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Quality of Life Over Time in Women Diagnosed with Ductal Carcinoma *In situ*, Early-Stage Invasive Breast Cancer, and Age-Matched Controls

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Abstract

Little is known about quality-of-life (QOL) differences over time between incident ductal carcinoma *in situ* (DCIS) and early-stage invasive breast cancer (EIBC) cases as compared with same-aged women without breast cancer (controls). We prospectively recruited and interviewed 1096 women (16.8% DCIS, 33.3% EIBC [25.7% Stage I, 7.6% Stage IIA], 49.9% controls; mean age 58; 23.7% non-white) a mean 6.7 weeks (T1), and 6.2 (T2), 12.3 (T3), and 24.4 months (T4) after surgery (patients) or screening mammogram (controls). We tested two hypotheses: (1) DCIS patients would report lower levels of QOL compared with controls but would report similar QOL compared with EIBC patients at baseline; and (2) DCIS patients' QOL would improve during 2-year follow-up and approach levels similar to that of controls faster than EIBC patients. We tested Hypothesis 1 using separate general linear regression models for each of the eight subscales on the RAND 36-item Health Survey, controlling for variables associated with at least one subscale at T1. Both DCIS and EIBC patients reported lower QOL at T1 than controls on all subscales (each $p < .05$). We tested Hypothesis 2 using generalized estimating equations to examine change in each QOL subscale over time across the three diagnostic groups adjusting for covariates. By T3, physical functioning, role limitations due to physical problems, energy/fatigue, and general health each differed significantly by diagnostic group at $P < 0.05$, due to larger differences between EIBC patients and controls; but DCIS patients no longer differed significantly from controls on any of the QOL subscales. At T4, EIBC patients still reported worse physical functioning ($P = 0.0001$) and general health ($P = 0.0017$) than controls, possibly due to lingering treatment effects. DCIS patients' QOL was similar to that of controls two years after diagnosis, but some aspects of EIBC patients' QOL remained lower.

Keywords

Breast cancer; ductal carcinoma *in situ* (DCIS); early-stage invasive breast cancer; quality of life

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Introduction

Ductal carcinoma *in situ* (DCIS) is a noninvasive breast cancer diagnosed with greater frequency due to more widespread use of screening mammograms [1] and accounts for nearly 25% of breast cancer cases in the United States [2]. Despite increased incidence, few studies have addressed the quality of life (QOL) of women with DCIS [3–6]. Since women diagnosed with DCIS and early-stage invasive breast cancer (EIBC) have similar treatment options (i.e., mastectomy or breast-conserving surgery and radiation therapy, each with or without hormone therapy, as indicated) [7], DCIS and EIBC patients may be similar in their QOL experiences following surgery. However, since women diagnosed with DCIS have an excellent prognosis and this diagnosis is clinically distinct from EIBC [8–12], QOL in women with DCIS might be more similar to QOL in women without a history of breast cancer over time. Thus, we sought to examine the impact of a DCIS diagnosis on QOL outcomes, by comparing women with DCIS, women with EIBC, and a comparison group of age-matched women without a history of breast cancer.

The results of QOL studies in women with DCIS have been inconsistent, largely explained by limitations due to small samples of DCIS patients [3, 5] or the lack of comparison groups of either healthy women [3] or women with invasive breast cancer [3, 4, 6, 13]. Many QOL studies of breast cancer patients have combined patients with *in situ* carcinoma and invasive disease in one group for analysis [14–17], and some studies that included DCIS patients were cross-sectional in design [3–5, 14]. In this longitudinal study, we used examined changes in QOL in a cohort of incident DCIS and EIBC cases and of women without any breast cancer (controls) beginning shortly after definitive surgical treatment (patients) or routine screening mammogram with benign/normal findings (controls). We tested two hypotheses: (1) women with DCIS would report lower levels of QOL compared with controls but would report similar QOL compared with women with EIBC at baseline and (2) DCIS patients' QOL would improve during 2-year follow-up and approach levels similar to those of controls faster than EIBC patients.

Methods

Participants

We prospectively recruited participants between October 2003 and June 2007 from the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine and from Saint Louis University School of Medicine in Saint Louis, Missouri. Patients diagnosed by surgical pathology with a first primary stage 0-IIA breast cancer (without neoadjuvant chemotherapy) were eligible. Controls were identified two weeks following normal/benign screening mammograms and were frequency-matched by age group (40–49, 50–69, 70) to patient participants. We included women age 40 and older, since screening mammography is recommended for women in this age group [18] and DCIS is primarily identified using mammography [19]. Additional eligibility criteria included no prior history of *in situ* or invasive breast cancer, the ability to speak and understand English and no evidence of cognitive impairment on the Orientation-Memory-Concentration (OMC) Test [20], administered to participants 65 years of age or older.

Procedures and measures

Following Institutional Review Board approval at each institution and obtaining participants' informed consent, computer-assisted telephone interviews were administered at 4–6 weeks (T1), 6 months (T2), 1 year (T3), and 2 years (T4) following definitive surgical treatment (patients) or screening mammogram (controls). We collected participants' demographic information and administered validated measures of QOL, social support,

comorbidity, and history of depression as well as a measure of menopausal symptoms developed for this study. All measures were selected because they were previously found (or hypothesized) to be associated with QOL in breast cancer patients.

QOL was measured using the eight subscales of the RAND 36-Item Health Survey 1.0 [21] – physical functioning, role limitations due to physical problems, role limitations due to emotional health, energy/fatigue, emotional well-being, social functioning, pain, and general health. Standardized scores range from 0–100 with higher scores reflecting better QOL. The reliability and validity of the subscales have been established in studies of both general and patient populations [22–25]. A subscale score change of 3–5 points is considered evidence for a minimally clinically important difference [26, 27].

The 19-item Medical Outcomes Study (MOS) Social Support Survey [28] was used to measure how often social support is available, if needed. Response choices range from “none of the time” (1) to “all the time” (5). Higher mean scores indicate greater availability of social support. We used Katz’ [29] validated adaptation of the Charlson Comorbidity Index [30] to measure history and presence of comorbid conditions. A weighted index taking into account both the number and severity of comorbid diseases was computed; higher scores indicate greater comorbidity. History of depression at study enrollment was determined using two questions: “Has a doctor ever told you that you had depression?” and “Have you ever been treated for depression with medication or psychotherapy?” An affirmative response to either or both questions was coded as having a history of depression. Participants rated the severity of menopausal symptoms (hot flashes, cold sweats, night sweats, and vaginal dryness) “in the last month” using a 5-point scale from “not at all” (1) to “all the time” (5). Higher mean scores on this 4-item scale [31] indicate more severe menopausal symptoms.

In addition, we obtained information about age at diagnosis, race, marital status, employment status, household income, education, height and weight to compute body mass index (BMI), and use of postmenopausal estrogen/hormone replacement therapy (HRT). Patients’ clinical data obtained from the medical record included cancer stage (DCIS, EIBC [stage I or IIA]) [32], surgery type (BCS, mastectomy, bilateral mastectomy), and receipt of adjuvant therapy (radiation therapy, chemotherapy, endocrine therapy) during the study.

Data analysis

We used chi-square tests and analysis of variance (ANOVA) to compare characteristics of participants and non-participants and to compare participants who did and did not complete all four interviews. We used multivariable logistic regression to identify independent predictors of study completion and report adjusted odds ratios (aOR) and 95% confidence intervals (CI) for that analysis.

To test the first hypothesis, we measured the association between diagnostic group (DCIS and EIBC versus controls) and each of the eight QOL domains at T1 in separate general linear regression models for each QOL domain, controlling for selected variables significantly associated with at least one of the QOL domains at T1. To test the second hypothesis, the change in each QOL domain over time across three diagnostic groups was examined using generalized estimating equations (GEE), which account for the correlation among repeated measures within subjects and allow for inclusion of all available data. On the basis of the correlation matrices for eight QOL domains within subjects, an exchangeable correlation structure was specified for the within-subject correlation. In the eight separate GEE models, each QOL domain was the dependent variable and diagnostic group, time since definitive surgery (continuous), and the interaction between diagnostic group and time since definitive surgery were the independent variables of primary interest.

The interaction between diagnostic group and time since definitive surgery was tested to determine whether the rates of change over time in each QOL domain (i.e., change in each QOL subscale per six months after definitive surgery) differed by diagnostic group. The procedure GENMOD in SAS (version 9.1, SAS Institute, Cary, NC) was used to fit the GEE models, which were adjusted for the selected covariates. We used the CONTRAST statement in PROC GENMOD to test if the change in each QOL domain over two years differed between DCIS and EIBC patients and between controls and each of DCIS and EIBC patients. Two-sided P values < 0.05 were considered statistically significant.

Results

We enrolled 549 patients (71.1% of 772 invited) and 547 controls (57.8% of 946 invited). A greater proportion of the 1096 participants than of 622 non-participants were white (76.2% vs. 59.0%; $P < .001$) and married (61.1% vs. 49.9%; $P < .001$); the two groups did not differ significantly by age or, among patients, by cancer stage or surgery type.

Descriptive statistics are included in Table 1. Telephone interviews were completed a mean 6.7 weeks (T1), 6.2 months (T2), 12.3 months (T3), and 24.4 months (T4) following definitive surgery (patients) or screening mammogram (controls). Retention was high with 1,011 participants completing T4 (92.2% overall; 514 [93.6%] patients, 497 [90.9%] controls). Participants who completed the study reported lower levels of comorbidity at T1 than participants who did not (mean [SD]: 0.5 [0.9] vs. 0.8 [1.3]; $P = 0.004$). Only race (aOR: 0.577, 95% CI: 0.353–0.943; $P = 0.028$) and marital status (aOR: 0.566, 95% CI: 0.350–0.915; $P = 0.020$) independently predicted study completion; a greater proportion of white than non-white (786/837 [93.9%] vs. 225/259 [86.9%]) and of married than unmarried (632/668 [94.6%] vs. 379/428 [88.6%]) participants completed the study. Moreover, non-white participants were less likely to be married (92/259 [35.5%] vs. 576/837 [68.8%]), and they reported higher levels of comorbidity at T1 (0.8 [1.2] vs. 0.4 [0.8]) than white participants (each $P < 0.001$).

DCIS patients were less likely to have had lymph nodes removed and to have received chemotherapy, radiation and endocrine therapy than EIBC patients (Table 1).

Unadjusted analyses

Table 2 shows the unadjusted mean QOL subscale scores at each interview by diagnostic group (DCIS, EIBC, controls) and the results of post hoc pair-wise comparisons for each subscale at each interview. All eight QOL subscales differed significantly by diagnostic group at T1 (each ANOVA test of main effects $P = 0.001$).

We examined collinearity among potential covariates (Tables 3 and 4). A higher proportion of high school graduates than non-high school graduates were employed at least part time (56.4% vs. 23.3%) and had household income \geq \$25,000/year (69.3% vs. 20.5%) (chi-square tests, $P < 0.001$). Since 7.3% of participants did not report household income and employment status could change over time, we included education as a covariate in addition to race, age, marital status, use of HRT, a history of depression, BMI, social support, comorbidity, and severity of menopausal symptoms.

Multivariable models

Figure 1 shows the adjusted means for each QOL subscale at each interview. For Hypothesis 1, we observed significant main effects by diagnostic group (DCIS, EIBC, controls) for all eight QOL subscales at T1, controlling for all covariates in the general linear regression models (each $P < 0.0001$). Controls reported better QOL at T1 on each subscale compared with DCIS patients (each $P < 0.02$) and with EIBC patients (each $P < 0.0001$). At T1, DCIS

patients reported better QOL than EIBC patients on the role limitations due to physical problems ($P = 0.0021$), energy/fatigue ($P = 0.0231$), and social functioning ($P = 0.0006$) subscales.

Both DCIS and EIBC patients showed improvements in QOL over the 2-year follow-up (Fig. 1). However by T2, there were still significant differences by diagnostic group overall in physical functioning ($P < 0.0001$), role limitations due to physical ($P < 0.0001$) and emotional ($P = 0.0053$) problems, energy/fatigue ($P = 0.0005$), social functioning ($P < 0.0001$), pain ($P = 0.0087$), and general health ($P < 0.0001$). Only emotional well being did not differ significantly by diagnostic group at T2. In support of Hypothesis 2, there were no statistically significant differences in post-hoc contrasts between DCIS patients and controls in any subscale but physical functioning at T2; however, all eight subscales at T2 differed significantly between EIBC patients and controls (each $P < 0.005$). In addition, DCIS ($P = 0.0118$) and EIBC ($P < 0.0001$) patients each reported worse physical functioning compared with controls at T2, and DCIS patients reported significantly better QOL on role limitations due to physical problems ($P < 0.0001$), energy/fatigue ($P = 0.0008$), social functioning ($P = 0.0004$), pain ($P = 0.0206$), and general health ($P = 0.0392$) than EIBC patients at T2.

By T3, there were still significant differences by diagnostic group overall in physical functioning ($P = 0.0337$), role limitations due to physical problems ($P = 0.0379$), energy/fatigue ($P = 0.0010$), and general health ($P = 0.0011$). In post-hoc contrasts, DCIS patients no longer differed significantly from controls on any of the eight QOL subscales, but EIBC patients still reported worse QOL than controls on physical functioning ($P = 0.0095$), role limitations due to physical problems ($P = 0.0155$), energy/fatigue ($P = 0.0131$), and general health ($P = 0.0002$). Moreover, EIBC patients reported worse energy/fatigue compared with DCIS patients at T3 ($P = 0.0004$).

By T4, the main effect of diagnostic group was significant only for physical functioning ($P = 0.0005$) and general health ($P = 0.0059$). In post-hoc contrasts, EIBC patients still reported worse physical functioning ($P = 0.0001$) and general health ($P = 0.0017$) than controls.

In GEE models (Table 5), we tested whether the rates of recovery differed between DCIS and EIBC by including an interaction term between diagnostic group and time since definitive surgical treatment. The rate of recovery differed significantly between DCIS and EIBC patients only for social functioning ($P = .03$).

Discussion

Our study contributes to the paucity of knowledge about changes in QOL over the first two years after a diagnosis of DCIS or EIBC and about differences in QOL between these two groups and between each patient group and women without breast cancer. Few studies have directly compared QOL between women with DCIS and EIBC [5, 33], and these studies did not include a comparison group of women without breast cancer. Other studies measuring QOL in breast cancer patients at various times after diagnosis were cross-sectional [3–5, 14, 16, 34–36]. Our findings can help inform treatment decisions and the design of interventions that address early on the QOL needs of DCIS and EIBC survivors, who comprise a growing proportion of all breast cancer survivors in the U.S. due to concomitant increases in early detection by screening mammography and receipt of adjuvant treatment [37]. Overall, the 5-year relative survival for 2001–2007 was 99% for breast cancer survivors with localized disease [38].

Our first hypothesis was that DCIS patients would report similar levels of QOL as EIBC patients 4–6 weeks following definitive surgery, since these patients receive similar surgical treatments. Although DCIS and EIBC patients reported similar levels of QOL on several

subscales in the multivariable analysis, DCIS patients reported significantly (and clinically meaningfully [26, 27]) higher scores on energy/fatigue, role limitations due to physical problems, and social functioning than EIBC patients at T1. Several factors might explain differences in these QOL subscales between DCIS and EIBC patients shortly after surgical treatment. Although QOL has been reported to differ by surgery type among breast cancer patients [39–41], these differences by surgery type may be due to lymph node removal to determine extent of invasive disease. Lymph node sampling to diagnose local spread of disease is standard surgical treatment for patients' with invasive breast cancer [42] but is used less frequently in patients with DCIS [43, 44]. A greater percentage of EIBC patients in our cohort received some type of lymph node sampling procedure than DCIS patients (Table 1). Lymph node removal [45] and the development of lymphedema following axillary lymph node dissection in particular [46–48] have been reported to be associated with poorer QOL outcomes, which may explain QOL differences between EIBC and DCIS patients at T1 in role limitations due to physical problems.

Differences in adjuvant treatment, which are reported to be associated with poorer QOL [33, 49–52], also might contribute to differences between DCIS and EIBC patients' energy/fatigue, role limitations due to physical problems, and social functioning at T1. Chemotherapy was only received by EIBC patients. In addition at T1, EIBC patients were more likely than DCIS patients to have received radiation therapy and endocrine therapy, which has been found to be associated with diminished QOL [53–55]. Lower social functioning would be expected while patients are receiving treatment. Thus, the lower proportion of DCIS patients than EIBC patients who received adjuvant treatment at T1 could explain poorer energy/fatigue, role functioning due to physical problems, and social functioning scores in EIBC than DCIS patients at T1.

Both DCIS and EIBC patients reported worse QOL than controls at T1. But, in support of Hypothesis 2, by T2, DCIS patients only reported significantly lower physical functioning than controls – a difference no longer apparent at T3. Although EIBC patients also showed improvements in QOL over time, DCIS patients reached QOL levels reported by controls sooner than EIBC patients did. Moreover, EIBC patients' physical functioning and general health did not reach levels reported by controls during the 2-year study period, which also might be attributable to receipt of adjuvant treatments [33, 52–56].

The rate of change in QOL domains was similar in DCIS and EIBC patients, except for social functioning; EIBC patients, whose social functioning was poorer than that of DCIS patients at T1, showed a greater rate of increase in social functioning after T2 than DCIS patients did. As shown in Table 2 and Figure 1, minimally clinically important changes of at least 3–5 points [26, 27] occurred in both DCIS and EIBC patients on all subscales except physical functioning and general health perceptions in the first six months after surgery, similar to changes reported elsewhere [15]. Like other longitudinal studies [13, 15, 17, 33, 57], we found that DCIS and EIBC patients reported significant improvements in QOL domains over time. Although rates of change for seven subscales were similar for DCIS and EIBC patients, DCIS patients reached QOL levels reported by controls on all eight subscales before EIBC patients did.

Similar to a previous report [33], emotional well being did not differ significantly between DCIS and EIBC patients at T1 despite DCIS patients' better prognosis and need for less aggressive treatment following definitive surgery. By T2, there was no significant main effect by diagnostic group in this subscale at all (Fig. 1). Similarly, investigators using the Nurses' Health Study data reported the relative risk of decline in emotional well being (from a pre-diagnosis assessment) was not significantly greater among incident breast cancer cases diagnosed 6–11 months ago (*in situ* and invasive disease combined) and controls without

any breast cancer [17]. Another study using these data observed clinically significant declines in social functioning and mental health in women diagnosed with DCIS < six months before the QOL assessment compared with controls [6], but incident invasive breast cancer cases were not included. It remains to be seen whether and to what extent our cohort of DCIS and EIBC patients and controls might differentially report QOL in these domains after longer-term follow-up.

Strengths of our study include our longitudinal design and high retention rates of a cohort of DCIS and EIBC patients and women without a history of breast cancer. We examined QOL over time in DCIS and EIBC patients separately, comparing each to one another and to a same-aged control group of women without breast cancer, which other studies [13, 15, 33, 57] did not. Although we lacked pre-diagnosis levels of QOL among the patients in our study, our findings of poorer QOL in patients compared with controls at T1 was not unexpected given the greater relative risk of decline in QOL observed among more recently diagnosed breast cancer patients (i.e., QOL assessment < six months after diagnosis) compared with women without a breast cancer diagnosis in the Nurses' Health Study; this relative risk of decline was attenuated with longer time since diagnosis [17]. However, since we recruited our patients and controls from a National Cancer Institute-designated comprehensive cancer center and another academic medical center in the same city, the generalizability of our findings may be limited. Additionally, our findings may not be generalizable to breast cancer patients who are younger than 40 years of age [47] or who have more advanced disease, since these patients may receive more aggressive treatment regimens. Although the representation of non-white patients in our sample (26%) was comparable to their distribution in the Siteman Cancer Center breast cancer patient population, 95% of non-white participants was African American, limiting generalizability of our findings to other racial/ethnic groups [58–60]. Finally, as reported elsewhere [34], participation rates were somewhat higher for patients than controls and for white than non-white women; a greater proportion of non-participants and of participants not completing the study were non-white and unmarried, thereby introducing potential selection bias.

In closing, our results supported our hypotheses for most QOL domains. DCIS and EIBC patients each reported poorer QOL compared with controls at T1 and showed improvements on all QOL subscales over two-year follow-up. Thus, in the short-term, there are differential QOL outcomes following different breast cancer treatments, and differences between DCIS and EIBC patients might be explained by treatments received. After two years, the significant differences between patients and controls in physical functioning and general health perceptions could be explained by lingering treatment effects among EIBC patients. Further examination of longer-term QOL outcomes in early-stage breast cancer survivors is warranted, since there is a paucity of data published on the impact of breast cancer radiation therapy on either short- or long-term QOL outcomes among DCIS and EIBC survivors [61, 62], and the late effects on QOL of some breast cancer treatments, e.g., brachytherapy and newer endocrine therapies, are largely unknown [55, 63].

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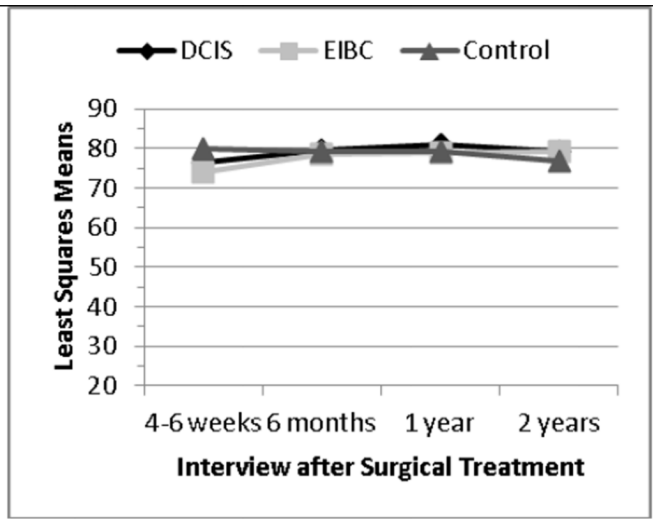
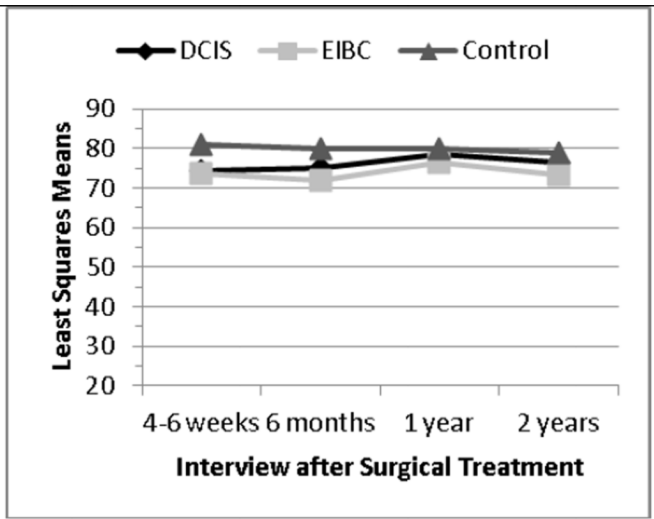
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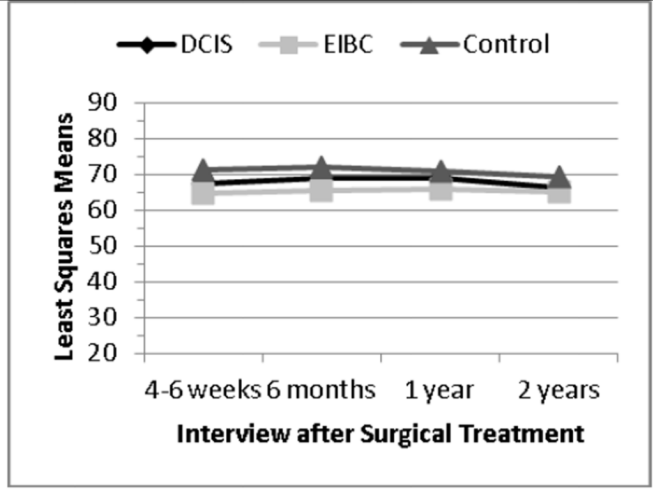
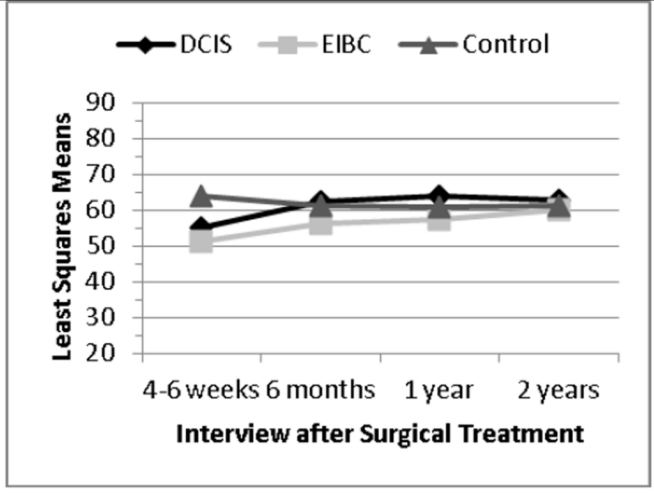
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Physical functioning

Emotional well-being



Energy/fatigue

General health

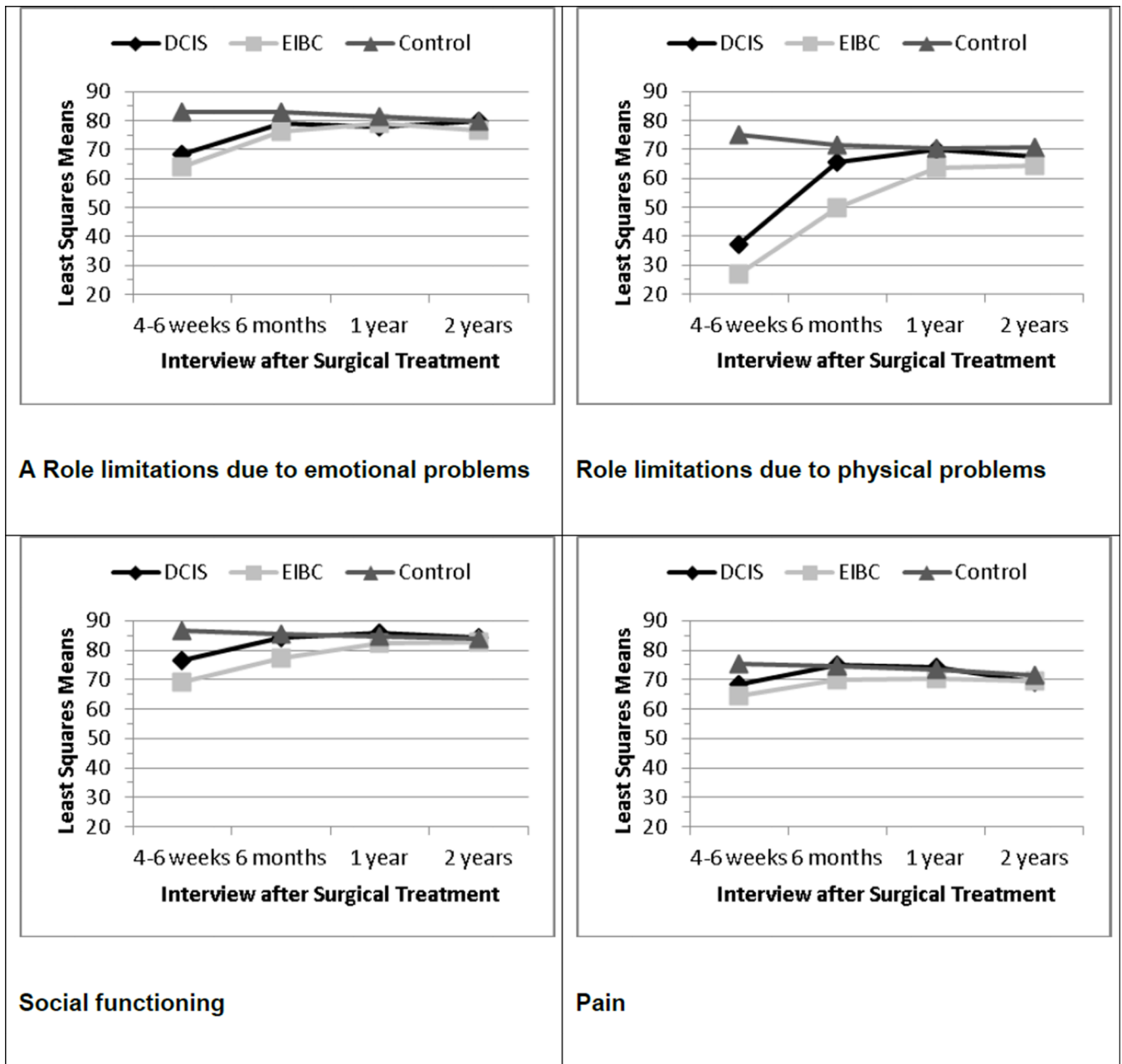


Fig. 1. Least-square means at each interview for RAND 36-item Health Survey subscales adjusting for all covariates in general linear models, by diagnostic group. Higher scores indicate better quality of life. *DCIS* ductal carcinoma *in situ*, *EIBC* early-invasive breast cancer

Table 1

Sample characteristics by diagnostic group at enrollment

	DCIS n = 184	EIBC n = 365	Controls n = 547	P value
Age, mean (SD)	57.2 (10.3)	58.9 (10.7)	57.2 (10.6)	.041
BMI, mean (SD)^a	28.4 (6.6)	28.5 (6.9)	28.4 (7.0)	.982
Menopausal Symptoms, mean (SD)	1.6 (0.8)	1.7 (0.8)	1.6 (0.7)	.669
Comorbidity, mean (SD)	0.5 (0.8)	0.6 (1.0)	0.5 (0.9)	.328
Social Support, mean (SD)	4.5 (0.7)	4.5 (0.7)	4.3 (0.8)	< .001
	<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>	
Race				0.019
White	146 (79.3%)	293 (80.3%)	398 (72.8%)	
Non-white	38 (20.7%)	72 (19.7%)	149 (27.2%)	
Marital status				0.306
Married	116 (63.0%)	215 (58.9%)	337 (61.6%)	
Widowed	17 (9.2%)	58 (15.9%)	57 (10.4%)	
Divorced/separated	36 (19.6%)	53 (14.5%)	90 (16.5%)	
Never been married	15 (8.2%)	39 (10.7%)	63 (11.5%)	
Employment status				0.070
Working at least part time	104 (56.5%)	176 (48.2%)	313 (57.2%)	
Retired	48 (26.1%)	105 (28.8%)	139 (25.4%)	
Homemaker	16 (8.7%)	27 (7.4%)	36 (6.6%)	
Unable to work/unemployed	16 (8.7%)	57 (15.6%)	59 (10.8%)	
Annual income				0.145
< \$25,000	46 (25.0%)	99 (27.1%)	117 (21.4%)	
\$25,000–\$75,000	68 (37.0%)	142 (38.9%)	207 (37.8%)	
> \$75,000	58 (31.5%)	93 (25.5%)	186 (34.0%)	
Refused/don't know	12 (6.5%)	31 (8.5%)	37 (6.8%)	
	<i>DCIS n = 184 (%)</i>	<i>EIBC n = 365 (%)</i>	<i>Controls n = 547 (%)</i>	<i>P value</i>
Education				0.383
< High school graduate	12 (6.5%)	31 (8.5%)	30 (5.5%)	
At least high school graduate	172 (93.5%)	334 (91.5%)	516 (94.3%)	
Refused	0 (0.0%)	0 (0.0%)	1 (0.2%)	
Postmenopausal hormone therapy				< 0.001
Previous use	86 (46.7%)	160 (44.0%)	183 (33.5%)	
Current use	2 (1.1%)	3 (0.80%)	98 (17.9%)	
Never used	96 (52.2%)	201 (55.2%)	266 (48.6%)	
Refused	0 (0.0%)	1 (0.3%)	0 (0.0%)	
History of depression				0.084
Yes	75 (40.8%)	123 (33.7%)	222 (40.6%)	

	DCIS n = 184	EIBC n = 365	Controls n = 547	P value
No	109 (59.2%)	242 (66.3%)	325 (59.4%)	
Patients only				
Surgery type				0.115
Breast-conserving surgery	111 (60.3%)	245 (67.1%)	---	
Mastectomy	73 (39.7%)	120 (32.9%)	---	
Lymph Node Removal				< 0.001
Yes	80 (43.5%)	358 (98.1%)	---	
No	104 (56.5%)	7 (1.9%)	---	
Radiation therapy during study				0.012
Yes ^b	104 (56.5%)	246 (67.4%)	---	
No	80 (43.5%)	119 (32.6%)	---	
Chemotherapy during study				< 0.001
Yes ^c	0 (0.0%)	136 (37.3%)	---	
No	184 (100.0%)	229 (62.7%)	---	
Endocrine therapy during study				< 0.001
Yes ^d	79 (42.9%)	265 (72.6%)	---	
No	101 (54.9%)	99 (27.1%)	---	
Unknown	4 (2.2%)	1 (0.3%)	---	

SD standard deviation, DCIS ductal carcinoma *in situ*, EIBC early invasive breast cancer (stages I and IIA)

Tests of significance were one-way analysis of variance for continuous variables and chi-square tests for categorical variables

^aBMI was not calculated for 5 women lacking height and/or weight data (1 DCIS, 2 EIBC, and 2 Control)

^b130 patients (55 DCIS, 75 EIBC) self-reported receipt of radiation therapy at T1

^c59 EIBC patients self-reported taking chemotherapy at T1

^d100 patients (29 DCIS, 71 EIBC) self-reported taking endocrine therapy at T1

Table 2
Unadjusted mean (SD) RAND 36-item Health Survey subscale scores at each interview, by diagnostic group

	DCIS												EIBC												Controls																																																																							
	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4																																																																								
PF	78.48 ^a (23.17)	80.06 (23.95)	81.53 (23.09)	80.50 (24.02)	76.46 ^b (22.56)	75.66 ^b (25.15)	77.68 ^b (23.94)	76.33 ^b (25.34)	84.07 ^{a,b} (21.13)	84.10 ^b (21.66)	83.48 ^b (21.40)	83.81 ^b (20.15)	42.26 ^{a,c} (42.92)	71.25 ^c (40.29)	75.00 (38.60)	74.71 (38.67)	32.74 ^{b,c} (39.92)	55.74 ^{b,c} (44.60)	66.86 ^b (42.55)	70.25 ^b (41.80)	78.56 ^{a,b} (35.82)	77.29 ^b (35.53)	75.48 ^b (37.39)	78.17 ^b (36.01)	74.28 ^a (39.61)	82.78 (32.00)	82.77 (34.03)	86.02 (31.69)	71.42 ^b (39.17)	80.35 ^b (35.56)	84.76 (31.76)	83.48 (34.05)	87.20 ^{a,b} (28.90)	77.29 ^b (35.53)	86.14 (29.87)	85.21 (30.94)	55.51 ^a (23.45)	61.75 ^c (23.23)	64.76 ^c (21.62)	63.39 (22.04)	51.99 ^b (22.69)	55.51 ^{b,c} (25.72)	58.34 ^{b,c} (23.97)	60.57 (24.00)	63.21 ^{a,b} (19.97)	61.72 ^b (20.25)	62.69 ^b (19.86)	62.32 (20.22)	77.61 (17.80)	80.13 (15.91)	82.36 (15.75)	81.56 (15.30)	76.50 ^b (18.34)	79.97 (17.40)	80.99 (17.33)	82.23 ^c (16.78)	80.76 ^b (14.98)	80.41 (15.79)	81.01 (14.29)	79.03 ^b (16.91)	78.53 ^{a,c} (25.86)	85.97 ^c (23.02)	87.57 (21.93)	87.57 (21.06)	72.36 ^{b,c} (28.29)	79.52 ^{b,c} (26.44)	83.71 (23.88)	85.92 (22.80)	88.16 ^{a,b} (21.15)	87.42 ^b (22.42)	86.82 (21.36)	86.77 (21.53)	70.35 ^a (25.41)	77.08 (22.81)	77.16 (23.43)	73.58 (25.11)	66.66 ^b (25.03)	71.90 ^b (25.58)	72.81 (24.38)	73.25 (24.18)	76.07 ^{a,b} (22.15)	77.14 ^b (24.11)	76.63 (22.73)	76.32 (23.91)	70.68 (21.51)	70.93 (18.76)	71.52 (19.45)	69.72 (22.24)	67.98 ^b (21.48)	67.17 ^b (22.46)	68.43 ^b (22.86)	67.99 ^b (22.55)	73.20 ^b (20.33)	73.81 ^b (20.80)	73.57 ^b (20.58)	73.42 ^b (21.08)

SD standard deviation, DCIS ductal carcinoma *in situ*, EIBC early invasive breast cancer (stages I and IIA), T1 first interview 4–6 weeks after definitive surgical treatment, T2 second interview 6-month follow-up, T3 third interview 1-year follow-up, T4 fourth interview 2-year follow-up, PF physical functioning, RP role limitations due to physical problems, RE role limitations due to emotional problems, E/F energy/fatigue, EWB emotional well being, SF social functioning, GH general health

Scores range from 0 to 100

^a Analysis of variance post-hoc comparisons between DCIS patients and controls significant at $P < 0.05$ at the same interview

^b Analysis of variance post-hoc comparisons between EIBC patients and controls significant at $P < 0.05$ at the same interview

^c Analysis of variance post-hoc comparisons between DCIS and EIBC patients significant at $P < 0.05$ at the same interview

Table 3

Unadjusted mean (SD) RAND 36-item Health Survey subscale scores in association with covariates of interest in 1096 study participants at the first interview

	PF	P value	RP	P value	RE	P value	E/F	P value
Race								
White	82.86 (20.23)	<.001	58.87 (43.73)	.025	81.00 (34.02)	.038	57.89 (21.78)	.511
Non-white	73.29 (26.45)		51.81 (44.83)		75.80 (38.88)		58.92 (23.14)	
Marital status								
Married	84.54 (18.92)	<.001	59.77 (43.60)	.019	83.13 (32.15)	<.001	59.30 (21.25)	<.001
Widowed	73.56 (26.65)		58.27 (41.91)		83.07 (33.40)		62.83 (20.52)	
Divorced/separated	75.06 (25.42)		48.37 (45.46)		70.20 (41.25)		52.31 (24.95)	
Never been married	74.42 (25.27)		55.34 (45.47)		72.08 (40.34)		55.51 (22.02)	
Employment status								
Working at least part time	86.07 (17.50)	<.001	63.41 (43.22)	<.001	80.72 (34.17)	<.001	59.28 (21.51)	<.001
Retired	77.23 (23.21)		57.02 (42.55)		86.87 (29.19)		61.28 (20.97)	
Homemaker	82.57 (21.03)		59.81 (43.38)		82.28 (34.93)		60.32 (20.64)	
Unable to work/unemployed	62.31 (28.00)		28.22 (40.32)		58.33 (43.85)		44.67 (23.47)	
Education^a								
< High school graduate	67.29 (23.21)	<.001	39.38 (42.06)	<.001	63.24 (41.66)	<.001	49.73 (23.09)	.001
At least high school graduate	81.59 (21.82)		58.53 (43.94)		80.94 (34.51)		58.76 (21.91)	
Postmenopausal hormone therapy								
Previous use	80.28 (21.00)	.026	56.18 (41.13)	<.001	81.47 (33.20)	.018	57.54 (22.03)	.027
Current use	86.22 (17.53)		75.00 (38.82)		86.73 (28.90)		63.72 (19.01)	
Never used	79.91 (23.64)		54.80 (45.03)		77.18 (37.62)		57.60 (22.57)	
History of depression								
Yes	76.53 (23.89)	<.001	49.52 (44.27)	<.001	68.17 (41.25)	<.001	50.32 (22.47)	<.001
No	83.12 (20.74)		61.98 (43.30)		86.98 (28.76)		62.98 (20.44)	
Patients only								

	PF	P value	RP	P value	RE	P value	E/F	P value
Surgery type								
Breast-conserving surgery	79.21 (23.23)	.004	44.59 (42.43)	<.001	71.91 (39.05)	.708	55.00 (22.75)	.007
Mastectomy	73.31 (21.40)		19.95 (33.32)		73.23 (39.86)		49.51 (23.01)	
Lymph node removal								
Yes	69.66 (25.36)	.002	28.08 (37.95)	.080	65.30 (42.10)	.099	54.26 (23.16)	.002
No	78.28 (22.14)		37.13 (41.53)		73.46 (38.79)		45.27 (20.21)	
Radiation therapy								
Yes	80.11 (21.77)	<.001	42.86 (42.09)	<.001	70.76 (39.57)	.203	54.27 (22.24)	.103
No	71.91 (23.57)		23.74 (36.48)		75.21 (38.78)		50.95 (24.12)	
Chemotherapy								
Yes	75.08 (23.16)	.368	23.16 (35.18)	<.001	64.46 (42.20)	.009	49.74 (22.64)	.146
No	77.28 (22.20)		38.43 (41.52)		75.55 (36.72)		53.32 (22.66)	
Endocrine therapy								
Yes	78.50 (21.34)	.062	38.44 (41.42)	.042	72.19 (38.92)	.892	53.15 (22.91)	.913
No	74.74 (24.77)		31.00 (40.20)		72.67 (40.07)		52.93 (23.26)	

	EWB	P value	SF	P value	Pain	P value	GH	P value
Race								
White	79.13 (16.20)	.261	82.50 (24.39)	.005	72.84 (23.36)	.034	73.04 (20.31)	<.001
Non-white	77.79 (18.42)		77.36 (28.65)		69.21 (26.06)		64.55 (22.01)	
Marital status								
Married	80.19 (14.92)	<.001	83.72 (23.63)	<.001	73.52 (22.86)	.003	73.84 (19.70)	<.001
Widowed	84.15 (23.49)		84.15 (23.49)		74.17 (22.67)		71.16 (19.49)	
Divorced/separated	73.10 (30.33)		73.10 (30.33)		67.16 (27.49)		64.81 (23.05)	
Never been married	77.14 (27.03)		77.14 (27.03)		68.40 (25.35)		64.69 (23.30)	
Employment status								
Working at least part time	79.29 (15.12)	<.001	83.83 (22.77)	<.001	74.70 (21.92)	<.001	74.06 (19.35)	<.001
Retired	83.29 (14.87)		84.20 (24.53)		73.49 (23.47)		71.95 (18.94)	
Homemaker	80.96 (14.64)		87.18 (19.51)		75.63 (23.32)		74.27 (19.84)	
Unable to work/unemployed	65.53 (21.64)		59.85 (31.84)		54.24 (27.50)		53.50 (24.76)	
Education^a								

	EWB	P value	SF	P value	Pain	P value	GH	P value
< High school graduate	72.55 (19.55)	.001	72.94 (27.48)	.004	67.23 (25.39)	.076	60.21 (19.82)	<.001
At least high school graduate	79.25 (16.46)		81.92 (25.28)		72.38 (23.87)		71.81 (20.92)	
Postmenopausal hormone therapy								
Previous use	80.22 (14.99)	.003	82.58 (23.97)	<.001	72.24 (23.18)	.296	70.18 (20.24)	.398
Current use	81.72 (13.87)		89.93 (16.61)		75.10 (20.97)		73.16 (21.58)	
Never used	77.19 (18.29)		78.69 (27.59)		71.16 (25.20)		71.31 (21.53)	
History of depression								
Yes	71.90 (19.56)	<.001	74.20 (27.77)	<.001	66.01 (24.72)	<.001	64.88 (22.78)	<.001
No	83.11 (13.01)		85.69 (23.00)		75.69 (22.89)		74.86 (18.89)	
Patients only								
Surgery type								
Breast-conserving surgery	76.99 (17.96)	.841	78.83 (25.17)	<.001	71.90 (23.71)	<.001	68.54 (21.36)	.616
Mastectomy	76.66 (18.54)		66.32 (30.10)		60.53 (26.23)		69.51 (21.82)	
Lymph node removal								
Yes	71.18 (20.48)	.004	66.10 (27.91)	.006	58.25 (23.31)	<.001	61.51 (23.95)	.002
No	77.75 (17.63)		75.71 (27.39)		69.38 (25.17)		70.01 (20.91)	
Radiation therapy								
Yes	76.26 (17.81)	.296	77.98 (25.12)	<.001	70.55 (23.90)	.001	68.58 (21.09)	.661
No	77.95 (18.74)		86.34 (30.12)		63.24 (26.76)		69.42 (22.26)	
Chemotherapy								
Yes	73.18 (19.75)	.007	64.34 (29.44)	<.001	62.28 (25.02)	.010	66.58 (23.16)	.340
No	78.48 (17.18)		77.13 (26.52)		69.27 (24.73)		68.80 (20.42)	
Endocrine therapy								
Yes	77.26 (17.78)	.531	75.76 (27.25)	.160	69.18 (24.93)	.110	69.76 (21.03)	.191
No	76.24 (18.20)		72.31 (28.21)		65.60 (25.58)		67.25 (22.42)	

PF physical functioning, *RP* role limitations due to physical problems, *RE* role limitations due to emotional problems, *E/F* energy/fatigue, *EWB* emotional well being, *SF* social functioning, *GH* general health

Scores range from 0 to 100

^aOne person did not report education level and was excluded. *n* = 1095.

Pearson product-moment correlations among RAND 36-item Health Survey subscale scores and covariates in 1096 study participants at the first interview

Table 4

	2	3	4	5	6	7	8	9	10	11	12	13
1. PF	.487 ^a	.282 ^a	.222 ^a	.435 ^a	.545 ^a	.460 ^a	.550 ^a	-.343 ^a	-.105 ^a	-.339 ^a	-.140 ^a	.164 ^a
2. RP		.298 ^a	.332 ^a	.613 ^a	.393 ^a	.531 ^a	.547 ^a	-.120 ^a	-.093 ^b	-.141 ^a	.007	.052
3. EWb			.636 ^a	.539 ^a	.433 ^a	.558 ^a	.387 ^a	-.075 ^c	-.239 ^a	-.071 ^c	.227 ^a	.319 ^a
4. RE				.465 ^a	.310 ^a	.409 ^a	.287 ^a	-.074 ^c	-.203 ^a	-.076 ^c	.171 ^a	-.200 ^a
5. SF					.394 ^a	.579 ^a	.532 ^a	-.115 ^a	-.169 ^a	-.328 ^a	.016	.153 ^a
6. GH						.508 ^a	.473 ^a	-.330 ^a	-.194 ^a	-.305 ^a	-.320 ^a	.228 ^a
7. E/F							.517 ^a	-.178 ^a	-.189 ^a	-.156 ^a	.135 ^a	.201 ^a
8. Pain								-.193 ^a	-.175 ^a	-.138 ^a	.071 ^c	.125 ^a
9. BMI ^d									.011	.214 ^a	-.010	-.095 ^b
10. Menopausal symptoms										.090 ^b	-.161 ^a	-.084 ^b
11. Comorbidity											.155 ^a	-.088 ^b
12. Age												.030
13. Social support												1.000

PF physical functioning, RP role limitations due to physical problems, EWb emotional well being, RE role limitations due to emotional problems, SF social functioning, GH general health, E/F energy/fatigue, BMI/body-mass index

^a $P < 0.001$

^b $P = 0.005$

^c $P < 0.02$

^d Five women lacked data to compute BMI, $n = 1091$.

Table 5

Test for differences in change in each RAND 36-item Short Survey quality-of-life domain per 6 months after diagnosis over 2-year follow-up, by diagnostic group.

	Change per 6 Months after Diagnosis (95% CI)			Test for Differences in Change between:			P value
	Controls	DCIS	EIBC	DCIS and EIBC	DCIS and Controls	EIBC and Controls	
PF	-0.29 (-0.64, 0.06)	0.75 (-0.09, 1.60)	0.33 (-0.32, 0.98)	0.38	0.08	0.31	
RP	-0.33 (-1.14, 0.49)	7.27 (5.25, 9.30)	9.22 (7.62, 10.82)	0.10	<0.0001	<0.0001	
EWB	-0.48 (-0.81, -0.14)	1.49 (0.84, 2.14)	1.85 (1.29, 2.40)	0.32	<0.0001	<0.0001	
RE	-0.73 (-1.44, -0.01)	3.48 (1.88, 5.08)	3.67 (2.31, 5.03)	0.84	<0.0001	<0.0001	
SF	-0.50 (-1.02, 0.02)	2.52 (1.42, 3.62)	3.91 (3.02, 4.79)	0.03	<0.0001	<0.0001	
GH	-0.11 (-0.44, 0.22)	-0.01 (-0.69, 0.68)	0.19 (-0.39, 0.76)	0.61	0.98	0.52	
E/F	-0.24 (-0.64, 0.17)	2.22 (1.31, 3.14)	2.46 (1.72, 3.19)	0.65	<0.0001	<0.0001	
Pain	-0.12 (-0.61, 0.37)	0.68 (-0.42, 1.77)	1.71 (0.82, 2.59)	0.10	0.23	<0.0001	

CI Confidence Interval, DCIS ductal carcinoma *in situ*, EIBC early invasive breast cancer, PF physical functioning, RP role limitations due to physical problems, EWB emotional well being, RE role limitations due to emotional problems, SF social functioning, GH general health, E/F energy/fatigue

Generalized Estimating Equation models were adjusted for age, race, education, marital status, BMI, social support, comorbidity, history of depression, menopausal symptoms, and hormone replacement therapy use