Experience of adjuvant treatment among postmenopausal women with breast cancer

Health-Related Quality of Life, symptom experience, stressful events and coping strategies

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To my family with love 'every day'

Abstract

In Sweden, breast cancer is today the most common type of cancer among women. Of the approximately 7,059 women who developed the disease in Sweden during 2006, about 73% were postmenopausal and aged 55 or older at time of diagnosis, and about 33% were aged 70 or older. Survival time for women with breast cancer has been extended due primarily to the development of new adjuvant treatments; however, these treatments may produce a wide variety of troublesome symptoms. There are limited descriptions in the literature of how Health-Related Quality of Life (HRQoL) is affected by adjuvant treatments in elderly populations. Nevertheless, it is common that in clinical practice these women are offered less aggressive treatment due to fears that the side effects may be greater for them.This thesis explores the experience of adjuvant chemotherapy (CT) and/or radiotherapy (RT) among postmenopausal women with breast cancer. More specifically, the thesis aims to examine how HRQoL develops over time, what factors predict overall HRQoL after treatment and if age is associated with HRQoL. A further aim was to describe stressful events experienced by these women and how they manage these stressful events or situations.

The participants were recruited from three centres in Sweden (Gothenburg, Stockholm and Skövde). In the first study, 150 women scheduled to receive adjuvant chemotherapy (CT, n=75) or radiotherapy (RT, n=75) were included. In the second study, 20 women with breast cancer were interviewed regarding their experiences during CT. The third and fourth studies included the same 75 women scheduled to receive adjuvant CT from the first study. Both inductive and deductive research methods were used. Data from the qualitative studies (II and IV) were analysed with content analyses (qualitative and quantitative). Data collected with quantitative methods were analysed using mainly non-parametric methods (Paper I and III).

No significant relationship was found between age and any of the HRQoL domains, except for dyspnoea and sexual functioning. Thirty percent of the diaries recorded no stressful events during adjuvant CT. Stressful events experienced during CT were more related to physical problems than to psychosocial problems. CT and RT affected many aspects of the women's HRQoL negatively. RT was associated with more localized problems, whereas CT was associated with systemic symptoms. Nausea/vomiting was one of the most stressful events reported by women undergoing CT, increased significantly during and after treatment and was also the most anticipated side effect of CT. Fatigue and depression increased over time and remained high at time of follow-up. Baseline predictors for overall QoL after CT were emotional functioning and pain, whereas overall QoL after RT was predicted by baseline emotional and physical functioning, lower tumour stage and less breast symptoms. Social support from family, friends and health care professionals was important for these women. The women employed many different coping strategies for each stressful event. Acceptance, relaxation and distraction were the most commonly used strategies.

In conclusion, CT and RT variously and seriously affect aspects of HRQoL in postmenopausal women. This indicates that the situation of these women cannot be understood as simply a function of chronological age, but as an individual process where the biological age is important. Patient care may be improved by focusing more attention on specific symptoms, notably fatigue, nausea/vomiting, and depression, and also on social and emotional functioning. Interventional studies are needed that specifically target identified pre-treatment predictors of later impaired QoL to determine if it is possible to prevent declines in QoL in these women. The deeper understanding of the coping strategies used by women to handle stressful events is also an important knowledge and a possible way for health care professionals to support in clinical practice.

ORIGINAL PAPERS

I.   Browall M., Ahlberg K., Karlsson P., Danielson E., Persson L-O. & Gaston- Johansson F. (2008). Health-Related Quality of Life during adjuvant treatment of breast cancer among postmenopausal women. *European Journal of Oncology Nursing* (Accepted)

II.   Browall M., Gaston-Johansson F. & Danielson E. (2006). Postmenopausal women with breast cancer: their experiences of the chemotherapy treatment period. *Cancer Nursing*, *29*, 34-42.

III.   Browall M., Ahlberg K., Persson L-O., Karlsson P. & Danielson E. (2008). The impact of age on Health-Related Quality of Life (HRQoL) and symptoms among postmenopausal women with breast cancer receiving adjuvant chemotherapy. *Acta Oncologica*, 47, 202-215.

IV.   Browall M., Persson L-O., Ahlberg K., Karlsson, P. & Danielson E. Daily assessment of stressful events and coping among postmenopausal women with breast cancer treated with adjuvant chemotherapy. (Submitted)

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ABBREVIATION

Adjuvant Treatment	Additional Treatment
CT	Chemotherapy
CMF	Cyclophosphamide, Methotrexate and 5-Flurouracil
DCA	Daily Coping Assessment
EORTC	European Organisation for Research and Treatment of Cancer
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire-C30
EORTC QLQ-BR23	European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire-Breast cancer specific module-BR23.
ER	Estrogen Receptor
FEC	5-Flurouracil, Epirubicin and Cyclophosphamide
HADS	Hospital Anxiety and Depression Scale
HER2-neu	Human Epidermal Receptor growth factor 2.
HRQoL	Health-Related Quality of Life
PR	Progesterone Receptor
QoL	Quality of Life
RT	Radiotherapy Treatment
TNM	Primary Tumor, regional lymp Nodes and distant Metasases
WMA	World Medical Association Declaration of Helsinki

INTRODUCTION

The main focus of this thesis is the postmenopausal women with breast cancers' experience of adjuvant chemotherapy (CT) and/or radiotherapy (RT). In Sweden breast cancer is today the most common type of cancer among women. Of the approximately 7,059 women who were diagnosed with the disease in Sweden during 2006, about 73% were postmenopausal and aged 55 or older at the time of diagnosis, and 33% were aged 70 years or older (National Board of Health and Welfare 2006). The median age for new breast cancer diagnosis is 60-64 years (Bergh *et al*. 2001). Cancer treatment of the elderly patient is therefore an increasingly important concern since the risk of developing breast cancer increases with age.

Survival time for women with breast cancer has extended due primarily to the development of new and more aggressive adjuvant treatments. However, it has also been shown that the disease process and treatments may produce a wide variety of troublesome symptoms (Schreier & Williams 2004; Wood *et al*. 2006; Miaskowski *et al*. 2006). Demographic, individual and disease characteristics are other factors that can influence patients' experiences (Armstrong 2003; Kim *et al*. 2005). All these factors may variously impact on the patient's Quality of Life (QoL) in different ways (De Jong *et al*. 2002; Ganz *et al*. 2003; 2004). The often lifelong consequences of breast cancer need to be recognized, addressed, and treated so that these women can go on to live normal lives (Schnipper 2001).

Previous research concerning the experience of symptoms and QoL in patients treated for breast cancer primarily include younger and middle-aged women (mean age <55 years) (Badger, Braden & Mishel 2001; Fortner *et al*. 2002; Dibble *et al*. 2003; Beck, Dudle & Barsick 2005) and rarely include elderly women (mean age > 65 years) (Rao & Cohen 2004). It is not certain whether findings from these studies of younger and middle-aged women can be accurately extrapolated to an elderly population (Yanick *et al*. 2001). There are also limited descriptions in the literature of how QoL is affected by adjuvant treatment in elderly populations (>65 years), however in clinical practice; it is currently common that these women are offered less aggressive treatment than are younger patients (Whiterby & Muss 2005; Eaker *et al*. 2006) due to fears that they may suffer greater side effects (Muss 2003). However, Muss and colleagues (2005) found that patients 51 to 65 years tolerate and benefit from standard CT regimens, and even more intensive regimens, almost as well as younger patients (< 50 years). Another limitation of prior research is that most studies are quantitative in nature and few qualitative studies have specifically studied elderly (> 65 years) women's experience of breast cancer treatment

(Crooks 2001; Ganz *et al.* 2003; Thomé *et al.* 2003; Thewes, Butow & Pendlebury 2004).

The more stressful the events are that breast cancer patients must endure, the more likely the patients are to have difficulty adjusting (Kornblith *et al.* 2001). In finding a link between the event or number of events and the degree of distress they give, the need is highlighted for these women to have support systems in place before the event occurs, to help them cope (Kornblith *et al*. 2001). Coping strategies have been shown to be associated with QoL after breast cancer diagnosis (Stanton *et al*. 2000; Avis, Crawford & Manuel 2005).

Several studies have indicated that it is important that elderly women (> 65 years) be carefully evaluated for adjuvant therapy (Shah *et al.* 2002; Beghe & Balducci 2005). At the same time, it has been stressed that in the elderly, biological age is more important than chronological age (Extermann 2002). Therefore, therapeutic decisions should be weigh in the patient's life expectancy, as well as treatment and risks and benefits (Kimmick & Muss 2001; Repetto & Balducci 2002). To meet this challenge health care professional need to gain more knowledge to better identify and meet patient's special needs, regardless of the patient's age and gender (Mackey & Sparling 2000). To further investigate how adjuvant treatment affects postmenopausal women with breast cancer, this thesis studied symptom experience, Health-Related Quality of Life (HRQoL), stressful events and coping strategies.

BACKGROUND

A literature search was conducted in Medline (PubMed), CINAHL, the Social Citation Index and PsycINFO databases, supplemented by a manual search.

Breast cancer

Breast cancer is the most common type of cancer among women in the Western countries. It accounts for 30% of all cancer among women, and the age-corrected incidence, compensating for ageing, has almost doubled since the start of the Swedish cancer registry in 1959. Treatment of elderly patients is an increasingly important concern since this part of the patient population is steadily increasing (National Board of Health and Welfare 2006). Although the incidence of breast cancer has increased since the 1960s, the death rate has decreased. The relative five-year survival rate for women diagnosed with breast cancer is 86%, and 10-year survival is more than 75% (National Board of Health and Welfare 2006).

Definition and histological type
Breast cancer is defined as cancer arising from cells in the breast tissues. When the cells invade through the basal membrane, the cancer is termed "invasive", otherwise the cancer is called "non-invasive" or "in situ". When the cells originate from the ducts in the breast, the cancer is called 'ductal cancer'. Ductal cancer is the most common type of breast cancer, constituting about 80% of all breast cancers. Cancer that arises from the glandular lobules in the breast is called "lobular carcinoma" and about 10% of all breast cancers are of this type. Other, rarer histological types are medullary carcinoma, tubular carcinoma, mucinous carcinoma and comedocarcinoma. These types together constitute about 10% of all breast cancers (Wood *et al.* 2005).

Etiology
Epidemiologic studies have provided much information on important risk factors for breast cancer. These include age, heredity, alcohol consumption, reproductive history and exposure to specific carcinogens (Key, Verkasalo & Banks 2001). Nulliparity, early menarche, late menopause, obesity in postmenopausal women, use of hormonal replacement therapy, and high concentration of endogenous ostradiol are all known risk factors. Therefore, hormones seem to play an important role in breast cancer development. Prolonged current or recent use of oral contraceptives has also been implicated as a cause of a small increase in the risk of breast cancer (Key *et al.* 2001).

Staging
The extent of axillary lymph node involvement in breast cancer is the dominant prognostic indicator of later systemic diseases (Henderson & Patek 1998). Tumour size is the second factor that predicts disease outcome and, together with lymph node status and presence or absence of distant metastases, it constitutes the basis of the primary tumour (T), regional lymph nodes (N), and distant metastases (M) TNM clinical classification (Fisher, Sass & Fisher 1987).

Histological grading has clear prognostic significance (Lundin *et al.* 2001), as does the patient's age. However, these prognostic factors are not as strong as lymph node status. Estrogen Receptor (ER), Progesterone Receptor (PR) and Human epidermal receptor growth factor 2 (HER2-neu) statuses are the most important and helpful predictive factors currently available, which must consequently always be classified in order to decide the adjuvant treatment (Goldhirsch *et al.* 2007).

Breast cancer treatment
Surgery is the main treatment for patients with breast cancer, and the majority of patients with unifocal tumours < 3 cm in diameter are treated with breast-conserving procedures (sector resection) (Bröstcancer regionalt vårdprogram 2006). For larger tumours, mastectomy is preferred. Axillary lymph nodes are investigated before further treatments are decided on. This can be done by axillary dissection, but more often today by sentinel node biopsy. In this procedure, the node in which the lymph flow from the breast primary has its drainage is examined. If this node is free of spread then no further dissection of other lymph nodes is required. After surgery, breast cancer patients need adjuvant treatment. This is given to minimize the risks of recurrence of the disease in the future. Depending on risk of future spread and the biology of the tumour (ER, PR and HER2 status), different kinds of adjuvant treatments are indicated for different patients (Goldhirsch *et al.* 2007). For most women postoperative RT is given at 8-10 weeks after surgery for 5 days per week over 5 weeks to decrease the risk of loco-regional recurrence (Rutqvist, Rose & Cavallin-Ståhl 2003). Women at high risk of recurrence are also frequently given systemic adjuvant CT and/or hormonal therapy (e.g. anti-oestrogen) (Goldhirsch *et al*. 2007). CT is started 4-6 weeks after surgery. It is clear from an overview of the Early Breast Cancer Trialists' Collaborative Group (2000) that in the adjuvant setting, combination CT is superior to single-agent treatment and that the proportional benefits of CT (like those of endocrine therapy) are similar in node-negative and node-positive patients. Hormone receptor positivity (i.e., ER or PR positivity) predicts response to antihormonal treatment, while HER2-neu positivity predicts response to trastuzumab (Smith *et al.* 2005).

Women's experiences of breast cancer and treatment

The impact of breast cancer is not represented by survival rates, and numbers cannot capture the physiological, psychological, and sociological impact of cancer or all the other losses the afflicted women most endure over a life span (Schneiderman *et al.* 2001). In a recently made meta-synthesis, Berterö & Wilmoth (2007) concluded that the diagnosis of breast cancer itself, as well as its treatment made the women conscious of their mortality, which for many led to a psychological journey - a life review. The diagnostic phase often provokes a range of emotional responses, including fear, shock, grief, anxiety and anger (Somerset *et al.* 2004). Vulnerable women experience uneasiness and conflicts from diagnosis through to surgery (Shapiro *et al.* 2001), and their lives, health and well-being are affected. Subsequent to primary treatment (surgery) of breast cancer, women encounter a range of physical and psychosocial problems, such as pain, lymphoedema, anger, depression, fear of recurrence and sexual difficulties (Rendle 1997). The loss of a breast can have a truly negative impact on patients' lives and well-being, especially since breasts are related to femininity, physical appearance and motherhood (Pikler & Winterowd 2003). Body image is merely an umbrella term that cannot capture and describe the complex psychosocial experience of losing a breast (White 2000).

Experiences of symptoms from adjuvant treatments can cause decreased QoL (De Jong *et al.* 2002; Ganz *et al.* 2004). Rostoen and Begnum (2000) points out in a literature review of QoL in women with breast cancer, that there is a lack of QoL studies that have attempted to differentiate significant subgroups of patients, e.g. different age groups. Few studies have considered age differences in symptom experience associated with breast cancer (Sammarco 2001). Studies on health status, life satisfaction and psychological distress among breast cancer survivors have reported small, age-related differences in HRQoL. Specifically, it was found that elderly patients were more highly satisfied with the overall quality of their lives and were much more likely to report higher levels of emotional well-being than were younger patients (Matthews *et al.* 2002; Zabora *et al.* 2001). On the other hand, it is important to keep in mind that the elderly have been found to be more vulnerable in terms of their physical health and functioning as a consequence of ageing (Sammarco 2001). The diagnosis of breast cancer, which in itself produces a great amount of distress (Shapiro *et al.* 2001), together with a variety of other stressors, such as symptom distress (Kuo & Ma 2002) and age (Schnoll *et al.* 1998), have been shown to be highly associated with coping and QoL after diagnosis (Avis, Crowford & Manuel 2005). Manuel *et al.* (2007) concluded that to be effective, and to be able to target different interventions, coping strategies may need to vary according to specific stressors. In studies of younger and middle-aged women treated with CT, various coping strategies, such as social support, acceptance, distraction,

and relaxation, have been shown to be helpful in reducing symptoms (Gaston-Johansson *et al.* 2000; Lauver, Connolly-Nelson & Vang 2007; Manuel *et al.* 2007).

Symptom experience

A symptom can be defined as a *"subjective experience reflecting changes in the bio- psychosocial functioning, sensations, or cognition of an individual"* (Larson *et al.* 1994, p. 273). In contrast, a sign is defined as any abnormality, indicative of disease that is detectable by the individual or by others (Dodd *et al.* 2001). In this thesis, we will focus on symptoms that are self-rated in the measurement instrument or expressed in the interviews by the patient.

According to Dodd *et al*. (2001), symptom experiences include an individual's perception of a symptom, evaluation of the meaning of a symptom and response to the symptom. "Perception of symptoms" refers to whether the individual notices a change from the way he or she usually feels or behaves. "Symptom evaluation" pertains to the individual's judgments about the severity, cause and treatability of the symptoms and about the effects of the symptoms have on their lives. "Symptom response" includes physiological, psychological, sociocultural and behavioral components. Understanding the interaction of these components of the symptom experience is essential for effective symptom management. Even when a disease is effectively treated, symptoms may often remain a continuing concern. Patients who have the opportunity to explore the symptom they experience, to learn about their disease, and to take participation in symptom management are better equipped to cope with their symptoms (Larson *et al.* 1994).

Symptom distress can be defined as the degree of discomfort, physical and mental upset, anguish or suffering experienced from a specific symptom or from a cluster of symptoms (Rhodes & Watson 1987, p. 234). According to Rhodes *et al.* (2000), assessing symptom distress helps to determine patients' perceptions of their needs and problems. Accurate measures of symptom experience, symptom distress and symptom occurrence are essential for symptom management and QoL (Rhodes *et al*. 2000). Frequency or intensity is not necessarily equivalent to distress, and there are other dimensions of symptom experiences, e.g., perceived importance, existential and spiritual aspects, that may also be significant for suffering or distress (Tishelman *et al.* 2005). Thus, the experience of symptom distress can vary from person to person and from situation to situation, and is composed of both cultural and personal meanings (Tishelman, Degner & Mueller 2000).

Health-Related Quality of Life

The term Health-Related Quality of Life (HRQoL) is commonly used to describe aspects of an individual's subjective experience that relate both directly and indirectly to health, disease, disability and impairment (Carr *et al.* 2001) and to the effectiveness of treatment. Quality of Life (QoL) is not a new concept; references to QoL date back to Ancient Greece (McCorkle & Cooley 1998). Since the early 1970s, the concept of QoL has gained increasing importance in research regarding evaluating of quality and outcome of health care. The World Health Organization (WHO) define QoL as the *"individual's perception of their position in life in the context of the culture and value systems in where they live, and in relation to their goals, expectations, standards and concerns"* (1998, p. 551). Their definition represents a broad view, focusing on the individual's evaluation of QoL in a cultural, social and environmental context. The WHO Quality of Life Working Group implicitly and widely introduced the QoL concept into health care when health was defined as a state of physical, mental, and social well-being and not merely the absence of disease or infirmity (Cooley 1998). This definition strongly emphasizes the multidimensional nature of health. Fayers & Machin (2000) also gave a broad definition of QoL, defining it as an overall experience of life satisfaction. QoL is also seen as one of a number of symptom outcomes; other outcomes include functional status, emotional status, self-care, costs and mortality (Dodd *et al.* 2001). Despite its extensive use in research in many different disciplines, there remains considerable conceptual confusion surrounding this term. QoL not only means different things to different people, but also has a variety of meanings in different areas of application (Fayers & Machin 2000). As discussed by Melin-Johansson (2007) in her thesis, there is still no consensus definition of QoL, nor do measurement models of common instruments capture all dimensions in measurements of the QoL.

Those who assume that a fully healthy life is equivalent to a high QoL (Testa & Simonson 1996), uses the terms "HRQoL", "health status", and "functional status" (Bradley 2001) interchangeably. This assumption may be challenged by the fact that patients with significant health and functional problems do not necessarily have commensurate QoL scores (Carr & Higginson 2001). A meta-analysis by Smith, Avis & Assman (1999) substantiated that QoL and health status are two distinct concepts, and should therefore not be used interchangeably. They argued that QoL is more related to mental health and health is more important to physical health. One of the first to promote a focused QoL definition that is specific to health care was Aaronson (1990), who in a way coined the term 'health-related quality of life' (HRQoL). HRQoL is often operationalised by assessing physical, mental/cognitive and social functioning domains and derives from the WHO definition of health (WHO

1998, p. 551). The European Organisation for Research and Treatment of Cancer (EORTC) has taken a consensus approach, focusing on health-related issues and a limited set of life domains (Aaronson *et al.* 1996). In the present thesis, we have utilized the EORTC instruments and accordingly adopted their definition of HRQoL. Hence, HRQoL is defined here as the subjective perception of health, i.e. the impact of disease and treatment on functioning, symptoms, subjective well-being, perceived health status and overall QoL. Furthermore, the EORTC instruments comprise those domains that we considered important to explore. Some instruments, such as the EORTC QLQ-C-30, merge the concepts global health status and QoL, and ask the patients to make separate assessments of perceived health and QoL, and then combine the two ratings into a single global (overall) QoL score. In this thesis, overall QoL is therefore a global score representing these two concepts (global health status and QoL).

Stressful events and coping

Human beings are confronted throughout their lives with a variety of stressful events and situations. The stress caused by illness and subsequent treatment may exceed the individual's ability to cope and thus negatively affect and threaten the individual's life and/or QoL (Manning-Walsh 2005) and cause much psychological distress throughout the course of the illness (Compas & Luecken 2002). Women with breast cancer need assistance in coping with the stress associated with these events immediately following diagnosis and during and after treatment (Kornblith *et al.* 2001). When a person is exposed to a stressful event, he/she evaluates the meaning of the event through a cognitive appraisal process that includes a primary and a secondary appraisal. In primary appraisal, the individual evaluates the significance of a stressful event for him/herself. Secondary appraisal addresses the question "What can I do?" Here, the individual evaluates the demands of the situation. The primary and secondary appraisals result in the stressful event being looked upon as irrelevant, positive or stressful. If it is stressful, it can be valued as engendering harm/loss, threat or challenge. It can also be a combination of the three (Folkman & Geer 2000). The appraisal also influences subsequent coping.

Lazarus and Folkman (1984) tried to overcome what they viewed as limitations of earlier approaches to coping by giving greater emphasis to the interaction between the individual and the environment. They defined coping as *"constantly changing cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person"(* 1984, p.141). According to Backer *et al.* (2000), this is the most commonly used definition in nursing literature. Coping refers to the thoughts and behaviours a person uses to regulate distress, manage the problems causing the stress and maintain positive well-being. According to Link *et al.*

(2005), although a variety of determinants of coping strategies have been identified, or at least theorized in patients with cancer, little is known about what factors contribute to the use of particular coping strategies from the cancer patient's perspective. To be able to provide effective self-care management programmes, health care professionals need more knowledge about how a person handles these stressful events (i.e. copes) (Link *et al.* 2005). In line with Lazarus and Folkman's (1984) definition of coping, repeated assessments and a specification of the demands are important for a more complete understanding of the coping process (Stone & Neale 1984; Lazarus 1993). Lazarus (2006) points out that although coping processes are commonly described in the literature they are almost always measured by quantitative standardized questionnaires. Therefore, a combination of qualitative and quantitative methods was used in this thesis to explore patients' experiences.

RATIONALE

Many issues are universal for all women with breast cancer, irrespective of differentiating factors such as age. However, we also know that although women with breast cancer share common concerns, experiences and anxieties, each woman encounters a unique set of problems. A review of the literature clearly reveals that the numbers of older women with breast cancer are increasing and that this patient population will need different adjuvant treatment. It is also apparent that virtually no research has been conducted on the symptom experience of older women who are diagnosed with breast cancer and offered adjuvant treatment. There is an indisputable need to advance scientific knowledge in this area to discover the physical and psychosocial effects of cancer treatment experienced by postmenopausal women and to determine their specific needs for care. We also need to assess their experience of treatment in longitudinal studies examining not only symptom experience, but also different dimensions of HRQoL, stressful events and coping strategies. This thesis will give a picture of how these postmenopausal women are affected by the multiple symptom experience and stressful events, how such factors affect HRQoL, and how these women cope with these stressful events. The knowledge gained can serve as a basis for developing of evidence-based interventions specially designed to decrease the severity of experienced symptoms and to improve coping strategies and HRQoL for postmenopausal women with breast cancer.

AIMS

The overall aim of this thesis was to explore how postmenopausal women (55 years and older) with breast cancer experience adjuvant (CT and RT) treatment over time.

Specific aims

The specific aims in papers I-IV were to:

I. Describe how HRQoL (perceived functioning and symptoms) and emotional distress develops over time in postmenopausal women undergoing adjuvant CT and RT, and, to identify the best predictors of global health and QoL (referred to as overall QoL in this article) after treatment from perceived functioning, symptoms, emotional distress and clinical/demographic variables measured at baseline.

II. Describe the experience of postmenopausal women with breast cancer who undergo adjuvant Chemotherapy treatment.

III. Analyse the impact of age on experienced HRQoL and symptoms in postmenopausal women with breast cancer before, during and 4 months after adjuvant CT.

IV. Describe stressful events experienced by postmenopausal women with breast cancer receiving adjuvant CT, and how these women handle these stressful events or situations.

METHODS

This thesis has its roots in health and care science. According to Leininger (1988), the nursing discipline is, of all the different health care professions, the one most concerned with investigating caring attitudes, processes and relationships. The overriding goal of this thesis was to contribute to our understanding of the impact that breast cancer and its treatment has on the patients' daily lives and, in so doing, shed light on potential avenues for improving the care of these patients.

The use of multi-method design may help to enrich our understanding of complex phenomena, such as that of human experience (Morse 2003) and, specifically, the experiences of postmenopausal women with breast cancer. All methods have limitations, and combining different types of methods may strengthen research findings. For example, patient questionnaires have the advantage of providing standardised and comparable data, whereas qualitative methods provides a deeper understanding in that they allow the patient to express his/her own thoughts and using his/her own words (Creswell 2002). According to Patton (2002), a combination of qualitative and quantitative data may help to elucidate complementary aspects of the same phenomenon. In this thesis, a pragmatic approach was taken, combining both qualitative and quantitative methods. As a researcher, I have some prior understanding and experience of working with patients with different cancer diagnoses, and with patients in different stages of their disease, but I had no previous experience of working with women with breast cancer.

The designs of studies comprising this thesis were descriptive, predictive, correlational and longitudinal. A descriptive design was used (study I, II-IV) to describe HRQoL at a group level between baseline, and over time. A correlational design was used to examine associations between HRQoL and symptoms, functional dimensions, socio demographic and clinical variables, etc. (Papers I, III) and to predict overall QoL (Paper I). Inductive and deductive methods were used, comprising both quantitative and qualitative analyses. In quantitative research, measurement instruments are often used and probability sampling is often required to permit statistical interferences to be made. The aim of the quantitative studies in this thesis was to gain knowledge that can be compared and generalised between different groups of patients. Qualitative research involves inductive reasoning and attempts to elucidate the individual's subjective perspective (Sandelowski 2007). The qualitative study was analysed using content analysis in order to obtain deeper knowledge about the experience of adjuvant treatment. Multi- methods were required to derive valid and meaningful data meeting the aims and research questions in this thesis. Furthermore, the use of multi-methods made it possible to acquire more

comprehensive and richer information about the adjuvant treatment period and how these postmenopausal women experienced their HRQoL, symptom experience, stressful events, and coping strategies over time than would have otherwise been possible by means of one method alone. Moreover, qualitative and quantitative methods are considered to complement each other (Polit & Beck 2004), and their use may therefore strengthen the results of this thesis. An outline of the included studies is given in Table 1

Table 1. Studies included in the thesis.

	Study design	**Subjects**	**Time frame**	**Measurements**	**Data analysis**
Paper I	Descriptive, longitudinal, and predictive, correlational	150 postmenopausal women	Before, during and after CT and RT	EORTC-QLQ-C30, BR23, HADS	Fishers test for pair wise comparisons. Multiple linear regression analyses
Paper II	Descriptive	20 postmenopausal women	After finished CT treatment	Interviews	Qualitative content analysis
Paper III	Longitudinal and correlational	75 of the original 150 postmenopausal women (In Paper I)	Before, during and after CT (4 months)	EORTC-QLQ-C30, BR23, HADS	Multiple linear regression Fisher`s test Pitman's test Kruskal-Wallis test
Paper IV	Descriptive	Same 75 women as in Paper III	During CT (cycles one, three and six)	Daily Coping Assessment (DCA), Diary entries	Combined qualitative and quantitative content analysis

Setting

In all the studies, an inclusion criterion of age-cut of ≥ 55 years was adopted to ensure the participating women were homogeneous with respect to menopause. This criterion limited the numbers of eligible patients and thus in order to enhance accrual the investigation was expanded to a multi-centre study involving two university hospitals (Sahlgrenska University Hospital: Department of Breast Surgery, Gothenburg, and Karolinska University Hospital: Department of Oncology, Stockholm) and one county hospital (Department of Surgery, Skövde).

Participants

Patient recruitment started at the centre in Gothenburg by the author. At the other hospitals, research nurses were recruited and requested to follow the same procedures for patient recruitment, inclusion and monitoring as those applied in Gothenburg. Unfortunately, due in part to logistics difficulties at the other centres, missing data and dropouts could only be accounted for at the Gothenburg centre. Hence, of the 86 eligible patients scheduled to receive CT in Gothenburg, 35 were lost due to different causes (i.e.18 had incomplete or missing data, 5 refused participation, 7 did not receive CT and 5 for other reasons), thus leaving a total of 51 patients. In Stockholm, 61 of 82 eligible

patients were lost for unknown reasons, leaving 21 at this centre. In Skövde 11 of 14 eligible patients were lost leaving 3 patients.

In Paper I, two groups of women were enrolled: (i) those scheduled to receive adjuvant CT (described above) (n=75) after prior surgery; and (ii) those scheduled to receive RT after surgery (n=75). In the RT group, 94 women met inclusion criteria and were age-matched to the CT group and were asked to participate. Of these, 16 refused participation and 3 were excluded due to language difficulties. Of the remaining 75 CT patients, a total of 10 women were lost (drop-outs) between cycles one and six (3 failed to send in the questionnaires and 7 had withdrew from adjuvant CT due to various medical problems). Five of the RT patients did not send in the questionnaire at the last collection (2 weeks after last treatment). The age range in the total patient sample was 55-80 years (mean age CT, 65 years; RT 64.5 years).

In Paper II, 21 women were asked to participate and one refused. All patients were included using the same inclusion criteria as in Paper I, III and IV, with the exception that they had completed adjuvant CT within the past year. Eleven of the patients had undergone their treatment at one of the university hospitals and 9 at the county hospital. Their age range were 55-70 (mean age 60.6 years).

In Paper III and IV, the sample consisted of the same 75 CT patients as in Paper I (age range here was 55-77 years: mean age 65 years). In Paper III, a total of 24% (n=18) of the original CT sample were lost to follow-up. Of these, 3 had withdrawn from the treatment for personal reasons, 7 had withdrawn during the sixth cycle because of medical problems, and 8 received all courses but did not return for the surveys. In Paper IV, 15 of the 75 patients did not participate (left no diaries). Of the total 60 participants in this study, 40 patients completed 15 diary (first, third and last treatment), 11 patients completed 10 diaries (first and third treatment), and 9 patients completed 5 diaries (first treatment).

Inclusion and exclusion criteria

Inclusion criteria for Paper I, III-IV were:

- must be postmenopausal women aged 55 years and older
- were newly diagnosed with histologically confirmed stage I - IIIa breast carcinomas
- were able to give informed consent; and
- were able to read and speak Swedish, and understood the purpose of the study.

Exclusion criteria were:

- evidence of dementia;
- known history of psychiatric disorder; and
- history of other kinds of cancer within the previous five years.

Procedure

In Paper II, data were gathered using interviews with one open question. Eligible patients were identified from patient records at two centres, over a period of 8 months during 2003. Registered nurses (RNs) at both hospital sites helped to extract information on the women who had been treated with adjuvant CT. Identified patients who were due back for another visit soon were approached by the RNs prior to the visit and asked to participate in the study. Women who were not scheduled for a visit for a while were contacted by telephone. Those who were interested in participating were contacted by the author and relevant information was sent to their homes. Most of the interviews were performed in the women's homes at their request and the rest were conducted in a private area at the hospitals in conjunction with a visit to the hospital. Prior to the interview, the author provided the participants with additional information about the study and written consent was obtained. The interviews lasted about 60 minutes, and were tape-recorded.

In Papers I, III and IV, the studies were carried out at the three hospitals described above (two university hospitals and one county hospital). Data were collected from November 2003 to November 2005. Information on all women scheduled to receive adjuvant treatment was collected from hospital charts and records at one of the university hospitals (Gothenburg) by the author. Due to long travelling distances from Gothenburg, two RNs on the staff at the other centres were recruited to identify eligible patients at those hospitals (Stockholm and Skövde). Patients meeting inclusion criteria were informed about the study and asked if they wanted more information about the study by the RNs. All women scheduled to receive CT treatment who met the inclusion criteria were consecutively asked to participate in the study. For each CT patient enrolled, a woman of the same age about to receive RT was asked to participate (Paper I).

Baseline data were collected during the week before treatment was started. In women about to receive CT baseline assessments were conducted approximately 4-6 weeks after surgery and in women scheduled for RT, 8-10 weeks post surgery. Women in the CT group scheduled for treatment at one of the university hospitals (Gothenburg) were interviewed and filled in questionnaires either at the hospital or at home. Women treated at the county hospital (Skövde) and the other university hospital (Stockholm) were interviewed by telephone due to long travelling distances. At subsequent data collections (1 week after the first, third and last cycles of CT) (Paper I), and at 4-month follow-up (Paper III), all patients were mailed the questionnaires together with a return envelope and a letter explaining the procedures and providing a telephone number where the interviewer could be reached. In the RT group, women scheduled for RT at one of the university hospitals were interviewed and filled in the questionnaires at the hospital at baseline. Subsequent questionnaires (after 3 weeks of treatment, and 2 weeks after completion of the treatment) were administered by mail. The same data collection procedures as those used for CT patients treated at the university hospital (Gothenburg) were used for RT patients at that hospital. All demographic and clinical data were collected from the patients or from the hospital charts.

All women receiving CT were also asked to complete diaries in which they were to assess daily stressful events and coping (Paper IV). Diaries were completed during a period of 5 consecutive days starting on the treatment days for cycle 1, 3 and 6. Women from the county hospital (Skövde) and one university hospital (Stockholm) were contacted by telephone and, if they agreed to participate, the diaries were sent to their homes by post. At subsequent data collection times, i.e. days 1-5 after the third and the last cycles of CT treatment all patients were mailed diaries, together with a return envelope and a letter explaining the procedures, again including the telephone number of the first author. All women participating in this study were also asked to complete a battery of questionnaires to during their treatments.

Methods for data collection

EORTC QLQ-C30 and EORTC QLQ-BR23
The core questionnaires used were the cancer-specific EORTC QLQ-C30 (Aaronson *et al.* 1993) version 3 and the tumour-specific breast cancer module EORTC QLQ-BR23 (Sprangers *et al.* 1996). The QLQ-C30 consists of 30 items assessing five multi-item functional scales that evaluate physical (5 items, ability to perform a variety of ordinary daily activities), emotional (4 items, psychological distress in physically ill patients), social (2 items, perceived disruption of normal family life and social contact), cognitive (2 items,

deterioration of memory and/or concentration) and role functioning (2 items, ability to perform daily work or household chores). In addition, an overall quality-of-life scale assesses global health status and quality of life. Symptoms commonly reported by cancer patients are assessed with three symptom scales: fatigue, (3 items, measuring only physical tiredness; Knobel *et al.* 2003), pain (2 items) and nausea/vomiting (2 items). Five single items assess the symptoms breathlessness or dyspnoea, sleep disturbance, appetite loss, diarrhoea, and constipation. An additional item assesses the financial impact of the condition and its treatment. All items are rated on a scale 1) "not at all", 2) "A little", 3) "Quite a bit", 4) "Very much", with the exception of "Overall QoL" which ranges from 1) "very poor" to 7) "Excellent" (Fayers *et al.* 1997). All scores are transformed to a percentile scale ranging from 0-100. High scores in the functional scales and overall QoL indicate high levels of functioning and overall QoL, whereas high scores in the symptom/problem scales indicate high levels of symptoms/problems.

The QLQ-BR23 module was developed to supplement the core questionnaire EORTC QLQ-C30 in order to assess specific HRQoL issues relevant to patients with breast cancer. It comprises 23 items divided in 4 functioning scales: body image (4 items), sexual functioning (2 items), sexual enjoyment (1 item), and future perspective (1 item); and 4 symptom scales: arm symptoms (3 items), breast symptoms (4 items), systemic therapy side effects (7 items), and upset by hair loss (1 item). The QLQ-BR23 is scored in the same way as the QLQ-C30 (Sprangers *et al.* 1996). The reliability of the Swedish version has been assessed in both healthy individuals and different groups of cancer patients (Michelson *et al*. 2000). In this thesis (Papers I and III), the internal consistency of the EORTC QLQ-C30 and BR23 was calculated using Cronbach's Alpha (Cronbach 1951). Alphas ranged between α= 0.75-0.94, except for nausea and vomit (α=0.37) and systemic therapy side effects (α=0.62), and cognitive functioning (α=0.69).

Hospital Anxiety and Depression Scale (HADS)
The Hospital Anxiety and Depression Scale (HADS) Zigmond & Snaith (1983) is a brief self-administered questionnaire used extensively in cancer settings. The HADS aims at identifying clinical cases (possible and probable) of anxiety disorders and/or depression among somatically ill, non-psychiatric patients. It consists of 14 items, 7 assessing anxiety (HAD-A) and 7 assessing depression (HAD-D). The patient rates the presence of problems during the preceding week on a four-point responses scale from 0 to 3. The scores for each subscale are summed, giving a maximum of 21. Two cut-off points were suggested by the original authors: scores of 0–7 represent no problems of clinical relevance (non-cases), scores of 8–10 suggest the need for further psychiatric investigation

(possible cases), and scores of 11-21 are indicative of a clinical level of anxiety/depression (probable cases). Studies have shown the HADS to be a reliable instrument for assessing anxiety and depression in breast cancer patients (Bjelland *et al.* 2002, Osborne *et al.* 2004). The reliability of the Swedish version has been assessed (Lisspers, Nygren & Söderman 1997). In this thesis (Papers I and III), the internal consistency (Cronbach's Alpha) for HAD-A α= 0.87 and HAD-D α= 0.86.

Daily Coping Assessment
(DCA)The Daily Coping assessment (DCA) questionnaire was developed by Stone and Neale (1984) specifically for the daily recording of coping with everyday stressful events (Paper IV). The DCA comprises four sections. The first section consists of a question asking patients to describe in their own words the most stressful event (illness related or not) of each day during five consecutively days. The second section assesses the distress occasioned by the described stressful event. Scores range from 1 (Not at all bothersome) to 7 (Extremely bothersome). The third section includes two questions concerning reactions to the stressful event: (1) How much control did you have over its occurrence? (No control, some, Quite a lot), and (2). Was it an expected stressful event or situation? (Completely unexpected, somewhat unexpected, somewhat anticipated, completely anticipated) The fourth part includes eight categories of strategies for managing the stressful event: distraction (thought about something else), situation redefinition (looked at the problem in a different way), direct action (did something about it), catharsis (expressed emotions), acceptance (accepted the problem), seeking social support (sought support from others), relaxation (relaxed), and religion (sought spiritual support). The patients report whether or not (yes/no) they use each of the strategies as a means of handling their recorded stressor for that day. The Swedish version (Wasteson & Nordin 1997, Appendix 1) of the DCA was used by Wasteson and colleagues (2002) for assessing patients with gastrointestinal cancer.

Interview
The targeted event in this thesis was the chemotherapy, and the overall purpose of the various studies was to gain an understanding about the experience of adjuvant chemotherapy treatment among a group of postmenopausal women. According to Mishler (1986), a research interview is a form of conversation, a dialogue, in which the interviewer and interviewee interact by 'talking together'. That is, the conversation is mutually created by the interviewer and interviewee. The interviews began with the following question*; 'Can you describe your experience of the chemotherapy treatment period'?* Because of the nature of this question, the women had the freedom to narrate their story, after which the interview focused on elements of the narrative. The participants

were encouraged to provide as many details as possible. In order to allow the participants to pursue their own lines of thought and introduce new topics that were of importance to them the interviewer remained silent during most of the interview, just nodding and saying "Yes", "I see", "Can you tell me more about", "How", "In what way", and so forth (Patton 2002).

Analyses

Statistical methods
Descriptive statistics were used to characterise the sample and to summarise HRQoL variables, anxiety and depression, levels of perceived distress, perceived control and perceived expectations at baseline and over time. Frequencies were computed of the use of the eight predefined coping strategies, of stressful events and of coping strategies. Non-parametric methods were used when analysing nominal and ordinal data due to small samples sizes and skewed data distributions (Altman 1991).

To describe the development of HRQoL over time (Paper I), a regression coefficient was calculated for each patient and each subscale, with the number of weeks from baseline on the x-axis and the value of the subscale on the y-axis. Fisher's test for pairwise comparisons (Good 2000) was used to determine whether the regression coefficients were significantly different from zero, i.e. whether there were any time trends from baseline through treatment in the two treatment groups. In examining potential baseline predictors of QoL after treatment, the EORTC QLQ-C30 scale Overall QoL was used as the dependent variable. All other scales in the QLQ-C30, BR23 and HADS, as well as clinical and demographic variables were treated as potential predictors. In this explorative search for strong predictors, correlations were first computed between all potential predictors at baseline and Overall QoL after treatment. Those variables showing significant correlations were then entered in multiple linear regression analyses (forward) to determine their unique predictive value for Overall QoL. We also investigated whether or not the mode of questionnaire administration (personal interview at home/at hospital versus telephone interview) correlated with HRQoL (Papers I, III). All analyses were performed within each treatment group. All tests were two-tailed and conducted at the 5% significance level.

In Paper III, linear regression coefficients were also calculated for each patient and each HRQoL subscale to describe trends with time from baseline through treatment. Fisher's test for paired comparisons was used to test if the regression coefficients were significantly different from zero, i.e. if there were any time trends from baseline through treatment. Differences between baseline and the mean of the first, third and the sixth cycle were calculated to elucidate the

difference between baseline and treatment time. Differences between baseline and the 4-month follow-up values were also calculated to elucidate the difference between baseline and follow-up. Correlations between age and baseline-follow-up differences were tested with Pitman's test (Good 2000). The non parametric Pitman's test, Fisher's permutation test or Kruskal-Wallis test was used, depending on type of variable, to test for relations between age and socio demographic as well as clinical variables. Patients with missing values on a variable were excluded from analyses in relation to that particular variable. All tests were performed with age as a continuous variable, but for descriptive purposes Tables and Figures show data divided into a younger group (55-64 years; n=36) and an older group (65+ years; n=39). This age cut-off was chosen for two reasons: 1) most clinical HRQoL studies of breast cancer have excluded patients over 65 years; 2) it divided the total group approximately at the median. A separate analysis of drop-outs was performed to study whether these patients differed regarding age and baseline HRQoL. All tests were two-tailed and conducted at 5% significance level.

In Paper IV, we used each diary as the unit of observation. We also performed analyses with each individual as the unit of observation, e.g. by examining the proportions of stressful events and coping strategies reported by each individual. These analyses yielded roughly the same results as those that are presented in the paper.

Content analysis
Content analysis has been defined as "*a research technique for making replicable and valid inferences from texts (or other meaningful matter) to the context of their use*" (Krippendorff 2004, p. 18). Content analysis was used by the church during the 18th century for inquisitorial purposes, but was not named content analysis until 1941 during World War II, when it was used in newspaper and propaganda analysis. There are now several approaches to qualitative content analysis with roots in literary theory, social sciences and critical scholarship. Thus, content analysis has evolved from its original use for analysis of the written word into a research method in its own right which enables data to be analysed with respect to their expressive contents, symbolic qualities and meanings (Krippendorff 2004). When analysing text quantitatively, manifest content little or no interpretation is used and only the visible surface is described. Krippendorff (2004) argues that content analysis should not only be restricted to summarise surface features of messages, but also interpret the meaning of content. Content analysis with interpretation is a form of qualitative analysis in which the underlying meaning, latent content is focused on. Data can be analysed by formulating categories or themes.

In Paper II, the analysis started only after all interviews had been carried out. The first step consisted of listening to, reading and summarising every interview in order to gain a general sense of the content. All interviews were read through several times by the first author. One of the co-authors read a sample of the text in order to obtain a sense of the whole. The text was then divided into meaning units (i.e. single words, parts of whole sentences), which were subsequently condensed in each interview into subthemes and labelled with a code. Coding refers to the process of transforming texts to analysable representations. All codes were back-checked several times to the meaning units and interview texts and some codes were changed. The codes were compared based on variations and similarities, and derived tentative themes were discussed and revised several times by the co-authors before they were finally sorted into subthemes. Subthemes were formed into themes, which constitutes the whole.

In Paper IV, the material for the analysis consisted of short descriptions of stressful daily events noted in the patient diaries. These descriptions were on a manifest and concrete level and the results were presented in categories and sub-categories. A quantitative content analysis (Weber 1995) was used to quantify the content of the qualitative data. The analysis of the diary entries was done in the same manner as in Paper II. All sentences and short accounts describing stressful experiences, occurring during the five days of treatment at cycle one, three and six, were read through several times by the first author. Two of the co-authors read a sample of the diaries to obtain a sense of the whole. Subsequently, all sentences and short descriptions were compiled into a single text document. This text was subsequently divided into meaning units, which were then condensed into codes of stressful events. All codes were cross-checked several times against the meaning units and entire diary texts and some were revised. The codes were also compared for differences and similarities with other codes and tentative categories were discussed and revised several times by three of the authors before they were finally formed into six categories (Weber 1995). From these categories, two major domains were observed: physical problems and psychosocial problems. Quantitative analyses could then be performed of these qualitatively derived categories and in relation to the DCA assessments of degree of distress, reactions and coping strategies used to manage stressful events. Citations were extracted from the diaries to exemplify the categories (Paper IV).

Ethics

The studies in this thesis comply with The World Medical Association Declaration of Helsinki (WMA 2004) ethical principles for medical research involving human subjects. Ethical considerations concerning autonomy and risk of causing emotional injury through questionnaires were adressed. All participants received oral and written information gave verbal and written consent and were informed about their right to disclosure at any time without reason. The potential risk of participation in the studies was of a psychological character, since it might be distressing to talk about the illness situation. Ethical considerations were also taken into account regarding the interviews. Hence, the principles of beneficence, doing good and doing no harm were abided by. The researcher was observant to patient's wishes to terminate interviews, either due to psychological distress or lack of energy. After the interview, all participants were given the opportunity to continue the conversation with the interviewer, if needed. There was a nurse at each centre that the participants could phone after the interview if needed. A nurse was also available at each centre to take phone calls from patients after the interviews, and the researcher also left her telephone number in the event that the participants wanted to contact her after the interview. All data were deidentified to ensure anonymity. To guarantee data security, the data are currently stored on discs kept in a locked file cabinet and may only be accessed for research purposes, and treated with confidentiality. The participants were informed of their right to withdraw from the study without having to give a reason and right to disclosure of the content of their registered data. The ethical committees of the Gothenburg University and Stockholm approved the study (No S-111-03 and No 03-441).

RESULTS

Paper I

In the CT group (n=75), 70 % of the women had co-morbidities, and cardiovascular disorders were the most common. Axillary clearance was performed in 75%, and 57% underwent mastectomy. Eighty-four percent of the women had CT combined with subsequent adjuvant RT and/or endocrine treatment. These subsequent treatments started about one month after the completion of the CT. Among the women that received RT (n=75), 64% had co-morbidities, the most common being musculoskeletal problems, followed by cardiovascular disorders. Sixty-four percent regularly received medication, of which endocrine therapy was the most common. Almost all women had breast-conserving surgery and a sentinel node biopsy was used in 64%.

Health-Related Quality of Life over time
In women receiving CT, a significant worsening was seen between baseline and the completion of last (six) cycle in overall QoL, physical, role, social and cognitive, functioning as well as body image and anxiety. Symptoms like fatigue, nausea/vomiting, dyspnoea, appetite loss, constipation, pain, systemic therapy side effects, hair loss and depression also worsened significantly during the same period.

In the women receiving RT, a significant worsening was noted between baseline and 2 weeks post-treatment in overall QoL, role and physical functioning, body image and anxiety. During the same period, the symptoms fatigue, dyspnoea, nausea/vomiting, pain, financial difficulties, constipation, systemic therapy side effects, arm and breast symptoms worsened significantly.

Predictors of overall Quality of Life
Significant correlations were found between overall QoL after the sixth cycle of CT and baseline values of ethnicity, musculoskeletal problems, physical, role, emotional and social functioning, fatigue, pain, anxiety and depression, and overall QoL. In the subsequent multi-variate linear regression analysis, better emotional functioning and less pain at baseline remained as predictors of post-treatment overall QoL. Together, they explained 24% of the total variance in overall QoL.

For women who received RT, significant correlations were found between overall QoL after treatment (i.e. 2 weeks after completed RT) and baseline values of ethnicity, tumour stage, sleep medication, physical, emotional, role, social and cognitive functioning, fatigue, pain, dyspnoea, financial problems and future perspective, body image, systemic therapy side effects, breast and

arm symptoms, anxiety and depression, and overall QoL. Subsequent multivariate linear regression analysis showed that lower tumour stage, better physical and emotional functioning and fewer breast symptoms at baseline remained significant predictors of post-treatment overall QoL. Together, they explained 48% of the variance in overall QoL.

Paper II

Nearly all of the 20 women in this interview study were married or cohabitating and most of the women had undergone adjuvant therapy within the past 6 months.

The experiences of the chemotherapy period
The findings of this study are based on analyses of data derived from interviews in which women with breast cancer were asked the question *'Can you describe your experiences of the chemotherapy treatment period?'* The analyses revealed a 'journey' in two parts, in which 4 themes and 12 subthemes emerged. The journey began with negative experiences that the treatment and disease brought about in the woman's and her family's life, expressed as 'fear of the unknown' and ´affects on body and mind`. The main part of the ´fear of the unknown` was felt in response to others, because the women realised that it was sometimes more difficult for her spouse than for herself to manage the situation. This led some of the women to hold back their own fears and worries, so as not to burden their relatives. This in turn led to a form of imbalance in their relationships, where the women felt that they lacked the support of those close to them.

Regarding the 'affects on body and mind*'*, the women vividly described the CT treatment as a strange feeling that circulated through the body. New and powerful images of the effects of CT treatment were given in the women's descriptions of how they had lost their own body smell and of how the treatment was experienced as an assault on the body. Some women experienced their loss of hair more negatively than they did the loss of a breast.

The journey then continued in a more positive but still somewhat negative manner. This phase was characterised by the need 'to get by' and by a 'transformed life', beginning already during the treatment, both for the women themselves and for their families. The women expressed the importance of support from significant others to meet the challenge 'to get by*'*. This was expressed in terms of both receiving support and perceiving a lack of support.

Support from health care professionals was also experienced both positively and negatively. Although professionalism was expected, other traits such as

empathy, respect and good support were considered more important. Support in the form of information was of significant importance, but many of the women thought that the amount of information given was stressful in itself. Some said that they wanted all sorts of information, even if it was negative.

The women's descriptions of the demands placed on them both by others and themselves help to illustrate how much the daily lives of these women were dominated by the CT. The women were completely focused on feeling as well as possible, which sometimes caused many of them to feel isolated. To live up to the roles of 'being a woman' and being expected to manage everything was described as difficult. It was repeatedly mentioned by the women who had chosen not to work that they felt pressured by society and the health care professionals to get back to work as soon as possible. Some of the women stated that they were not afraid of dying, but that they wanted time to prepare everything. Several women explained that maintaining their normalcy and identity and not becoming just another 'cancer case' was of the utmost importance.

Paper III

Patients included in this study were those from the CT group in Paper I. Please see Paper I above for patient demographics and clinical status.

Health-Related Quality of Life over time and the impact of age
The only significant correlations between age and the HRQoL domains were with dyspnoea and sexual functioning. Age was inversely related to worsening of dyspnoea over time, while perceived sexual functioning was lower at baseline for older women. Furthermore, among the demographic and clinical variables, age was significantly related to retirement, education level, cardiovascular disorders, as well as cardiovascular medication.

All women, irrespective of age, showed significant worsening in global health status/QoL (overall QoL), body image, sexual enjoyment, and physical, role, social and cognitive functioning during the CT treatment period. Of these, only social and cognitive functioning had fully recovered to baseline levels at 4-month follow-up. Depression, upset by hair loss, systemic therapy side effects, nausea/vomiting, constipation, fatigue, dyspnoea, appetite loss and pain also significantly worsened over the treatment period. Of these, only nausea/vomiting, appetite loss, constipation and upset by hair loss had fully recovered to baseline levels at 4-month follow-up. For all women, anxiety levels decreased during treatment and were significantly lower at the time of follow-up compared with baseline levels. Similarly, sleep was significantly worse at baseline and improved significantly to time of follow-up.

Paper IV

For a description of patient demographics and clinical status, please see Paper I above.

Daily assessment of stressful events and coping
This paper analysed patient diaries both qualitatively and quantitatively. Six categories were found: 'nausea/vomiting', 'fatigue', 'other symptoms', 'isolation and alienation', 'fear of the unknown' and 'being controlled by the treatment'. These categories illustrate how the participants experienced the first five days of adjuvant CT at cycles one, three and six. From these categories, two major domains were observed, namely, physical problems and psychosocial problems. The domain physical problems subsumed the categories 'nausea/ vomiting', 'fatigue', 'other symptoms' and the domain psychosocial problems consisted of 'isolation and alienation', 'fear of the unknown' and 'being controlled by the treatment'.

Stressful events and coping strategies
Almost 30 % of the diaries (217 diaries) recorded no stressful event during treatment (cycle 1, 3 and 6). Only one event could be recorded per diary/day and thus a total of a 538 diaries (755-217) recorded some kind of stressful event. The most frequently mentioned stressful event was 'nausea/vomiting' and the least mentioned was 'fear of the unknown'. Events associated with the domain physical problems were almost three times as frequent as those associated with the domain psychosocial problems. In addition to describing an event, patients also rated how bothersome (level of distress) it was perceived. Although the experiences of 'isolation and alienation' and 'fear of the unknown' were relatively rare, they were associated with the highest mean levels of distress. In contrast, 'being controlled by the treatment', also rarely mentioned, was associated with the lowest level of distress. 'Nausea and vomiting' was the most anticipated symptom and the event 'other symptoms' was the least anticipated.

In total, 1,790 coping strategies were reported in relation to the 538 stressful events. Hence, several different coping strategies were used to manage each stressful event, with a mean of 3.33 coping strategies per stressful event (1.790/538). The most commonly used strategies were acceptance, relaxation and distraction (thinking about something else). The least used strategy was religion (seeking spiritual support).

Coping strategies in relation to stressful events
In this paper, acceptance, relaxation, distraction and direct actions (doing something about it), were commonly used coping strategies for all types of stress. Acceptance and relaxation were particularly frequent in relation to the events 'fatigue', 'nausea and vomiting' and 'being controlled by the treatment'. Seeking social support and situation redefinition (looking at the problem in a different way) were most commonly used to handle 'fear of the unknown'. Situation redefinition was also commonly used for 'isolation and alienation', 'being controlled by the treatment' and the domain psychosocial problems. Religion was rarely used as a coping strategy, except in relation to 'fear of the unknown'. Catharsis (expressing emotions) and seeking social support also tended to be used in connection with this event. The greatest mean number of coping strategies was used in relation to 'fear of the unknown' and the least for 'other symptoms' (data not shown). Acceptance was the most frequently used coping strategy in the stress event domain physical problems, whereas distraction was the most frequently used in the domain psychosocial problems.

DISCUSSION

Through this thesis we have gained insight into the experience of adjuvant treatment over time among postmenopausal women with breast cancer. The results highlight some important aspects of the patients' experiences which need to be discussed.

Health-Related Quality of Life

Many of the different HRQoL domains were significantly affected in the postmenopausal women both during and after CT and RT (Papers I, III). The consequences and negative effects of adjuvant treatment on HRQoL among women with breast cancer have recently been reported in several other studies e.g. (Brandberg *et al.* 2003; Lee *et al.* 2005; Hopwood *et al.* 2007). In studies including both younger and older women receiving CT, it appears that younger women experience a greater decrease in physical functioning and well-being compared with older women (Arora *et al.* 2001; Watters *et al.* 2003).

Results for the women that underwent RT were similar to those for women receiving CT. For example, both groups reported increased fatigue and decreased overall QoL and physical functioning (Paper I). This is in agreement with recent studies by other authors showing that fatigue increased over the RT period (Geinitz *et al.* 2001; Knobf & Sun 2005) and that overall health status was also negatively affected (Lavdaniti *et al.* 2006). Hence, fatigue continues to be described as the most common and distressing symptom associated with different adjuvant treatments (De Jong *et al.* 2002; Payne 2002; Mock 2004; Iop, Manfredi & Bonura 2004). In our qualitative interview study (Paper II), the women described both bodily and mental fatigue, expressed by symptoms such as fainting from strain, difficulties in concentrating, and deteriorated memory. Patients with breast cancer frequently describe changes in cognitive functioning after adjuvant CT with the term ''chemobrain'' (Hess & Insel 2007). In a cohort of older women receiving adjuvant CT, Hurria and colleagues (2006a) found that a subset of these women experienced a decline in cognitive function from pre-CT to 6 months post-CT. Other studies in the literature corroborate CT-associated cognitive function declines in subsets of younger breast cancer survivors who received adjuvant CT (Tchen *et al.* 2003; Wefel *et al.* 2004; Bender *et al.* 2006). Among the postmenopausal women in our quantitative studies, we did not find any statistically significant declines in cognitive function during the study period. However, it is possible that our follow-up period was too short. It would therefore be of interest and importance to follow-up our patients up to two years to see if their cognitive function changes and if declines occur and if they impact on the women's lives.

Among the women who received RT, an increase was also seen over time in more localised symptoms, e.g., arm and breast symptoms (Paper I). These problems probably reflect the immediate local effects of RT, such as skin reaction and swelling of the irradiated area. Similar results have recently been reported by Knobf and Sun (2005) in a study of older women with breast cancer. In that study, about one-third of the patients had an increase of breast oedema over time and these problems persisted after the treatment was completed. Wengström and colleagues (2000) reported that skin problems steadily increased from the third week of RT treatment and peaked at the completion of therapy in middle-aged women.

Many breast cancer studies report that despite advances in the prevention and treatment of emesis, nausea and vomiting is still considered to be among the most severe, feared and distressing symptoms of CT (Lee *et al.* 2005; Viale 2006; Booth *et al*. 2007), despite the widespread use of 5-HT^3 antagonists (Lee *et al.* 2005). Nausea/vomiting in our studies increased significantly over both the CT and RT period (Paper I), but returned to baseline levels at 4-month follow-up after CT (Paper III). Most of the functional changes described in QoL studies have been found to be attributable to CT-induced nausea and vomiting (Bergkvist & Wengström 2006; Bloechl-Daum *et al*. 2006).

In our interview study (Paper II), the women's need for social support was very apparent from their narratives. The family was described as an important part of their support system and the role of the spouse was described as a 'lifeline'. These findings are consistent with those described by others (Drageset & Lindstrom 2003; Manning-Walsh 2005) indicating that social support from family members and friends helps to decrease the negative effects of symptoms on QoL. The interviews also highlighted the importance of support from health care professionals. The women's narratives indicated that they desired professional health care support that emphasises different aspects of caring, such as empathy, respect and information. In a recent study Berg, Skott & Danielson (2007) examined caring relationships in a medical context, and identified three themes that formed the basis of the caring relationship, namely, patients and nurses respect for each other and for themselves, their responsibility to reach out to each other and engagement. To create a caring relationship with the patients is one of the most important tasks in nursing such as support to patients in difficult care situations. According to Walker *et al.* (2003), patient satisfaction may be enhanced when health care professionals help the patients with their psychosocial needs associated with the disease (Walker *et al.* 2003). In a recent study by Arving (2007), it was also concluded that there is a need for psychosocial support among breast cancer patients and that this need may be met by specially trained nurses as effectively as by psychologists.

Depression increased during treatment and at 4 month follow-up in the women undergoing CT (Papers I, III). Some researchers have concluded that the diagnosis of cancer itself produces a greater amount of distress than other diagnoses e.g. (Shapiro *et al.* 2001). Earlier studies have shown that women with substantial symptoms of depression and anxiety often experience increased physical side effects, which may lead to an experience of reduced overall QoL (De Jong *et al*. 2002; Badger *et al.* 2004; Schreier *et al.* 2004; Massie 2004). Symptoms of depression and anxiety also decrease women's abilities to mobilize critical support when the need for it is greatest (Manne *et al.* 2004).

The impact of age on Health-Related Quality of Life

Age did not seem to have any impact on the HRQoL domains except for dyspnoea and sexual functioning (Paper III). Age was inversely correlated to change in dyspnoea from baseline to follow-up (i.e., the younger the age, the greater the decrease in dyspnoea at follow-up), whereas older women perceived their sexual functioning as significantly lower at baseline. These results indicate that in our consecutively selected sample of postmenopausal patients aged 55-77 years undergoing adjuvant CT, age was not a predictor of decreased HRQoL. Muss and colleagues (2005) found that older patients tolerate and benefit from more aggressive CT almost as well as do younger patients and concluded that older patients with breast cancer in otherwise good health should therefore be offered participation in ongoing clinical trials with adjuvant CT. Similar results were reported in a review by Burdette-Radoux and Muss (2006). However, in some studies elderly patients experience greater toxicity than younger patients, leading to loss of cognitive function (Hurria *et al*. 2006a) and decreases in QoL and loss of physical function (Hurria *et al.* 2006b). Co-morbidity and increased age is seen as key considerations in offering systemic adjuvant treatment to older women, since they can minimize the potential benefit of any adjuvant therapy, and may even increase the side effects of breast cancer treatment (Yanick *et al.* 2001; Whiterby & Muss 2005; Fehlauer *et al.* 2005). As shown in Paper III, the women in the older age group experienced more cardiovascular disorders. This result is consistent with the findings of Yanick *et al*. (2001) where approximately 30% of those aged 65-69 years had one or more major co-morbidities. Our results, together with those from earlier research suggest that age, co-morbidities and side effects should be carefully considered in treatment decision making. Treatment decisions should be made cautiously, carefully weighing the risks against the beneficial effects of treatment. As health care professionals we must therefore learn more about how older women with breast cancer experience and cope with the advanced treatments that are becoming available. We must also make efforts to ascertain what the needs of these women are so that we can offer them the best care available.

Predictors of overall Quality of Life

Significant correlations were found between overall QoL after the last cycle (sixth) of CT and baseline emotional functioning and pain (Paper I). This result indicates that women who have better emotional functioning and less pain before they start their treatment have a better chance of a higher overall QoL when the treatment is over. In patients undergoing RT, emotional functioning was also one of several important baseline predictors, together with tumour stage, physical functioning, and breast symptoms. Here, better physical and emotional functioning, fewer breast symptoms and lower tumour stage at baseline seemed to predict better overall QoL at the end of RT.

Our finding that emotional functioning seems to predict overall QoL, for both CT and RT-treated patients is in line with current knowledge concerning emotional reactions. It is known that emotional reactions to stressful life events may lead to anxiety, tension, and depression (Lazarus 2006). These in turn may lead to increased physical side effects and ultimately to reduced overall QoL (De Jong *et al.* 2002; Badger *et al.* 2004; Schreier *et al.* 2004; Massie 2004). In a recent study by Östlund and colleagues (2007) in lung cancer patients and their relatives, emotional functioning was found to be an independent predictor of overall QoL, together with fatigue. Emotional functioning may become a major focal point for health care investigations in the future due to its strong relationship with overall QoL in women. Knowledge about these predictors may add relevant knowledge for clinical practice to increase the understanding of important areas of QoL in assessment of care.

Stressful events and coping strategies

Surprisingly, almost 30% of the diaries in Paper IV did not document any stressful events during CT. This may suggest that the everyday lives of these breast cancer women are not dominated either related to the disease. Physical problems were reported three times as often as psychosocial problems (Paper IV), this was also described in a powerful way in the theme affects on body and mind (Paper II). Nausea/vomiting was among the most frequently recorded stressful events, was also the most anticipated one (Paper IV), and was also seen to increase over time (Papers I, III). The fact that nausea/vomiting was the most anticipated stressful event probably reflects the information that is given by health care professionals before treatment and what the general public knows about CT and its side effects (Paper IV). This finding also indicates that health care professionals still do not seem to know which pharmacologic or non-pharmacologic treatments offer best relief from CT-induced nausea/vomiting, and suggests the need for further research on this well-known symptom. In the diaries, women described feelings of being left 'outside', of feeling down, and

of loneliness, which in the analyses were subsumed under the category 'isolation and alienation' (Paper IV). On a similar note, in Paper II the lack of support from significant others was found to led to a feeling of imbalance in the relationship and a feeling of loneliness. Isolation and alienation were associated with the highest levels of distress in Paper IV, and these stressful events could possibly be seen as a form of psychological distress (depression and anxiety). Psychological distress is one of the most commonly reported symptoms in relation to the diagnosis of cancer and its treatment (Trask 2004; Kissane *et al.* 2004; Sharpley & Christie 2007) and was also seen to increase during treatment in Papers I and III.

Acceptance, relaxation and distraction were the most commonly used coping strategies for managing all stressful events among the postmenopausal women (Paper IV). Correspondingly, they were also the most frequently used strategies to handle stressful events in patients with gastrointestinal cancer in a study by Wasteson and colleagues (2002). Acceptance, relaxation and distraction in particular were frequently used by the women in relation to the experience of fatigue and nausea/vomiting (Paper IV). Similar coping strategies were found to be used to manage dyspnoea by patients with lung cancer in a recent study by Henoch, Bergman and Danielson (2007). The benefits of using these coping strategies to reduce fatigue were recently documented by Cohen and Fried (2007), who found relaxation and guided imagery helped to reduce fatigue. Relaxation therapy has also been shown to improve QoL (Walker 1999) and to reduce depressed mood, anxiety and pain (Hernandez-Reif *et al.* 2005) in women with breast cancer. Also, non pharmacologic interventions, such as self-hypnosis, relaxation and distraction have been shown to relieve CT-induced nausea (Roscoe *et al*. 2003; De Carvalho, Martins & dos Santos 2007).

The women recorded the use of a wide variety of coping strategies and an average of 3.33 different coping strategies was observed per reported stressful event (Paper IV). In other words, the women did not rely on a single coping strategy but rather employed many different strategies to deal with the same stressful event. This has been confirmed by other studies of patients with different cancer diagnoses. For example, Miedema and colleagues (2007) reported that young adults use various coping strategies to come to terms with the disease and its treatment. Link and colleagues (2004) found that younger cancer patients use many coping strategies and thought of them as methods of control, were more confident of being cured and used more proactive strategies, e.g., lifestyle changes. In another interview study by Persson and Ryde´n (2006), it was suggested that well-adjusted persons with somatic disabilities and/or chronic illness use several types of coping strategies that complement each other. In a recent intervention study by Schneider and Hood (2007), it was suggested that using distraction is most effective during the initial CT, when

patients are more anxious and less likely to have developed coping skills for the stressful situation. However, they also stated that more studies are needed to explore the timing of the intervention. Further research is needed to better understand the relationship between stressful events and the different coping strategies used by postmenopausal women. Taken together, these data support the feasibility of and need for further research studies involving daily assessments and short recall times.

METHODOLOGICAL CONSIDERATIONS

The use of both quantitative and qualitative methods strengthened the results of the thesis, and it seems like a multi-method is suitable for reaching the experience of a difficult time in these women's lives.

Quantitative studies

Various steps were taken in this thesis to attempt to ensure the validity of our findings. In general, consecutive inclusion of patients enhances the generalisability of study results; however, systematic drop-out of patients represents a threat to both generalisability and internal validity. Possible criticism could also be levelled against the sample size (Papers I, III-IV) which may lack in power, since this was not tested. Although we consecutively included patients to the studies, about 24% of the women with CT were lost to follow-up (Paper I, III-IV). Although these women did not differ from those remaining in the studies regarding baseline HRQoL, the possibility that they differed over the course of treatment may be a potential source of confounding. No significant correlation between age and questionnaire completion at follow-up was found, and those who were lost to follow-up were equally distributed in the younger and older age groups, as were those who withdrew during the 6-cycle treatment programme due to medical problems. In the RT group, there was a 5% loss at follow-up (Paper I). All tests in Paper III were performed with age as a continuous variable, but for descriptive purposes data were divided into a younger group (55-64 years) and an older group (65+). A pilot study was performed to evaluate study logistics using 10 of the 75 patients in the CT group (Paper I); no adjustments to the study protocol were required. We also investigated whether or not the mode of questionnaire administration (personal interview at home/hospital versus telephone interview) (Paper I and III) influenced HRQoL ratings and response rates; no significant differences were found between methods regarding either of these. The sample in Papers I and III was not randomised, which may weaken the external validity of these studies because random selection minimizes the influence of systematic biases. Another weakness is that in Paper III, most of the women who had a dose reduction during treatment were older (5 of 7).

The internal consistency reliability of the various questionnaires used in this thesis was evaluated with the Cronbach's alpha coefficient, which is a function of both the average inter-item correlation and the number of items in a scale (Cronbach 1951). The instruments used in Papers I and III (EORTC QLQ-C30, BR-23, and HADS) are all well-known and widely used internationally. The reliability of the Swedish versions has been assessed in healthy individuals

(Lisspers *et al*. 1997; Michelson *et al*. 2000) and in different groups of cancer (Michelson *et al*. 2000; Osborne *et al.* 2004) Reliability coefficients should be at least 0.70 in HRQoL instruments for use in clinical trials (Whalen & Ferrans 2001). The alpha values in this thesis were above 0.70 in all scales and items, except for the EORTC QLQ-C30 scales cognitive functioning and nausea/vomiting and BR23 systemic therapy side effect.

We also compared our results pertaining to the EORTC QLQ-C30 and BR23 with those from two earlier studies performed in a healthy population in Sweden (Michelson *et al.* 2000) and in Canada in women with breast cancer (Watters *et al.* 2003). Briefly, we found that the elderly women in our study had significantly better physical functioning at baseline compared to both the healthy Swedish reference group and the older Canadian breast cancer patients. However, our results also showed that our older women experienced worse HRQoL and more symptoms during treatment. No other significant differences were seen at baseline between these different study groups, which we think strengthens the use of EORTC in this thesis.

Finally, our ability to generalise our findings to all postmenopausal women with breast cancer is limited by relatively small patient sample sizes. There is also a risk of selection bias, as indicated by the fact that baseline functioning levels in most domains were similar in younger and older patient groups (Paper III). The strengths of the studies comprising this thesis are the demographic and diagnostic homogeneity of the consecutively included sample, as well as the use of consistent inclusion criteria and validated questionnaires (Polit & Beck 2004).

Qualitative studies

The qualitative methods applied in this thesis were guided by criteria recommended by Lincoln & Guba (1985) and Leininger (1994). These criteria include credibility, dependability, confirmability and transferability.

Credibility refers to the 'believability' of the findings. To enhance credibility, efforts were made to create conducive conditions for the interviews (Paper II), such as providing patients with comprehensive information about the study, optimal settings for the interviews (own homes/private place at hospital), adequate time for the interviews, an open question to allow the women to freely narrate their story (Paper II) and the opportunity to ask questions about the diary (Paper IV). Efforts were also made to describe the categories and themes in as much detail and as vividly as possible, so as to communicate the findings as clearly as possible. The use of a diary has the advantage of providing

information regarding the frequency of occurrence of symptoms, which in turn gives a more comprehensive picture of how symptoms change from day to day. In contrast, standardised questionnaires often ask about the most commonly occurring and/or typical problems during the past week.

Dependability pertains to the stability of data over time. According to Lincoln & Guba (1985), credibility cannot exist without dependability and they suggested that a thorough description of credibility is needed to establish dependability. They also think that dependability is closely related to confirmability. To strengthen confirmability in a qualitative study the researcher needs to describe the data analysis process clearly and succinctly (Hilton 2001). We have tried to do so by carefully describing the content analysis procedures used here. Quotations extracted from the texts were also used to illustrate and provide more concrete examples of thoughts, feelings or moods of the participants` diary entries and interview texts (Paper II, IV). In this thesis, the interviews and diaries were independently analysed by two (Paper II) and three (Paper IV) authors and then discussed and compared with the other authors. In our analyses of the interview material a form of saturation was reached as the subthemes and themes that emerged during our initial analyses of the first 10 interviews required only minor revisions after the remaining interviews had been analysed.

Transferability refers to how well the findings in a qualitative study can be applied to another, similar setting and depends on the degree of similarity between the study populations and the actual settings. Transferability from our results is strengthened through the fact that similar results were shown in the quantitative studies (Paper I, III).

CONCLUSIONS

The overall aim of this thesis was to explore how postmenopausal women with breast cancer experience adjuvant treatment. The following are the major findings of this thesis:

- There were no significant relationships between age and any of the HRQoL domains, except for dyspnoea and sexual functioning. Age was inversely correlated to change in dyspnoea from baseline to follow-up, while older women reported significantly lower sexual functioning at baseline.
- A high proportion (30%) of the diaries recorded no stressful events during the adjuvant CT.
- Among the women who experienced stressful events while undergoing adjuvant treatment, more of the events were related to physical problems than to psychosocial problems.
- Although RT and CT impacted on HRQoL in a similar manner, the women receiving CT reported more localised problems directly related to the treatment and earlier surgery.
- The women that received CT experienced several symptoms. Nausea/vomiting was one of the most stressful events and this problem increased significantly during treatment and up to four months after treatment. It was also the most anticipated stressful event by the women.
- Fatigue also increased during treatment and remained high at time of follow-up. Both bodily fatigue and mental fatigue were described in the interviews. This symptom covaried with aspects of cognitive functioning, such as fainting from strain, difficulty concentrating and deteriorated memory.
- Depression also increased during the CT period and remained high at time of follow-up. In the diaries, depression was expressed as a feeling of isolation and alienation. The latter were considered to be the most distressing stressful events the women experienced.
- Social support was generally described as positive and important (a 'life line') by the women. They felt that they received good social support from their families and friends, as well as from health care professionals. The women also related some negative experiences; for example, they mentioned that lack of support from close ones led to them to feel that their lives were out of balance. Moreover, they felt that empathy was lacking in the support they received from health care professionals.
- Baseline predictors for better overall QoL after adjuvant CT were better emotional functioning and less pain. In contrast, in women that received RT, baseline predictors were better emotional and physical functioning, lower tumour stage and less breast symptoms at baseline.

- Many different coping strategies were employed for each stressful event. Acceptance, relaxation and distraction were the most common coping strategies for all stressful events.

IMPLICATIONS FOR CLINICAL PRACTICE AND RESEARCH

The findings in this thesis on how postmenopausal women with breast cancer experience adjuvant treatments can be useful in both clinical practice and research. Our findings add new knowledge that may be implemented in and help to advance the care of these women. For example, we found that fatigue and nausea/vomiting continue to be commonly experienced CT and RT-induced symptoms, indicating that health care professionals still do not know which pharmacologic or non-pharmacologic treatments are optimal in assisting these women. Social and emotional functioning are also important issues to take into consideration in treatment planning and care of these women.

Our results also gave some hints about what needs to be further studied. For example, our finding that the women used several different coping strategies to manage the same stressful event suggests the need for research to determine which strategies may be most effective in efforts to manage this disease and its treatment. More broadly, there is a need for research that sheds light on relationships between stressful events and coping strategies used by these women. Results from such research could potentially aid us in our endeavours to more effectively help and support these patients. Such studies could benefit from research designs involving daily assessments, short recall times and larger samples.

Our finding that overall QoL was predicted by emotional and physical functioning, pain, tumour stage, and breast symptoms may also have important implications for the development of individual care strategies for these women. Studies should be performed to evaluate if interventions targeting these predictors help to prevent decreases in overall QoL during and after adjuvant treatment.

To date, few studies in the research literature have evaluated elderly patients' experiences of adjuvant treatment. Given that the current growth of this patient group it is of utmost importance to further investigate if more aggressive adjuvant treatments are suitable for this group of women and, if not, why they are unsuitable. Larger studies are needed to verify our finding that age had no impact on overall QoL in older patients with breast cancer during and after adjuvant therapy.

We believe that all of these findings are important for health care professionals to acknowledge, particularly when designing interventions to support women with breast cancer, but also in research to evaluate such interventions. Clearly, not all issues regarding these women's experiences could be addressed in this

thesis. There is much left to be done, and it is obvious that these women's situation cannot be understood as simply a function of chronological age. Future investigations combining qualitative and quantitative methodologies and involving multiprofessional teams in larger studies could possibly help to enrich our understanding of the problems faced by women with breast cancer and promote more solid results.

ACKNOWLEDGEMENTS

I would like to express my deep gratitude to everyone who has contributed to this thesis by sharing their experiences and knowledge with me and by being supportive throughout the long process of completing this work. I particularly want to thank the following persons:

All patients, for generously sharing your experiences and thoughts with me.

Professor Ella Danielson, my main supervisor during the last years and our seminar leader during the whole doctoral programme, for your great support and guidance throughout my work on this thesis. Thanks for your engagement, warm friendship and concern about the well-being of us doctorial students. Your constructive criticism made me believe that I could reach a higher level.

Professor Fannie Gaston-Johansson, my main supervisor during the first four years of my doctorial studies, for guiding me thorough the research process during these years, and for believing in my capacity.

Senior Lecturer Karin Ahlberg, supervisor, for your support and encouragement and for challenging me to apply for the doctoral programme a long time ago. The discussions with you helped me to understand my own thoughts and writing so much better.

Associate Professor Lars-Olof Persson, supervisor, for giving me so much of your time and engagement, for sharing your great knowledge and experience of research. I am grateful for all constructive and enlightening discussions about measurements and research findings and for all good advice and help during the analyses and writing of this thesis.

Associate Professor Per Karlsson, supervisor, for all your medical advice during the writing of this thesis, for your excellent knowledge about the care of patients with breast cancer and for taking part in the studies and sharing your experiences and ideas with me.

The Institute of Health and Care Sciences, for making this thesis possible by providing scholarships and research assistantships.

The staff at the Sahlgrenska University Hospital: Department of breast Surgery, Gothenburg, and Karolinska University Hospital, Department of Oncology, Stockholm and Skövde Department of Surgery, for kindly receiving me, helping me in the inclusion of patients and giving me a place to meet the patients during the data collection period.

my sister Alida and their families, for your love and encouragement during the work with this thesis.

And last but not least, I would like to thank my family for your patience when my whole world was paper and statistics. My husband Roger, for loving and caring about me and for making me laugh. You are my best friend and I am so glad that I have you near. My 'prince and princess', Therese and Mattias, for being such loving and caring children and for not reproaching me for not always being around. You are the most important people in my life and I am so very proud of you, and I love you both 'every day'.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Upplevelsen av tilläggsbehandling hos postmenopausala kvinnor med bröstcancer, hälsorelaterad livskvalitet, symtom upplevelse, besvärande händelser och bemästringsstrategier.

Bakgrund

Fokus för denna avhandling har varit postmenopausala kvinnor, 55 år och äldre med bröstcancer och deras upplevelse av tilläggsbehandlingar med cytostatika och/eller strålbehandling. I Sverige är bröstcancer den vanligaste formen av cancer bland kvinnor och medianåldern för insjuknande är 60-64 år. Av alla som insjuknade i bröstcancer under 2006 så var 73 % av dessa kvinnor 55 år eller äldre. Behandlingen av den något äldre kvinnan är därför ett viktigt område för forskning eftersom antalet i denna patientgrupp ständigt ökar. Studier har visat att överlevnaden för kvinnor med bröstcancer har ökat mycket tack vare allt mer intensiva behandlingsstrategier. Samtidigt har man sett att olika symtom av dessa behandlingar påverkar kvinnor på ett negativt sätt som i förlängningen ger en försämring av livskvaliteten. De flesta av de studier som är gjorda för att följa och utvärdera dessa nya behandlingsstrategier och dess påverkan på upplevd livskvaliteten är gjorda på yngre eller medelålders kvinnor. Frågan blir därför om man kan överföra kunskapen om yngre kvinnors upplevelse till de äldre? Vidare visar studier att äldre kvinnor inte erbjuds samma intensiva behandlingar som yngre på grund av risken för att oönskade sidoeffekter skulle påverka de äldre mer negativt än de yngre. Vissa studier har dock visat motsatsen, att de äldre tolererar och har lika många fördelar av dessa behandlingar som yngre, men fortfarande så finns det kunskapsluckor angående vad dessa tilläggsbehandlingar gör för den upplevda livskvaliteten under och efter avslutad behandling. För att lära oss mer om hur äldre kvinnor upplever och klarar av nya mer intensiva tilläggsbehandlingar och för att kunna vidta adekvata åtgärder för att förbättra patienternas livskvalitet finns det behov av ytterligare forskning.

Syfte

Det övergripande syftet med avhandlingen var att beskriva hur postmenopausala kvinnor, 55 år och äldre, med bröstcancer upplever tilläggsbehandling med cytoststika och/eller strålbehandling.

Metod

Avhandlingens upplägg är beskrivande och består av två kvalitativa studier och två kvantitativa, där både intervjuer, dagboksanteckningar och frågeformulär användes. Kvinnor från tre olika sjukhus i Sverige ingick i studien. I en av studierna genomfördes intervjuer med 20 kvinnor som under det senaste året genomgått en tilläggsbehandling med cytostatika. Kvinnorna fick med egna ord berätta om hur de upplevt denna tid av cytostatika behandling. I två av studierna användes frågeformulär som besvarades av 150 kvinnor, 75 som fick cytostatika och 75 som fick strålbehandling. Frågeformulär mäter den upplevda hälsan och livskvaliteten, olika symtom, funktioner, samt oro och ångest. De besvarades före start av behandling, under pågående behandling samt en tid efter avslutad behandling. I den sista studien användes dagböcker, med frågan 'vad har varit mest besvärande för dig under dagen'. Dessa fylldes i av de kvinnor som fick cytostatika med start på behandlings dagen och påföljande fyra dagar. I dagböckerna skulle kvinnan också beskriva vad man själv gjort för att må bättre, detta upprepades under tre av de totalt sex cytostatika- behandlingarna.

Resultat

Det fanns inga signifikanta samband mellan ålder och de symtom och funktioner som undersöktes under cytostatikabehandlingen, förutom för andnöd och sexuell funktion. Desto yngre kvinnan var ju mer andnöd upplevde hon efter avslutad behandling jämfört med tiden före behandlingen startade. Sexuell funktion var nedsatt ju äldre kvinnan var vid start av behandling. Trettio procent av alla dagböcker som fylldes i under behandlingen uppgav inga besvär under dagen som gått. Bland de kvinnor som upplevde några besvär under behandlingen med cytostatika var det fler som var relaterade till kroppsliga problem än till psykosociala problem. Konsekvenserna av dessa två tilläggsbehandlingar var på många sätt väldigt lika. Kvinnorna upplevde en mängd olika symtom och försämring av olika funktioner samt livskvalitet. Strålbehandlingen påverkade dock kvinnorna mer lokalt, direkt kopplat till operations och det strålbehandlade området, medan de som fick cytostatika upplevde en påverkan på hela kroppen. Illamående/kräkningar var ett av de symtom som ökade mest under behandlingen, kvarstod upp till fyra månader efter avslutad cytostatikabehandling och visade sig också vara det symtom som var mest förväntat av kvinnorna. Trötthet och depression ökade också över behandlingstiden och kvarstod med ökat värde fyra månader efter avslutad behandling. Socialt stöd visade sig vara viktigt för dessa kvinnor; från både anhöriga och vänner men också från sjukvårdspersonalen. När faktorer som kunde förutspå hur livskvaliteten under behandlingen utvecklades visade det sig att för kvinnor som erhöll cytostatika så innebar en bättre känslomässig funktion vid start av behandlingen tillsammans med mindre smärta en högre sannolikhet

för bättre total upplevd livskvalitet vid fyra månader efter avslutad behandling. För de kvinnor som fick strålbehandling var det bättre känslomässig och fysisk funktion, lägre tumörstadie och färre symtom från det opererade bröstet vid start av behandlingen som var faktorer som kunde förutspå en förbättrad livskvalitet två veckor efter avslutad behandling. Kvinnorna använde en mängd olika strategier för att hantera sina besvär och de vanligaste strategierna som användes var att acceptera problemet som det var, att kunna slappna av samt att tänka på något annat.

Diskussion

Sammanfattningsvis har denna avhandling visat att de postmenopausala kvinnor, 55 år och äldre, som vi undersökt påverkas på en mängd olika sätt av dessa tilläggsbehandlingar. Åldern i sig verkar dock inte påverka livskvaliteten under och efter tilläggsbehandling. Vården för dessa kvinnor kan förbättras genom att fokusera speciellt på specifika symtom som t.ex. illamående, kräkning, trötthet, depression samt social och känslomässig funktion. Interventionsstudier skulle behöva göras med specifik inriktning på de faktorer som framkommit för att se om man i ett tidigt skede av sjukdomen möjligen kan förebygga att den totala livskvaliteten försämras efter avslutad behandling. Fortsatt forskning för att bättre förstå de relationer som finns mellan symtom och de olika hanteringsstrategier som dessa kvinnor använder skulle kunna vara till hjälp för vårdpersonal att mer effektivt hjälpa och stödja dessa kvinnor till att på bästa sätt klara av tilläggsbehandlingar.

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