosocial consequences affecting their HRQL by conducting research with high participation and well-validated questionnaires. Such information will benefit the development of individually based care for the family caregivers.

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