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ORIGINAL ARTICLE

Quality of life of women treated with radiotherapy for breast cancer

T. S. Lee · S. L. Kilbreath · K. M. Refshauge · S. C. Pendlebury · J. M. Beith · M. J. Lee

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Abstract
Goals of work Radiotherapy is routinely used in the treatment of early breast cancer, particularly in women who have undergone lumpectomy. Its impact on the quality of life of patients is important and is taken into consideration when making informed choices about treatment from both a patient's and health professional's point of view. This study reports on the quality of life of women at baseline, the completion of radiotherapy and 7 months after the completion of radiotherapy.
Materials and methods European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C-30 and BR-23 questionnaires were used to evaluate quality of life of 61 women treated with radiotherapy for breast cancer. Additionally, demographic and treatment variables were analysed in relation to quality of life outcomes to determine if there were any significant predictors of quality of life.
Main results There was no difference in quality of life of women at baseline, completion and 7 months after completion of radiotherapy. Fatigue and breast symptoms increased during radiotherapy but returned to baseline levels at 7 months. Fatigue was the strongest predictor of poor quality of life in women after radiotherapy.
Conclusion Women retain a high quality of life and return to baseline function by 7 months after radiotherapy. Treatment may best be targeted to alleviate fatigue and breast symptoms during radiotherapy.

Keywords Breast cancer · Radiotherapy · Quality of life · Fatigue

T. S. Lee (✉) · S. L. Kilbreath · K. M. Refshauge · M. J. Lee
School of Physiotherapy, University of Sydney,
P.O. Box 170, Lidcombe 1825, Australia
e-mail: tlee8503@mail.usyd.edu.au

S. C. Pendlebury
Department of Radiation Oncology, Sydney Cancer Centre,
Royal Prince Alfred Hospital,
Sydney, Australia

J. M. Beith
Sydney Cancer Centre, Royal Prince Alfred Hospital,
Sydney, Australia

Introduction

Patients are becoming more autonomous when it comes to making decisions about their health care, and women are routinely seeking information relating to their breast cancer treatment and side effects to make informed choices about their treatment [17, 23]. Women diagnosed with early breast cancer are confronted by the choice of either mastectomy or the combination of lumpectomy and radiotherapy. Concerns about radiotherapy were reported to significantly influence women's choice of mastectomy over lumpectomy [28, 33, 41]. These concerns include side effects of radiotherapy [41].

Radiotherapy causes a number of side effects, the risk of which depend on the number and placement of radiation fields, dosage, fraction size and radiosensitivity [29]. Skin irritation such as erythema, desquamation, swelling and arm or breast pain commonly occur in the treatment area, and generalised fatigue is also experienced by some women [4, 15]. Less common side effects are acute pneumonitis [20, 35], rib fracture [32, 34], ischaemic heart disease [16] and second malignancy [18, 44].

Research concerning the quality of life of women during and after radiotherapy for breast cancer is surprisingly scarce. There have been a total of two randomised controlled trials examining the effects of radiotherapy on quality of life of women after breast cancer. Both of these trials administered

radiotherapy treatment using the outdated Cobalt-60 machines, known to cause more acute toxicity than megavoltage treatment [10]. Of these trials, Whelan et al. [43] found that women who underwent radiotherapy have a lower quality of life than women not receiving radiotherapy at 1 and 2 months, but Rayan et al. [36] found no difference between these groups at 3, 6 or 12 months after surgery. Two prospective trials evaluated the effects of radiotherapy using current treatment protocols with linear accelerators and tangential megavoltage energy fields on quality of life. Wengstrom et al. [42] found an improvement in quality of life from the start of radiotherapy to 2 months after its completion, and Back et al. [4] found radiotherapy to have no effect on quality of life at 6 weeks after the completion of treatment. These studies present differing results, and no conclusion can be derived on the effects of radiotherapy on the quality of life of women after breast cancer.

The primary aim of this study was to describe the quality of life of women undergoing radiotherapy for breast cancer. The secondary aim was to identify any prognostic factors contributing to the quality of life of women receiving radiotherapy. Identification of adverse prognostic factors may help health professionals target women who are at risk of deteriorations in quality of life.

Materials and methods

Participants

The participants of this study were the same participants engaged in a randomised controlled trial evaluating the effects of a pectoral stretching programme for women undergoing radiotherapy for breast cancer [19]. Women were included if they had undergone breast cancer surgery and were receiving radiotherapy to the breast or chest wall in either two fields (medial and lateral tangents: 50 Gy in 25#, or 42.5 Gy in 16#) or three fields including a supraclavicular fossa field (50 Gy in 25#). Women were excluded if they received radiotherapy to the axilla. Sixty-four consecutive women were referred to the study by the radiation oncologist. Two women were excluded because they received radiotherapy to the axilla, and one was excluded because of transport problems.

The mean age was 54±12 years ($\bar{x}$±SD), and the mean body mass index (BMI) was 26.6±4.8 for the cohort (Table 1). The average time after surgery for entry into the trial was 3.6±1.9 months. Approximately half of the participants in each group had breast cancer on their dominant side; that is, surgery was performed on the side of the upper limb they normally use. Ten women were diagnosed with ductal carcinoma in situ (DCIS), 44 women had early stage breast cancer (stages I and II) and seven women had stage III tumours. Sixteen women did not receive axillary surgery, 21 women had sentinel node biopsies and 24 women had full axillary dissections.

Table 1 Participants' characteristics

Participants' characteristics		Mean (SD)[a] or n[b]
Age[a]		54 (12)
BMI[a]		26.6 (4.8)
Affected side (dominant/non-dominant)[b]		31:30
Time since surgery (months)[a]		3.6 (1.9)
Cancer stage grouping[b]	DCIS	10
	Stage I	21
	Stage II	23
	Stage III	7
Surgery type (mastectomy/lumpectomy)[b]		13:48
Axillary surgery[b]	None	16
	Sentinel node biopsy	21
	Axillary dissection	24
Chemotherapy[b]		34
Tamoxifen or Arimidex[b]		49

[a] Mean (SD)
[b] Number of patients

Protocol

Women were randomised into one of two groups, a control or a stretch group throughout the radiotherapy period. Quality of life questionnaires were completed by 61 women before the start of radiotherapy (baseline) and at the completion of radiotherapy (within 7 days of the completion date). At 7 months follow-up, 57 women completed the questionnaires. Participants were assessed 7 months after the completion of radiotherapy because hospital protocol was to review patients at 1 month after radiotherapy, then 6 months after that appointment; hence, the final follow-up was a total of 7 months after the completion of radiotherapy. Three patients were lost to follow-up as they were not available for assessment or were not contactable. Ethics approval was granted by the Sydney South West Area Health and University of Sydney Human Ethics Committee. Written informed consent was obtained from all participants.

Questionnaires

The European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire and its breast cancer module (QLQ-BR23) were used to measure quality of life in this study. These questionnaires have been tested and confirmed as reliable and valid when measuring quality of life outcomes for cancer patients [1, 39]. The EORTC QLQ-C30 consists of 30 questions organised into five functional scales (physical, role, cognitive, emotional and social), nine symptom scales (fatigue, nausea and vomiting,

pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea, financial difficulties) and a global health status scale that assesses overall quality of life. The QLQ-BR23 module consists of 23 questions organised into four functional scales (body image, sexual functioning, sexual enjoyment and future perspective) and four symptoms scales (systemic side effects, breast symptoms, arm symptoms and upset by hair loss).

For both questionnaires, a four-point response scale was used to assess each item concerning functions or symptoms, and a seven-point scale was used for global health status/quality of life. Raw scores were linearly transformed into a score of 0–100 for processing according to the EORTC manual [9]. Higher scores for the functional and global health status/quality of life scales represented better function and quality of life. In contrast, higher scores indicated greater problems for the symptom scales. The mean score (±SD) was calculated for each scale at each time of measurement. Consistent with previous studies, only differences greater than ten points on the transformed questionnaire scale were considered clinically meaningful [25, 31].

To determine whether there was a change in questionnaire scores throughout the duration of the study, two-way repeated-measures analysis of variance was used. The within-group factor was time (baseline, completion of radiotherapy, 7 months follow-up) and the between group factor was group allocation (control, stretch). Cases lost to follow-up were excluded from the repeated-measures tests; hence, there were 57 complete data sets from the cohort. Linear regression was conducted to determine if any patient or treatment characteristics explained the variance in quality of life. The dependent variables included whether the affected side was dominant (yes or no), cancer stage group (DCIS, stage I, II or III), type of cancer surgery (mastectomy or lumpectomy), type of axillary surgery (none, sentinel node biopsy, axillary dissection), number of radiotherapy fields (two or three), application of electron boost (yes or no), chemotherapy (yes or no), hormone therapy (yes or no), age and BMI. The same dependent variables were used in a second linear regression to determine predictors of fatigue. Additionally, linear regressions were performed to see if any of the EORTC symptom or function items predicted global health status/quality of life scores at each of the time points measured. Statistical analyses were performed using SPSS Version 12.0 software (SPSS, Chicago, IL).

Results

No difference was found between the control and stretch group for the items reported on the EORTC QLQ-C30 and the QLQ-BR23 module at any of the time points measured. For the BR-23 module at baseline, 34 of the participants found the question about sexual enjoyment not applicable, and 40 participants found the question about hair loss not applicable. These items were therefore omitted from the analysis. Unless otherwise stated, the results are reported in mean scores±SD for the whole cohort.

The global health status scores reflecting quality of life were high. Radiotherapy did not affect quality of life, although there was a trend towards improvement in quality of life between the completion of radiotherapy (71±20) and 7 months (78±17; Fig. 1). Physical, emotional, cognitive and social functioning scores were consistently high. Role functioning increased from a mean of 78±29 at the completion of radiotherapy to a mean of 90±20 at 7 months (Table 2).

Fatigue increased during radiotherapy but it resolved with time, returning to baseline levels at 7 months after treatment (Fig. 2). No change was found for pain, dyspnoea, insomnia, appetite loss, constipation and diarrhoea during the period of the study. Financial difficulties remained stable throughout the study.

Breast symptoms increased from baseline (14±15) to completion of radiotherapy (33±21), but this returned to baseline level by 7 months (Fig. 3) and was the only clinically meaningful change obtained from the QLQ-BR23 questionnaire.

High radiotherapy dosage predicted 13% of the variance in quality of life at the completion of radiotherapy, with high dose (50 Gy as opposed to 42.5 Gy) and more fractions (25# as opposed to 16#) associated with lower quality of life. No other cancer or treatment characteristics

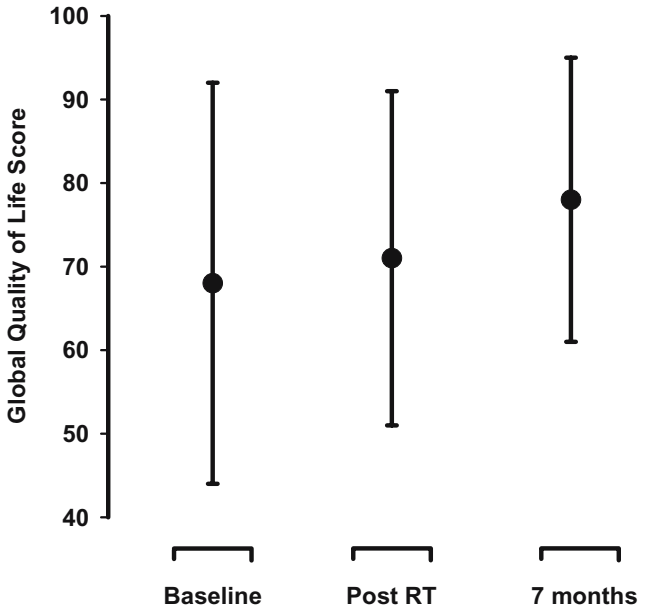

Fig. 1 Global quality of life scores at the time points measured

Table 2 EORTC scores at measurement time points

	EORTC Item	Baseline		Postradiotherapy		7-month follow-up	
		Mean (SD)	Number	Mean (SD)	Number	Mean (SD)	Number
QLQ-C30	Global health status/quality of life	68 (24)	61	71 (20)	61	78 (17)	57
	Physical functioning	87 (16)	61	87 (17)	61	90 (24)	57
	Role functioning	80 (27)	61	78 (29)	61	90 (20)[a]	57
	Emotional functioning	81 (21)	61	79 (23)	61	80 (20)	57
	Cognitive functioning	83 (25)	61	81 (24)	61	93 (14)[a]	57
	Social functioning	79 (23)	61	78 (24)	61	78 (21)	57
	Fatigue	24 (23)	61	33 (26)	61	23 (22)[a]	57
	Nausea and vomiting	7 (15)	61	4 (10)	61	2 (7)	57
	Pain	16 (27)	61	22 (27)	61	13 (19)	57
	Dyspnoea	11 (18)	61	13 (24)	61	11 (19)	57
	Insomnia	26 (31)	61	33 (33)	61	28 (29)	57
	Appetite loss	11 (26)	61	12 (20)	61	3 (12)	57
	Constipation	14 (27)	61	11 (23)	61	8 (18)	57
	Diarrhoea	4 (11)	61	5 (12)	61	2 (11)	56
	Financial difficulties	15 (28)	61	17 (31)	61	14 (29)	57
BR-23	Body image	78 (27)	61	84 (23)	61	87 (22)	57
	Sexual functioning	80 (22)	60	83 (17)	60	78 (20)	55
	Sexual enjoyment	53 (28)	27	60 (19)	26	55 (29)	28
	Future perspective	60 (33)	61	65 (27)	61	68 (24)	57
	Systemic side effects	20 (29)	61	17 (15)	61	14 (12)	57
	Breast symptoms	14 (15)	61	33 (21)[a]	61	16 (17)[a]	57
	Arm symptoms	13 (16)	61	18 (19)	61	14 (20)	57
	Upset by hair loss	33 (39)	21	58 (32)	4	42 (50)	8

[a] Indicates a greater than or equal to ten-point difference from previous measurement occasion

predicted quality of life. Linear regression of symptoms from the EORTC questionnaires found fatigue at the completion of radiotherapy to be highly predictive of lower quality of life at the same time point (R^2=0.55). Similarly, fatigue at 7 months after radiotherapy was highly predictive of lower quality of life at the same time point (R^2=0.48). Baseline fatigue was not predictive of quality of life at any time point. Linear regression of the treatment and demographic variables found chemotherapy to be a weak predictor (R^2=0.18) of baseline fatigue, but chemotherapy was not a predictor of fatigue at any of the follow-up time points.

Discussion

Women maintained their quality of life in the early period up to 7 months after radiotherapy. Radiotherapy had little effect on the quality of life of breast cancer patients, although those who were fatigued during radiotherapy had a lower quality of life. There was less than ten points difference in global health status scores between baseline and completion of radiotherapy and between completion of radiotherapy and 7 months. The mean global health status scores at baseline, completion of radiotherapy and at 7 months follow-up were all comparable to those scores found in the general female population [38]. This is consistent with the findings from other studies evaluating the effects of radiotherapy for breast cancer survivors on quality of life [4, 36, 40].

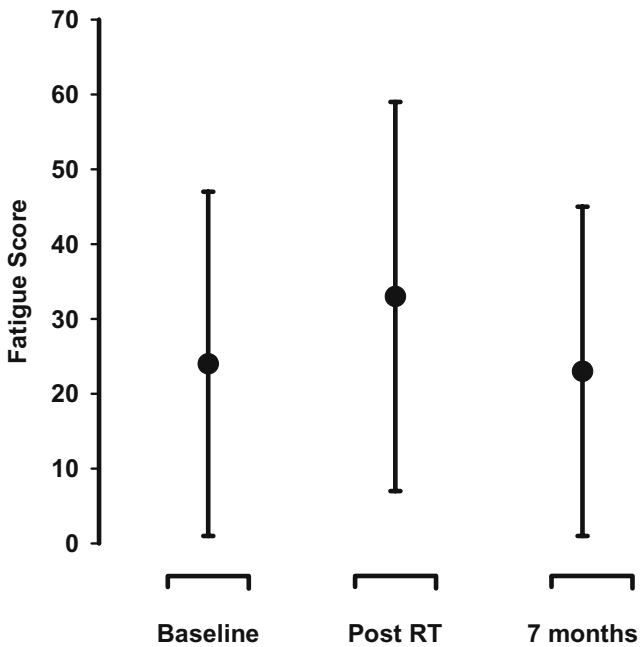

Fig. 2 Fatigue scores at the time points measured

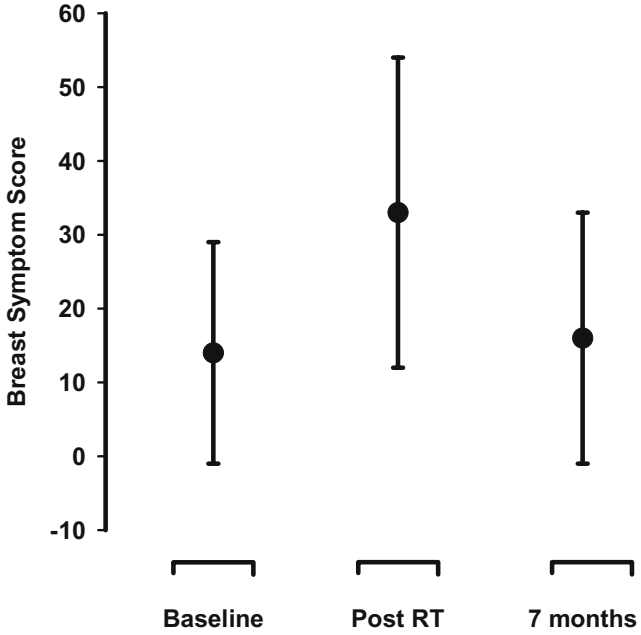

Fig. 3 Breast symptom scores at the time points measured

There was no difference in the quality of life of women who performed the stretching program during radiotherapy and the control group. One explanation may be that both groups benefited from weekly appointments with a physiotherapist throughout the radiotherapy treatment period. Regardless of whether or not the participant had therapeutic intervention, they were able to communicate with physiotherapists about any issues they may have been experiencing at each appointment. Research suggest that constructive communication with health professionals, characterised by caring, compassion, respect and trust, can significantly help cancer patients adjust better to their illness and thereby increase their quality of life [5, 11, 13, 24]. Cancer patients often need re-assurance from their health professional about the normalcy and legitimacy of their reactions and concerns [37]. They may also seek support from their health professional because of decreased body image and self-esteem during or after breast cancer treatment [37]. Provision of such support to all participants in this study may have inflated their quality of life scores at the completion of radiotherapy.

Consistent with a previous study [3], one of the main findings from this study was that fatigue is a strong predictor of poor quality of life. Wengstrom et al. [42] assessed the severity of fatigue in women at the completion of radiotherapy and found that although the majority of women experienced mild to moderate fatigue, 30% rated fatigue as severe to intolerable. Exercise has been reported to be effective in addressing the symptoms of fatigue during radiotherapy. Women who performed aerobic exercise such as a walking programme during radiotherapy have better physical functioning and less fatigue, anxiety and insomnia than women who did not exercise [8, 26]. If exercise has the ability to reduce fatigue, then it would seem logical to implement a programme during the course of radiotherapy. Radiotherapy regimens for women with breast cancer require their presence at the treatment centre 5 days per week for 4 to 6 weeks. This presents an ideal time to implement a supervised exercise programme because it can be monitored daily at their treatment facility, maximising compliance and effective performance.

Breast symptoms increased during the period of radiotherapy but returned to baseline levels by 7 months after radiotherapy. These symptoms are associated with the acute toxicity of radiotherapy on the treated skin and subcutaneous tissues and are normally transient in nature [4, 15]. As the degree of skin toxicity is directly related to treatment dosage and schedule, patients would benefit from appropriately planned treatments that maximise their survival rate, whilst minimising the side effects of treatment. Additionally, some consideration can be made to the use of topical creams to relieve the acute symptoms in the area treated with radiotherapy. Although there remains a degree of uncertainly regarding the best type of topical treatments to prevent or treat radiotherapy associated skin reactions, there is an abundance of research addressing this issue [6, 12, 22, 30].

High radiotherapy dosage and long schedule was a predictor of low quality of life at the completion of radiotherapy. This may be explained by the relationship that exists between high radiotherapy dosage, invasive disease and surgery, and poorer prognosis. In addition to increased acute skin toxicity caused by high radiotherapy dosage and intensive schedule [7], quality of life can be reduced because of the disruptive nature of the treatment schedule on family, social and working roles, such that the longer schedule further delays the woman's return to normal function. Wallace et al. [40] previously explored the relationship between dose/schedule and quality of life. Their study found that women receiving high dosage and long schedules (50 Gy in 25#+boost 15 Gy in 5#) for breast cancer had greater disruption of private life and a less positive outlook on the completion of radiotherapy treatment compared to women receiving low dosage and short schedules (40 Gy in 15#+boost 15 Gy in 5#). However, their results needed to be interpreted with care because women in the long-schedule group had a greater incidence and severity of depression before commencing irradiation; hence, the differences in quality of life at the completion of radiotherapy may not be attributed to dosage or schedule per se.

Chemotherapy was not found to be a predictor of quality of life in this study. Measurement of quality of life several months after the completion of chemotherapy in our study may indicate a period of time when women are not troubled

by the acute side effects of chemotherapy (nausea, vomiting, hair loss, neutropaenia). Long-term follow-up (>5 years) of patients suggest chemotherapy is a predictor of poor quality of life [2, 14, 27], but consideration needs to be given to the long-term side effects of chemotherapy such as menopausal symptoms and infertility. Our study was not powered to investigate the association between chemotherapy and quality of life, but interestingly, a larger trial [21] (2,236 participants) evaluating quality of life of breast cancer survivors at a median of 6.4 months after cancer diagnosis also found no differences in overall quality of life or physical, psychological and social domain scores in women who have undergone chemotherapy compared to women who did not undergo chemotherapy. Women in our trial and in the study of Lu et al. [21] may be experiencing a high quality of life simply because they have completed treatment and survived breast cancer.

Breast cancer survivors and health professionals should feel confident that despite fatigue and breast symptoms at the completion of radiotherapy treatment, women retain a high quality of life and return to baseline function by 7 months after radiotherapy. Treatment may best be targeted to alleviate fatigue and breast symptoms during radiotherapy.

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