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Health-Related Quality of Life in Long-Term Breast Cancer Survivors: Differences by Adjuvant Chemotherapy Dose in CALGB Study 8541

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Abstract

Background—The Survivor's Health and Reaction (SHARE) study examined health-related quality of life (HRQL) in breast cancer patients who had participated in CALGB 8541 from 1985–1991.

Methods—A total of 245 survivors (78% of eligible patients) who were 9.4–16.5 years post-diagnosis (mean 12.5 years) completed HRQL surveys relating to 5 domains. Analyses examined HRQL domains by the three chemotherapy doses administered in the original treatment trial: low-dose=Cyclophosphamide/Doxorubicin/Flouracil (CAF) at 300/30/300×2 mg/m^2 over 4 cycles, standard-dose=CAF at 400/40/400×2 mg/m^{2}over 4 cycles, and high-dose=CAF at 600/60/600 mg/m^{2}over 4 cycles.

Results—In univariate analyses, a statistically significant difference was found in SF-36 physical role functioning by treatment group, with the standard treatment arm showing lower mean scores (mean=65.05) compared to the low-dose (mean=74.66) or high-dose (mean=84.94) arms (p=<0.0001). Multivariate analysis, however, revealed that treatment arm was no longer statistically significant, while the following factors were associated with decreased physical role functioning: age ≥60 (OR=3.55, p=0.006), increased comorbidity interference total score (OR=1.64, p=0.005), lower vitality (OR=1.05, p=0.0002) and increased menopausal symptoms (OR=1.04, p=0.02).

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IRB statement: All patients gave informed consent before participating in this study.

Conclusions—At 9.4–16.5 years post-diagnosis, differences in physical role functioning among breast cancer survivors who received three chemotherapy doses were explained by clinical and demographic variables, such as age, fatigue, menopausal symptoms and comorbidities. Prospective studies are needed to further assess the role of these factors in explaining HRQL and physical role functioning among long-term survivors.

Keywords

breast cancer; survivorship; quality of life; chemotherapy

Introduction

Advances in early detection and treatment have led to increased numbers of breast cancer survivors, totaling approximately 2.4 million in 2007.[1, 2] This increase in survivors raises concerns about the long-term effects of cancer treatment on health-related quality of life (HRQL).

Several studies have reported good overall HRQL among long-term survivors, but have identified issues such as sexual concerns, psychosocial problems and physical symptoms, including pain and lymphedema.[3–7] Adverse effects of systemic adjuvant therapy (chemotherapy) on global HRQL, physical functioning, bodily pain and sexual functioning have been shown to worsen 5–10 years after diagnosis among breast cancer patients.[3,6]

Ahles et al. revealed gaps in knowledge regarding the effects of cancer treatment in long-term breast cancer survivors, as few studies exist.[8] Ganz et al. found few differences in the effects of adjuvant treatment on HRQL and emotional functioning in breast cancer survivors 3 years post-treatment, but discovered significant differences in global HRQL, general health, physical and social functioning after 6 years of follow-up.[9] Bottomley et al. reported declines in HRQL 3 months after treatment, but found that these effects had largely diminished 3 years post-treatment.[10] Ahles et al. also emphasized the importance of assessing the impact of chemotherapy on HRQL to make cancer survivors aware of potentially negative outcomes of cancer treatment, and for the development of interventions to cope with negative side effects of treatment.[8] Thus, past studies have shown inconsistent results regarding the effects of adjuvant chemotherapy on long-term HRQL. This issue has important implications for breast cancer survivors, and, therefore, needs further study.

The theoretical framework for this study was derived from the Quality of Life model adapted for cancer survivors by Dow, Ferrell and colleagues (Figure 1).[5, 11] The model identifies four major areas of HRQL in cancer patients: physical, psychological, social and spiritual well-being. It has been tested in several studies with specific issues identified within each domain.[12, 13] In the present study, the social well-being area was subdivided into social and economic well-being. Thus, 5 domains plus medical and demographic variables were assessed.

The primary goal of this paper was to assess whether adjuvant chemotherapy dose of a commonly used breast cancer treatment regimen (Cyclophosphamide/Doxorubicin/Flouracil (CAF)) was associated with differences in 5 HRQL domains (physical, psychological, social, spiritual, and economic) among long-term breast cancer survivors (9–16 years post-diagnosis) who had participated in Cancer and Leukemia Group B (CALGB) treatment trial 8541. Due to conflicting evidence from past studies and because these women had survived 9–16 years, we hypothesized that there would be differences among the treatment arms, which could result in higher or lower HRQL. The secondary goal was to identify factors that currently exhibited significant differences by treatment arm, such as co-morbidities,

treatment variables and demographic variables, including age, education and socioeconomic status (SES). Identification of these factors may be useful for interventions to improve HRQL among long-term survivors.

Methods

1. Setting

The current study (CALGB 79804) examined HRQL in breast cancer patients who had participated in CALGB 8541 from 1985–1991. The goal of CALGB 8541 was to determine whether a dose-dependent relationship existed between disease-free survival, dose, and dose-intensity for stage II breast cancer patients randomly assigned to receive one of the following (CAF) adjuvant therapy regimens for surgically resected breast cancer: low-dose (CAF 300/30/300×2 mg/m^2 over 4 cycles), standard-dose (CAF 400/40/400×2 mg/m^2 over 6 cycles); and high-dose (CAF 600/60/600 mg/m^2 over 4 cycles).14,15

The results of the trial showed that after 3.4 median follow-up years, women treated with high- or standard-dose/intensity had significantly longer disease-free survival ($p<0.001$) and overall survival ($p=0.004$) than low-dose/intensity patients in log rank comparisons (3 degrees-of-freedom).14, 15 The difference in survival between the two groups treated with standard- or high-dose/intensity was not significant.

Of 1,572 women randomized to CALGB 8541, approximately 618 were alive and cancer-free when the present study began in 1999. Since accrual for CALGB 8541 occurred from 1985–1991, participants in this study were 9.4 to 16.5 years post-diagnosis (mean 12.5 years). The study was approved by the Institutional Review Boards of each participating institution.

2. Procedures

Details of the study methods have been provided elsewhere.16 In brief, clinical research associates (CRAs) at CALGB treating institutions were notified of patient eligibility by the CALGB Statistical Center. CRAs confirmed patient disease status (alive and disease-free) and informed the treating physician of the study. CRAs then either contacted the patient about the study or an introductory letter was sent from the principal investigator (EP) noting the physician's permission to contact the patient. A consent form and questionnaire were sent, which were completed, signed and returned by women who wished to participate. Non-respondents were contacted by phone to complete the survey (N=8), if necessary. Upon questionnaire completion, patients were registered with the CALGB Statistical Center.

In total, 618 women from 42 CALGB institutions were identified by the CALGB Statistical Center for potential participation in this study. Eligibility criteria consisted of: participation in CALGB 8541, breast cancer-free for 12 months, free of other cancers in the past 5 years (except basal/squamous skin or in-situ cervical cancers), physician approval to participate, and could complete English-language questionnaire. Figure 2 shows exclusions that were made. Reasons for ineligibility included death or disease recurrence and lack of physician approval. Thus, 314 women were eligible to participate and 245 (78%) returned the surveys. Participants did not differ significantly from non-participants (CALGB 8541 survivors who were not eligible to participate in the follow-up study) by age, treatment arm, number of nodes or age/year of entry in CALGB 8541 (data not shown). More white survivors, however, versus non-white survivors chose to participate (93% versus 81%, $p<0.0001$).

3. Measures

The following questionnaires were used to assess HRQL domains by treatment arm in this study, with higher scores representing increased levels of the outcome being assessed.

Quality of Life

a.) SF-36: Overall HRQL was assessed using eight dimensions: physical functioning, role limitations, bodily pain, general health perceptions, vitality (fatigue), social functioning, emotional well-being, and perceived changes in health status.17, 18 Subscales were scored from 0–100, with higher scores indicating better HRQL. Lower vitality scores indicated greater fatigue.

Psychological Well-being

b.) CES-D (20 items): Depression was measured with a total score that was dichotomized using a score ≥16 to reflect the possible presence of depression.19

c.) Breast Cancer Anxiety and Screening Behavior Scale(BCAS): This modified 21-item scale assessed the emotional and cognitive aspects of breast cancer,20 showing high validity with breast cancer worries and generalized anxiety scales.20–23 All subscales were examined, including intrusive and avoidant thoughts, and total cognitive distress.

Social Well-being

d.) MOS Social Support Survey: This validated 20-item survey measured 4 areas of perceived social support: emotional/informational, tangible, affectionate, and positive social interaction.24, 25 All subscale scores and total score were examined.

e.) Life Events Scale: Stress was assessed with this 11-item survey, which has been used in past studies.26 Both the number and frequency of events were examined.

Spiritual Well-being

f.) System of Beliefs Inventory: Religious/spiritual beliefs were measured with this 15-item scale.27 Two subscales, spiritual beliefs practices and community social support, and total score, were examined.

Economic Well-being

g.) Employment and Insurance Difficulties Attributed to Cancer: The overall impact of breast cancer diagnosis on employment and insurance was assessed with 2 questions from this survey,28 which were developed for prior CALGB survivor studies.7,29

Physical Well-being

h.) Your Health-Short Form: This modified version of the validated OARS Co-Morbidity list30 assessed the following illnesses/comorbidities (no/yes): heart disease, osteoporosis, high blood pressure, diabetes, circulation problems in arms/legs, stroke, depression, chronic liver/kidney disease, stomach/intestinal disorders, osteoporosis, arthritis, glaucoma, and emphysema. An “Interference Score” (with daily activities) was assessed using a 3-point scale (‘not at all’=1, ‘somewhat’=2, ‘a great deal’=3).30

i.) Pain and Lymphedema Questionnaire: This 12-item module documented the occurrence and duration of treatment-related swelling and pain in the arms/hands.31

j.) Menopause and Reproductive Health Questionnaire: This 47-item survey asked participants if they had experienced particular physical symptoms (yes/no) and if the severity was mild, moderate or severe. A total score assessed both frequency and severity.

Medical Information/Demographics—k.) The medical file in the CALGB 8541 database provided demographics and the following information: date of study entry, treatment arm, menopausal status (at diagnosis), number of positive nodes at diagnosis, tumor size, histological grade, estrogen receptor (ER) status, and performance status (Karnofsky Performance Scale32). Current demographics, such as age, education, income and insurance status were obtained from a supplemental demographic survey for the current study.

5. Analysis

Statistical analyses were performed by statisticians at the CALGB Statistical Center (JEH and KD). Descriptive statistics were used to characterize HRQL domains and clinical characteristics of survivors by treatment arm. Power analyses for this study revealed 90% power to detect a clinically significant difference in physical role functioning, where one group differed from the other groups by more than 0.5 standard deviations, assuming alpha = 0.05 (2-sided) and sample sizes of 74, 93, and 78 for the low, standard and intensive-dose groups, respectively.33

Due to skewed distributions and a ceiling effect for many of the survey scores, the non-parametric Kruskal-Wallis test was used to compare survey scores by treatment arm. All other categorical data were analyzed using Fisher's exact test. The Jonckhere-Terpstra34 test was used to test for a dose-response relationship between treatment dose and survey score. Statistical tests were calculated using exact methods from Monte-Carlo simulations and were two-sided, using alpha=0.05. The null hypothesis in these comparisons was that there were no differences in survey scores between treatment arms. The alternative hypothesis was that at least one arm had a significantly higher or lower score compared to the other arms.

The relationship between treatment arm and physical role functioning was analyzed using logistic regression. Physical role functioning, which was the outcome for this analysis since it was the only HRQL variable that showed a statistically significant association with treatment arm (p=0.001), was dichotomized (100 versus <100) due to the discrete nature of the distribution. Higher SES was defined as having private health insurance, household income ≥$20,000, and being a high school graduate; otherwise, women were classified as having lower SES.35 Other variables in the logistic regression analysis were: age at interview (≥60 years versus <60), number of co-morbidities (0 versus ≥1), type of surgery (lumpectomy versus mastectomy), ER status (negative versus positive), hormone therapy (no versus yes), radiation therapy (no versus yes), high blood pressure interfering with daily life (no/not applicable versus yes), diabetes interfering with daily life (no/not applicable versus yes), vitality score, menopausal symptom score, comorbidity interference total score, and time since diagnosis, which was stratified by its median (12.3 years). Variables significant at the 25% level based on Wald's chi-square test were included in the multivariate model using stepwise selection methods. The selection criterion was based on the Score chi-square statistic, using alpha=0.05. The Wald chi-square statistic was used to determine if a factor should remain in the model (alpha=0.05).

Results

Table 1 shows the distribution of demographic and clinical characteristics of participants by treatment arm. Seventy-four patients (30%) had received low-dose chemotherapy, 93

patients (38%) had received the standard dose, and 78 patients (32%) had received the highest dose. Age and race did not differ significantly between groups. Differences were evident regarding education, whereby patients who received standard therapy were somewhat less-educated (p=0.04). No significant differences were found in the distribution of co-morbidities interfering with daily life by treatment group (results not shown).

Table 2 shows the distribution of SF-36 subscales by treatment arm. The mean scores were highest for the intensive treatment arm and lowest for the standard arm for all but the mental health subscale, with the only statistically significant difference seen in physical role functioning (p<0.0001). Trends toward significance were seen for general health perceptions (p=0.06), emotional role functioning (p=0.07), and vitality (p=0.09), with lower scores found in the standard treatment arm. There were no significant dose-response relationships by treatment arm (results not shown).

Table 3 displays the HRQL domain items examined by treatment arm. Overall, approximately 80% of women indicated having one or more comorbidities and 20% of women had possible depression (CES-D≥16). They also showed high levels of MOS social support (mean scores>78). In examining the social support systems of belief subscale, a trend towards significantly higher social support was seen in the standard treatment arm (p=0.07). There were no significant dose-response relationships by treatment arm (results not shown).

The association of demographic and medical characteristics with decreased physical role functioning were analyzed using logistic regression. The univariate results (Table 4) showed a highly significant relationship between treatment arm and decreased physical role functioning (OR=3.17, p=0.0009). Other factors associated with reduced physical role functioning were: lower SES (OR=2.76, p=0.0004); age≥60 (OR=1.85, p=0.03); ≥1 co-morbidities (OR=4.76, p=0.0001); lower vitality (OR=1.06, p<0.0001); increasing menopausal symptom score (OR=1.07, p<0.0001), higher comorbidity interference total score (OR=2.81, p<0.0001), and positive ER status (OR=2.17, P=0.009).

Variables significant at the 25% level in the univariate analysis were included in the stepwise selection process to derive the multivariate model (Table 5). Vitality, menopause symptoms, age and comorbidity interference total score all had significant associations with physical role functioning, but treatment arm and SES were no longer significant. Older patients (OR=3.55, p=0.006), patients with higher comorbidity total interference scores (OR=1.64, p=0.005), patients with higher menopausal symptom scores (OR=1.04, p=0.02), and women with reduced vitality (fatigue) (OR=1.05, p=0.0002) were more likely to report decreased physical role functioning.

In further exploring these associations, two specific co-morbidities reported as interfering with daily life, high blood pressure and diabetes, were highly related to decreased physical role functioning in univariate analyses (p<0.001). Patients with a high school education or less tended to have more health problems compared to those having at least some college education (not shown). Significant differences by education level were seen in circulation trouble (p=0.01), depression level (p=0.01), and diabetes (p=0.06) interfering with daily life.

Discussion

The primary purpose of this study was to compare differences by treatment group in HRQL domains (physical, psychological, social, spiritual and economic) among long-term breast cancer survivors. When HRQL measures were examined by treatment arm, physical role functioning emerged as the only statistically significant outcome. Trends toward significance were seen in variables such as general health perceptions, vitality, emotional

role functioning and social functioning. These results are similar to Ganz et al., who found that 6-year survivors treated with adjuvant therapy reported lower levels of physical role functioning, as well as general health, bodily pain, physical functioning, and social functioning.[6,36] Ahles et al. also found significantly lower scores in social and physical domains among 10-year survivors who received chemotherapy versus local therapy.[37] Others have reported poorer physical role functioning among patients 5 years post-chemotherapy compared to patients without cancer[38] and to patients who received adjuvant chemotherapy.[3]

Unlike previous studies, where a dose-response relationship was found, the present study showed the lowest SF-36 subscale means in the standard group, followed by the low-dose and high-dose groups. Survivors in the standard arm also showed significantly higher levels of systems of belief social support in the spiritual domain. These findings may be due to survivors in the standard group having less education or perhaps being less healthy than the other groups. Future studies should examine similar dose-intensities and their effect on HRQL.

In further examining the relationship of physical role functioning by treatment arm, logistic regression analyses revealed that treatment arm was no longer significantly associated with HRQL after adjusting for factors such as age, fatigue, menopausal symptoms and comorbidities interfering with daily life. A recent prospective study found lower levels of physical role functioning among women one year after receiving high-dose chemotherapy, which remained stable over 4 years but had small effect sizes that were clinically irrelevant.[39] In that study, when age and menopausal status were assessed as covariates, postmenopausal women exhibited lower physical role functioning scores. Other studies have also shown lower levels of HRQL in physical/role functioning domains in high-dose chemotherapy patients that returned to baseline 1 year post-treatment.[40–42] The current results, however, provide information on who may be at risk for reduced physical role functioning following the receipt of any dose of this adjuvant therapy regimen.

Age was significantly related to physical role functioning in this study, and has typically been associated with lower HRQL in past studies. Older survivors have reported decreased physical role functioning,[43, 44] more physical problems, depressed mood and days affected by fatigue.[45,46]

Comorbidities interfering with daily life, which were significantly related to physical role functioning in this study, have consistently been shown to affect HRQL. Depression, diabetes and circulation trouble were also evident in women with lower education levels. Past studies have shown that poorer HRQL among lower SES groups may be related to increased co-morbidities and reduced access to care. Patients with lower education level have reported more physical symptoms, such as tiredness, decreased sexual interest and painful muscles.[39]

Fatigue was significantly related to physical role functioning in this study. Fatigue is often reported as a long-term side effect of breast cancer treatment that persists years after active treatment.[6,7,47,48] Co-morbidities, such as high blood pressure, which were prevalent in this study, have been shown to be related to fatigue in previous studies.[48] The presence of joint and muscle pain have also been associated with fatigue.[49,50,51] Patients who most frequently reported symptoms, such as pain and fatigue 5 years post-treatment, scored significantly lower on HRQL at baseline compared to other patients.[39] Future studies should assess these domains at baseline, and possible interactions with other factors, as differences may be predictive of future outcomes.

Regarding menopausal symptoms, which showed a statistically significantly association with physical role functioning, Schultz et al. concluded that despite "complex interactions" between HRQL indicators and physiologic effects of treatment, menopausal symptoms may not be different for breast cancer survivors and should not be confused with quality of life/ psychosocial issues.52 Others have demonstrated that HRQL differences could not be explained by menopausal symptoms alone and that more research is needed in this area.38

There were several strengths of this study. First, it focused on the HRQL domain of physical role functioning, and factors influencing this domain, which have not been explored in previous studies. Second, it examined survivors who were 9–16 years post-diagnosis, which few studies have included. Third, the women were diagnosed at relatively the same disease stage received one of 3 known chemotherapy regimens within the same clinical trial, thus reducing variability due to treatment and stage of diagnosis. Many previous studies have used heterogeneous populations in examining stage and treatment.

Limitations of this study include reliance on self-reported co-morbidities, such as lymphedema and osteoporosis. Information on temporal changes in HRQL was not assessed since HRQL was examined at only one time point. Also, a survival bias may have occurred, whereby patients with better HRQL were more likely to be long-term survivors, and thus, eligible to participate in the follow-up study. However, analyses showed few differences between CALGB 8541 survivors who did and did not participate in this study. These limitations emphasize the need for prospective long-term studies of HRQL in breast cancer survivors from treatment through survivorship.

While chemotherapy provides a great survival benefit for cancer patients, it provides potential long-term side effects that may greatly impact HRQL. The current study demonstrated that while adjuvant chemotherapy dose was initially related to lower HRQL in physical role functioning, this effect was actually explained by demographic and clinical factors, which can be used in targeting HRQL interventions for long-term survivors. The clinical significance of these factors and their role as potential areas for interventions in improving HRQL needs to be further explored in prospective studies of HRQL in long-term breast cancer survivors.

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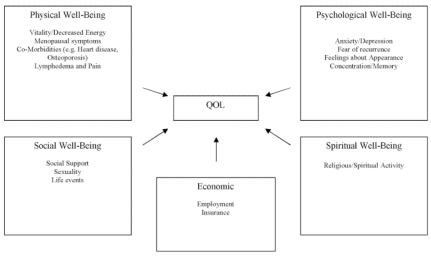

Figure 1. Quality of Life Model Adapted for Breast Cancer Survivors*
*adapted from Dow et al.5 and Ferrell et al.11

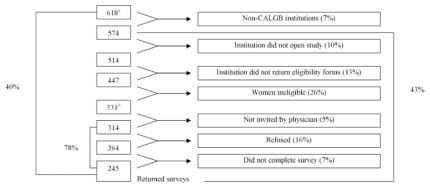

Figure 2. Accrual/Eligibility to SHARE

[a]There were 618 potentially eligible patients

[b]There were 331 Eligible patients

Table 1

Demographic and Clinical Characteristics of Study Participants by Treatment Trial Arm*

Variable Total # of Patients	Low Dose n = 74 n(%)	Standard Dose n = 93 n(%)	Intensive Dose n = 78 n(%)	All Patients n = 245 n(%)	P-Value
Age (years)					0.31
30 – 39	1(1)	0(0)	2(3)	3(1)	
40 – 49	4(5)	10(11)	6(8)	20(8)	
50 – 59	28(38)	26(28)	24(31)	78(32)	
60 – 69	30(41)	32(34)	30(38)	92(38)	
70 +	11(15)	25(27)	16(21)	52(21)	
Mean(SD)	61.3(8.8)	63.4(10.5)	61.1(9.8)	62.0(9.8)	
Race					0.34
White	70(95)	84(90)	75(96)	229(94)	
Other	4(5)	9(10)	3(4)	16(6)	
Education					0.04
0 – 12 years	29(41)	54(61)	39(54)	122(55)	
13 + years	42(59)	34(39)	33(46)	109(47)	
Income					0.12
Under $10,000	4(6)	3(4)	5(8)	12(6)	
$10,000 – $19,999	9(14)	13(16)	8(13)	30(14)	
$20,000 – $29,999	4(6)	19(24)	7(11)	30(14)	
$30,000 – $44,999	10(16)	18(23)	10(16)	38(18)	
$45,000 – $59,999	9(14)	6(8)	11(17)	26(13)	
$60,000 – $79,000	8(13)	9(11)	10(16)	27(13)	
$80,000 +	20(31)	12(15)	13(20)	45(22)	
Socioeconomic Status					0.51
Lower	32(47)	47(54)	31(46)	110(49)	
Higher	36(53)	40(46)	37(54)	113(51)	
Type of Treatment					0.12
Mastectomy	62(84)	75(81)	55(71)	192(78)	
Breast Conservation	12(16)	18(19)	23(29)	53(22)	
Received Radiation Therapy					0.13
Yes	13(18)	19(20)	24(31)	56(23)	
No	60(82)	74(80)	53(69)	187(77)	
Received Tamoxifen					0.89
Yes	32(44)	42(45)	32(42)	106(44)	
No	41(56)	51(55)	45(58)	137(56)	
Received Any Hormone					0.89

Variable Total # of Patients	Low Dose n = 74 n(%)	Standard Dose n = 93 n(%)	Intensive Dose n = 78 n(%)	All Patients n = 245 n(%)	P-Value
Yes	34(46)	44(47)	34(44)	112(46)	
No	40(54)	49(53)	44(56)	133(54)	
Estrogen Receptor Status					0.55
Negative	26(35)	25(27)	25(32)	76(31)	
Positive	46(62)	65(70)	48(62)	159(65)	
Borderline	2(3)	3(3)	1(1)	6(3)	
Time Since Diagnosis (years)					
Mean(SD)	12.4(1.9)	12.5(1.7)	12.5(1.9)	12.5(1.8)	0.89

* Note: Frequencies within education, income, socioeconomic status, Tamoxifen use, estrogen receptor status, and prior radiation therapy columns do not sum to column total due to missing data

Table 2

SF-36 Subscales and Treatment Arm for Patients Enrolled in CALGB 79804

	Treatment Arm						
	Low (n=74)		Standard (n=93)		Intensive (n=78)		P-value*
MOS SF-36 Subscale:	Mean(SD)	Median	Mean(SD)	Median	Mean(SD)	Median	
Physical Function	75.14(30.64)	85.00	73.01(30.74)	85.00	82.31(22.91)	90.00	0.17
Role Functioning-Physical	74.66(39.42)	100.00	65.05(41.56)	75.00	84.94(30.24)	100.00	<0.0001
Role Functioning-Emotional	86.94(31.12)	100.00	77.78(36.23)	100.00	87.89(26.99)	100.00	0.07
Social Function	87.50(23.77)	100.00	82.07(27.06)	100.00	87.18(21.13)	100.00	0.36
Bodily Pain	73.69(24.14)	84.00	71.37(24.34)	74.00	77.27(21.22)	84.00	0.32
Mental Health	77.70(16.56)	80.00	76.58(17.35)	84.00	76.08(15.86)	80.00	0.74
Vitality	61.40(22.65)	65.00	56.81(22.06)	55.00	64.62(17.33)	70.00	0.09
General Health Perceptions	74.50(21.49)	75.00	68.92(20.58)	72.00	75.35(17.99)	77.00	0.06

*Kruskal-Wallis test.

Table 3

Quality of Life Domains by Treatment Arm for Patients Enrolled in CALGB 79804

Treatment Arm				
	Low (n=74)	Standard (n=93)	Intensive (n=78)	
Domain/Items	**Mean(SD)[a]**	**Mean(SD)[a]**	**Mean(SD)[a]**	**P-Value**
Physical Well-Being				
Menopausal Symptoms Score	22.53(18.16)	24.53(17.99)	21.21(18.45)	0.31[b]
Vitality (Fatigue)	61.40(22.65)	56.81(22.06)	64.62(17.33)	0.09[b]
Lymphedema & Pain				
Swelling Since Surgery				0.55[c]
Yes	26(35%)	28(30%)	21(27%)	
No	48(64%)	65(70%)	57(73%)	
Arm/Hand Pain				0.76[c]
Yes	18(24%)	18(19%)	18(23%)	
No	55(74%)	73(78%)	60(77%)	
Co-morbidities:				
None	15(20%)	23(25%)	18(23%)	0.81[c]
>1	59(80%)	70(75%)	60(77%)	
Interference Total Score	1.35(2.27)	1.80(2.34)	1.10(1.79)	0.13[b]
Psychological Well-Being				
CES-D Total Score	9.52(9.96)	9.78(8.01)	9.30(7.79)	0.64[b]
Score≥16	15(20%)	21(23%)	15(19%)	0.88[c]
Score<16	59(80%)	72(77%)	63(81%)	
Breast Cancer Anxiety & Screening Subscales:				
Total Cognitive Distress	10.88(6.44)	11.31(6.21)	10.57(6.33)	0.86[b]
Intrusive Thoughts	4.16(4.26)	4.15(3.70)	4.00(4.18)	0.81[b]
Avoidant Thoughts	2.90(3.08)	3.39(3.13)	2.69(2.68)	0.34[b]
Appearance Assessment	26.09(8.12)	26.16(7.35)	24.97(7.19)	0.54[b]
Difficulty Concentrating				
Yes	10(14%)	17(18%)	17(22%)	0.45[c]
No	61(82%)	75(81%)	60(77%)	
Social Well-Being				
MOS Social Support Score MOS Subscales:	83.04(17.96)	77.53(23.27)	79.16(20.43)	0.34[b]
Positive Interaction	85.70(17.96)	79.71(24.96)	82.59(22.32)	0.44[b]
Affection	85.59(22.89)	81.54(26.20)	83.33(20.81)	0.29[b]
Emotional Support	83.24(17.79)	78.14(23.51)	78.41(22.61)	0.41[b]

Treatment Arm				
	Low (n=74)	**Standard (n=93)**	**Intensive (n=78)**	
Domain/Items	**Mean(SD)[a]**	**Mean(SD)[a]**	**Mean(SD)[a]**	**P-Value**
Tangible Support	80.07(23.03)	73.12(27.04)	76.12(23.25)	0.20[b]
Life Events Score	5.79(5.79)	7.26(6.38)	5.85(4.91)	0.14[b]
Spiritual Well-Being				
Systems of Belief Score	2.31(0.78)	2.39(0.78)	2.29(0.73)	0.12[b]
Religious-Spiritual	2.49(0.79)	2.54(0.72)	2.45(0.72)	0.30[b]
Social Support	1.96(0.94)	2.12(1.00)	1.95(0.86)	0.07[b]
Economic Well-Being				
Perceived Negative Socio-Economic Impact	0.01(0.12)	0.08(0.27)	0.06(0.25)	0.20[b]
Perceived Positive Socio-Economic Impact	0.03(0.16)	0.02(0.03)	0.03(0.16)	1.00[b]

[a] Frequencies and percentages are displayed for categorical variables

[b] Kruskal-Wallis test

[c] Fisher's exact test

Table 4

Univariate Logistic Regression Analysis: Association of Demographic and Medical Characteristics With Decreased Physical Role Functioning

Variable	Odds Ratio	95% CI	P-Value
Treatment Arm:			
Low vs. High	1.62	0.80,3.28	0.75
Standard vs. High	3.17	1.64,6.12	0.0009
Age at Time of Interview: ≥60 years old vs. <60	1.85	1.08,3.23	0.03
Number of Co-Morbidities: * None vs. ≥1	4.76	2.13,10.0	0.0001
Type of Surgery: Lumpectomy vs. Mastectomy	0.97	0.52,1.79	0.91
Estrogen Receptor Status: Negative vs. Positive	2.17	1.22,4.00	0.009
Hormone Therapy: No vs. Yes	0.64	0.38,1.09	0.10
Radiation Therapy: No vs. Yes	0.91	0.49,1.68	0.77
High Blood Pressure Interference: No or N/A vs. Yes	0.11	0.04,0.33	0.0001
Diabetes Interference: No or N/A vs. Yes	0.12	0.03,0.43	0.001
Vitality Score (Fatigue)	1.06	1.05,1.09	<0.0001
Menopausal Symptom Total Score	1.07	1.05,1.09	<0.0001
SES: Lower vs Higher	2.76	1.57,4.85	0.0004
Time Since Diagnosis <12.3 vs. ≥12.3	1.14	0.68,1.92	0.62
Comorbidity Interference Total Score	2.81	2.10,3.76	<0.0001

* Comorbidities included (interfered with daily life): other cancers/leukemia, arthritis/rheumatism/other connective tissue disorder, glaucoma, emphysema/chronic bronchitis, high blood pressure, heart disease, circulation problems in legs/arms, diabetes, stomach/intestinal disorders, osteoporosis, chronic liver/kidney disease, stroke, and depression

Table 5

Multivariate Logistic Regression Analysis: Association of Demographic and Medical Characteristics With Decreased Physical Role Functioning

Variable	Odds Ratio	95% CI	P-Value
Age at time of interview: ≥60 years old vs. <60	3.55	1.45,8.62	0.006
Vitality Score (Fatigue)	1.05	1.02,1.08	0.0002
Menopausal Symptom Total Score	1.04	1.01,1.07	0.02
Comorbidity Interference Total Score	1.64	1.17,2.31	0.005