

Scientific Article

A prospective study of quality of life in breast cancer patients undergoing radiation therapy

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Received 21 November 2015; received in revised form 20 January 2016; accepted 28 January 2016

Abstract

Purpose: The purpose of this study was to examine the impact of radiation therapy on quality of life (QOL) of breast cancer patients during and until 1 year after radiation therapy treatment.

Methods and materials: Thirty-nine breast cancer patients treated with breast-conserving surgery were enrolled in a prospective study before whole breast radiation therapy (50 Gy plus a 10-Gy boost). No patient received chemotherapy. Data were collected before, at week 6 of radiation therapy, and 6 weeks and 1 year after radiation therapy. The primary outcome variable was quality of life (QOL), measured by Medical Outcomes Study 36-Item Short Form Version 2 (SF-36). Risk factors potentially associated with total SF-36 scores and its physical and mental health component summary scores were also examined, including age, race, marital status, smoking history, menopausal status, endocrine treatment, cancer stage, sleep abnormalities (assessed by the Pittsburgh Sleep Quality Index), and perceived stress levels (assessed by the Perceived Stress Scale). Mixed effect modeling was used to observe QOL changes during and after radiation therapy.

Results: Total SF-36 scores did not change significantly during and up to 1 year after radiation therapy compared with baseline measures. Nevertheless, increased body mass index (BMI) and increased perceived stress were predictive of reduced total SF-36 scores over time ($P = .0064$, and $P < .0001$, respectively). In addition, increased BMI was predictive of reduced physical component summary scores of the SF-36 ($P = .0011$), whereas increased perceived stress was predictive of worse mental component summary scores ($P < .0001$). Other proposed potential risk factors including skin toxicity from radiation therapy were not significant.

Conclusions: Radiation therapy did not worsen QOL in breast cancer patients. However, pre-radiation therapy patient characteristics including BMI and perceived stress may be used to identify women who may experience decreased physical and mental function during and up to 1 year after radiation therapy.

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Sources of support: This work was supported by National Institutes of Health, National Cancer Institute grants R21 CA155511 and P30CA138292. Conflicts of interest: None.

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<http://dx.doi.org/10.1016/j.adro.2016.01.003>

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Introduction

Breast cancer is the most common noncutaneous malignancy diagnosed in women in the United States, with 1 in 8 women developing breast cancer in her lifetime.¹ Localized disease accounts for 61% of all breast cancers diagnosed in the United States, and the 5-year survival rate for this population approaches 98%.² Given the large number of breast cancer survivors, increasing attention is being paid to the impact of cancer treatments on quality of life (QOL), because it represents a potentially significant public health concern.

Previous studies have shown that chemotherapy significantly worsens QOL in breast cancer patients.^{3,4} In these studies, the Medical Outcomes Study 36-Item Short Form Version 2 (SF-36), which has been validated in a population of healthy women, has been one of the most commonly used instruments to assess QOL. Although chemotherapy has been consistently shown to worsen SF-36 scores and decrease QOL, few studies have examined the impact of breast radiation therapy (RT) on QOL. Research on breast RT has been limited by cross-sectional design and by the inclusion of patients treated in a heterogeneous manner (eg, lumpectomy, mastectomy, with or without prior chemotherapy).⁵⁻¹⁰

Radiation therapy after breast-conserving surgery is the standard of care for the majority of breast cancer patients, because RT significantly reduces breast cancer recurrence.¹¹ Nevertheless, many women will forego RT from “fearing the unknown,” “getting burnt,” “damaging internal parts,” and “anticipating tiredness.”¹² Fear of how RT may impact QOL both during and after RT may decrease compliance with treatment and, ultimately, increase the risk of cancer recurrence.^{11,13} However, QOL changes during and after RT have not been prospectively assessed with the SF-36 instrument in a longitudinal study of homogeneously treated patients, and risk factors for poor QOL over time have not been studied. Thus, the purpose of this study was to explore QOL changes and risk factors for poor QOL in early breast cancer patients before, during, and after RT following breast-conserving surgery in the absence of prior exposure to chemotherapy treatment.

Methods and Materials

Study design

Subjects were recruited from Emory University Department of Radiotherapy Oncology from March 2010 to March 2013. After receiving breast-conserving surgery, stage 0-II breast cancer patients who were recommended whole-breast RT were approached for enrollment. All enrolled subjects provided written informed consent, and

all procedures were a priori approved by the Emory University Institutional Review Board.

Patients were excluded if they received chemotherapy for their breast cancer. They were also excluded for comorbid conditions including uncontrolled cardiovascular, metabolic, pulmonary, or renal disease, pregnancy, and history of major psychiatric disorder, such as schizophrenia, bipolar disorder, or substance abuse/dependence, which may impact QOL.

Based on previous QOL studies, pre-RT patient and tumor characteristics, including age, body mass index (BMI), race (Caucasian vs African American), marital status (married [married or living with significant others] versus unmarried [single, divorced, or widowed]), smoking history (no vs yes), menopause status (pre/peri vs post), cancer stage (0 vs ≥ 1), and skin toxicity from RT, were recorded to determine their impact on QOL.^{6,9,14-16}

RT

All patients were treated with 50 Gy to the whole breast followed by a 10-Gy boost to the lumpectomy cavity given in 2-Gy fractions with 6-MV photons and/or 18-MV photons using standard tangential field-in-field technique to promote dose homogeneity. Radiation therapy plans were generated according to the International Commission on Radiotherapy Units-50 guidelines.¹⁷

Patients were assessed before (within the week before starting RT), at week 6 (first day of boost treatment), 6 weeks, and 1 year post-RT. Endocrine therapy was prescribed to patients who were hormone receptor positive and was not initiated until after RT completion. Skin toxicity was graded by physicians at each time point using the Radiation Therapy Oncology Group grading criteria.

Behavioral measures

Quality of life was measured by the SF-36, which is one of the most commonly used generic health-related QOL questionnaires, with well-documented validity and reliability in various populations,¹⁸⁻²⁰ including patients with breast cancer.^{21,22} There are 8 multi-item subscales: physical functioning, role limitations because of physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations from emotional problems, and mental health. The scores for the subscales range from 0 to 100, with 100 being the most favorable score. The US general population norm scores are publicly available for the subscales.²³ In addition, the scores from the 8 subscales can be combined into 2 component summary scores reflecting physical and mental health.²⁴ The 2 component summary scores are standardized with a mean score of 50 and 1 standard deviation of 10. A score of 60 signifies 1 standard deviation above the

general population mean, and a score of 40 is 1 standard deviation below the general population mean. A total QOL score was calculated as the average of the physical health component summary and the mental health component summary scores, with higher scores indicating better QOL.

Previous studies have indicated that sleep and stress are major behavioral factors that may impact QOL.^{16,25,26} The Pittsburgh Sleep Quality Index (PSQI) was used to assess subjective sleep quality and disturbances over the prior month in our subjects. This questionnaire has high internal consistency and test-retest reliability and can distinguish good sleepers from bad sleepers among breast cancer patients.^{27,28} The PSQI contains 15 multiple-choice items and 4 write-in items, which generate scores for 7 subscales: duration of sleep, sleep disturbance, sleep latency, day dysfunction from sleepiness, sleep efficiency, overall sleep quality, and medications for sleep. The score for each subscale ranges from 0 (no difficulty) to 3 (severe difficulty). The 7 subscale scores are summed to produce a global score ranging from 0 to 21. A PSQI global score greater than 5 is considered to be suggestive of significant sleep disturbance.²⁷

The Perceived Stress Scale (PSS) is one of the most widely used instruments to assess stress and has been previously used in patients with breast cancer.^{29,30} The PSS is a well-verified questionnaire for measuring nonspecific perceived stress that exceeds a person's coping abilities in the past month.³¹ Ten items are included in the PSS, and each item is scored by using a 5-point Likert scale ranging from 0 to 4, with 0 representing never and 4 representing very often. Higher scores mean more perceived stress.

The SF-36, PSQI, and PSS assessments were performed at all 4 study time points.

Data analysis

Descriptive statistics were used for demographic and clinical characteristics. Mean and standard deviation were presented for categorical variables, and frequency and percentages were used for continuous variables. Mixed effect modeling was generated to assess the change in trajectories of QOL over time and the impact of variables of interest on QOL over time. Variables included in the model were sleep, stress, age, BMI, race, marital status, smoking history, menopause status, endocrine treatment, cancer stage, and skin toxicity from RT. Only variables that showed a significance level of 0.10 on bivariate analyses were included in the final regression model. In addition, one-half standard deviation from normal mean values of SF-36 scores was used in this study as a minimal clinically important difference.³² All analyses were done using SAS 9.3 (SAS Institute, Inc., Cary, NC) with a significance level of 0.05.

Results

Patients' characteristics

Thirty-nine patients were enrolled in the study following breast-conserving surgery. Demographic and clinical characteristics of participating subjects are listed in Table 1. The average BMI was 30.66, with 23% of patients having a BMI below 25, 36% having a BMI between 25 and 30, and 41% with a BMI above 30. Sixty-two percent of participants were Caucasian and 54% were unmarried (defined as single, separated, divorced, or widowed). Forty-six percent of subjects had stage 0 breast cancer, whereas 54% had stage I or II disease. Among the enrolled subjects, 100%, 97%, 92%, and 64% completed SF-36 measures at baseline, week 6 of RT, and 6 weeks and 1 year after RT, respectively.

QOL over time

The total QOL score did not change significantly during or after RT (Table 2). In addition, no change was observed in the physical or mental health component summary scores over time. Of the 8 subscales, only the role physical subscale score exhibited a significant improvement from pre- to post-RT ($F = 5.59$, $P = .002$). Post hoc comparisons using least significant difference test revealed that the role physical subscale scores at both 1 year post-RT was significantly higher than the pre-RT and 6 weeks of RT scores ($P = .025$ and $P = .008$, respectively).

Table 1 Demographic and clinical characteristics (N = 39)

Variables	Mean \pm SD or N (%)
Age (y)	59.38 \pm 9.24
BMI	30.66 \pm 7.23
Race	
Caucasian	24 (62)
African American	15 (38)
Marital status ^a	
Married	18 (46)
Not married	21 (54)
Smoking history	
No	31 (80)
Yes	8 (20)
Menopause status	
Pre/peri	9 (23)
Post	30 (77)
Stage	
0	18 (46)
I/II	21 (54)

BMI, body mass index; SD, standard deviation.

^a Married includes patients married or living as married; not married includes patients who are single, separated, divorced, or widowed.

Table 2 SF-36 subscale and component summary scores over time

	Mean \pm SD			
	Baseline (n = 39)	Week 6 of RT (n = 38)	6 weeks after RT (n = 36)	1 year after RT (n = 32)
Physical functioning	76.28 \pm 27.19	74.34 \pm 26.54	79.58 \pm 27.27	76.56 \pm 28.38
Role physical ^a	66.67 \pm 39.87	64.47 \pm 38.83	75.00 \pm 39.19	86.72 \pm 26.17
Bodily pain	71.51 \pm 22.67	70.18 \pm 22.40	73.61 \pm 19.28	70.50 \pm 19.78
General health	75.77 \pm 17.20	76.21 \pm 15.84	75.22 \pm 17.08	76.62 \pm 16.85
Vitality	65.00 \pm 19.40	63.03 \pm 22.23	66.94 \pm 22.30	66.41 \pm 22.69
Social functioning	80.45 \pm 21.80	82.23 \pm 19.42	86.11 \pm 22.51	88.67 \pm 23.19
Role emotional	84.62 \pm 33.20	86.84 \pm 28.52	85.19 \pm 31.31	86.46 \pm 27.90
Mental health	79.79 \pm 15.97	87.79 \pm 10.76	85.22 \pm 15.32	84.50 \pm 16.28
Physical component summary	47.98 \pm 10.49	46.12 \pm 9.77	48.91 \pm 10.49	49.28 \pm 9.83
Mental component summary	52.94 \pm 8.79	55.76 \pm 6.36	54.70 \pm 9.92	54.92 \pm 9.48
Total score	50.46 \pm 6.32	50.94 \pm 6.27	51.81 \pm 7.13	52.10 \pm 6.61

RT, radiation therapy; SD, standard deviation.

^a $P < .05$.

Sleep and stress

Patients' sleep scores did not change significantly over time ($P = .583$); however, more than half of the patients had PSQI scores were >5 at each time point (51%, 47%, 49%, and 58%, at pre-, week 6, 6 weeks, and 1 year post-RT, respectively). Patients' perceived stress levels decreased significantly from pre- to 1 year post-RT ($P = .005$).

Risk factors for reduced QOL over time

Table 3 reveals that BMI and perceived stress were the only variables that were significantly associated with total QOL scores. Patients who had a higher BMI or higher PSS scores were more likely to have reduced total QOL scores. In addition, higher BMI was predictive of worse scores on the physical component summary score of the SF-36 over time, whereas exhibiting higher perceived stress was predictive of worse scores on the mental component summary score. Of note, PSQI scores were not associated with any QOL scores. Other proposed potential risk factors, including skin toxicity from RT, were not significant in the final model.

Discussion

This is one of the few studies to prospectively evaluate the effect of RT on the QOL of nonchemotherapy-treated breast cancer patients before, during, and after RT using the SF-36 instrument. Given that most studies on QOL in early breast cancer patients have included subjects treated with RT and chemotherapy, this study was uniquely positioned to evaluate the effect of RT alone on the QOL of early-stage breast cancer patients following breast conserving surgery.

QOL change over time

Radiation therapy does not appear to significantly change patients' QOL. Patients in our study had relatively stable QOL with a trend toward better from pre- to 1 year after RT. That RT may not change QOL has been demonstrated in several studies using other QOL questionnaires in cohorts of patients heterogeneously treated with various systemic regimens consisting of chemotherapy and/or endocrine treatment.³³⁻³⁶ For example, a large phase 3 randomized clinical trial compared early-stage breast cancer patients receiving postlumpectomy with or without RT.³⁴ Quality of life, measured by the European Organization for Research in the Treatment of Cancer instrument, were identical between treatment arms within 15 months after surgery. A study with a 15-year follow-up period also demonstrated that women treated with surgery and RT had very high QOL assessed by the European Quality of Life-5 Dimensions, and the patient scores were comparable to those seen in an otherwise normal adult female US population.³⁷

Our study found that patients' role limitations resulting from physical health, measured by the role physical subscale of the SF-36, improved significantly from pre- to 1 year post-RT. This improvement indicates that physical health-related difficulties with working or other daily activities before and during RT, improved over time. Our statistical analysis further showed that this improvement was specifically significant at 1 year post-RT compared with pre-RT treatment or at week 6 of RT. Ganz and colleagues²¹ also assessed role physical using SF-36 for breast cancer patients from pretreatment until 1 year posttreatment. Similarly, they found substantial improvements over time for role limitations resulting from physical health.

Overall, our study found that patients' QOL does not change significantly during and after RT; however,

Table 3 Association between demographic and clinical characteristics and SF-36 over time

	Estimates	SE	P
SF-36 total score			
The first model with all variables $P < .1$			
Age	-0.02	-0.44	.6625
BMI	-0.18	-2.85	.0067
Marriage: not married ^a	1.83	2.03	.0481
PSS score	-0.38	-6.14	<.0001
PSQI score	-0.21	-1.73	.0914
Time: baseline ^b	-1.06	-0.70	.4895
Time: 6 weeks of RT ^b	-2.51	-1.62	.1130
Time: 6 weeks post-RT ^b	-2.05	-1.21	.2342
The final model with only variables $P < .05$			
BMI	-0.19	0.07	.0064
PSS score	-0.41	0.06	<.0001
Physical Component Summary Score			
The first model with all variables $P < .1$			
BMI	-0.42	0.12	.0011
The final model with only variables $P < .05$			
BMI	-0.42	0.12	.0011
Mental Component Summary Score			
The first model with all variables $P < .1$			
Age	-0.01	-0.07	.9447
Marriage: not married ^a	3.35	2.39	.0214
PSS score	-0.60	-6.61	<.0001
PSQI score	-0.23	-1.29	.2024
Time: baseline ^b	-1.40	-0.75	.4567
Time: 6 weeks of RT ^b	-1.11	-0.67	.5051
Time: 6 weeks post-RT ^b	-2.46	-1.33	.1893
The final model with only variables $P < .05$			
PSS score	-0.61	0.09	<.0001

BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; PSS, perceived stress scale; RT, radiation therapy; SE, standard error; SF-36, Medical Outcomes Study 36-Item Short Form.

^a The reference group was married.

^b The reference group was the time at 1 y post-RT.

limitations in their daily activities and work they may experience from their physical health improves remarkably during this period. Previous studies have shown that patients' fear of RT decreases the compliance of RT, which may eventually reduce the rate of local control and long-term survival.^{11,13} Our findings indicate that patients who undergo RT do not experience a worse QOL resulting from the treatment and provide evidence for clinicians to share with patients who may anticipate significant life-changing side effects and poor QOL from RT.

Risk factor for QOL over time

Although BMI and perceived stress were significant risk factors for total QOL, the significant risk factors for each of the 2 component summary scores of QOL were different. BMI was more predictive of reduced physical function, whereas perceived stress predicted for mental

health function. This finding indicates the distinctive components underlying physical and mental health might lead to the divergent risk factor profiles for these different QOL components. Carver and colleagues¹⁴ found similar results, which showed different components of QOL may have different types of predictors including demographic, medical, and psychosocial patient characteristics.

Our study indicates that BMI is a significant independent risk factor for QOL, and specifically for physical function. Similar findings have been presented in previous studies using either the SF-36¹⁶ or different QOL questionnaires.⁵ The effect of BMI on physical health may even last up to 40 months after diagnosis.¹⁶ The exact reason for this relationship is not well documented; however, higher BMI usually is related to higher incidence of lymphedema and other treatment-related symptoms.¹⁶ Lower physical activity³⁸ associated with a higher BMI may also explain poor QOL.

Our data also support the hypotheses that high perceived stress may contribute to poor QOL, more specifically to the mental health component summary score, during and after breast cancer RT. This relationship has been shown in many other studies, especially studies using psychosocial behavioral interventions to reduce stress.^{39,40} Although the majority of these studies did not directly use the perceived stress measurements, they used measurements related to mental or emotional health for the outcome measure of stress reduction.

Research has demonstrated that breast cancer patients with poor sleep quality usually report worse total QOL.⁶ However, our study showed that sleep problems had only a trend effect on mental component summary score. This trend is probably from the relatively small sample size. In addition, our study did not show any effect of sleep problems on the physical component summary score, which is not consistent with other recent studies. One recent study found that poor sleep quality was most strongly associated with physical and functional well-being instead of emotional and family well-being.⁴¹ Another group found that poor sleep has an influence on both physical and mental health.²⁶ Although all of the 3 studies used the same sleep quality questionnaire, PSQI, and investigated patients before, during and after treatment, their studies used different QOL questionnaires and included patients treated with chemotherapy. It is not clear whether these differences could explain the discrepancies among results. Further studies in terms of the effect of sleep on different domains/components of QOL are warranted.

Conclusions

This prospective longitudinal study provides a unique perspective by only examining patients receiving RT following lumpectomy. Our findings provide value for

clinicians and researchers by examining QOL before, during, and up to 1 year post-RT, which is not a well-studied treatment period. Overall, our study showed that early breast cancer women's QOL did not change or decrease significantly during or after RT. Instead, patients' role limitations resulting from physical health improved at 1 year. Nevertheless, several risk factors for poor QOL were identified, including increased BMI and increased perceived stress. Future prospective studies with a larger cohort are needed to substantiate our findings and design interventional trials to improve QOL in breast cancer patients at risk for overall decreased QOL during and after RT.

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