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ORIGINAL ARTICLE – BREAST ONCOLOGY

The Effects of Surgery Type and Chemotherapy on Early-Stage Breast Cancer Patients' Quality of Life Over 2-Year Follow-up

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ABSTRACT

Background. We examined the effects of surgery type and adjuvant chemotherapy on change in early-stage breast cancer patients' quality of life (QOL) over time.

Methods. A cohort of 549 patients (33.5 % ductal carcinoma in situ, 66.5 % stages I/IIA) were interviewed a mean 6.1 weeks (Time1), and 6.2 (Time2), 12.3 (Time3), and 24.4 (Time4) months following definitive breast-conserving surgery (BCS) or mastectomy. QOL was measured using the total Functional Assessment of Cancer Therapy-Breast (FACT-B). Adjusting for demographic, psychosocial, and clinical variables, multiple linear regression models estimated the associations between QOL and each of surgery type, chemotherapy, and their 2-way interaction at each interview. Adjusted generalized estimating equation (GEE) models tested Time1–Time4 change in QOL.

Results. At Time2, chemotherapy ($P < .001$) and BCS ($P < .001$) were independently associated with worse QOL in adjusted linear regression, and the adverse effect of chemotherapy was prominent among patients who received BCS compared with those who received mastectomy ($P_{\text{interaction}} = .031$). In the GEE model, QOL significantly improved over time among patients who received BCS ($P_{\text{trend}} = .047$), mastectomy ($P_{\text{trend}} = .024$), and chemotherapy ($P_{\text{trend}} < .001$), but not among patients who did not receive chemotherapy ($P_{\text{trend}} = .720$). All patients completed adjuvant chemotherapy and radiation by Time3. Regardless of surgery type, patients receiving chemotherapy reported lower QOL following surgery, and QOL improved after completion of adjuvant treatment.

Conclusions. Chemotherapy had a short-term negative impact on QOL after definitive surgical treatment regardless of surgery type. QOL rebounded after completion of adjuvant treatment.

Much of the increase in early-stage breast cancer incidence over the past several decades has resulted from widespread use of screening mammography and early detection of breast cancers, including ductal carcinoma in situ (DCIS, stage 0) and early-invasive breast cancer (EIBC, stages I/IIA).[1] Although DCIS is clinically distinct from EIBC and offers excellent prognosis, DCIS and EIBC patients are offered similar surgical-treatment options (i.e., mastectomy or breast-conserving surgery (BCS) and radiation therapy, and hormone therapy, as indicated).[2–7] The equivalence of BCS and mastectomy in prevention of DCIS/EIBC recurrence, morbidity, and mortality has been demonstrated.[8–10] However, with growing numbers of breast cancer survivors enjoying longer life expectancy, quality of life (QOL) outcomes are increasingly important considerations when making treatment decisions.[11]

Many studies (largely cross-sectional) have examined QOL outcomes after early-stage breast cancer treatment.[12–21] Reports of equivalent QOL outcomes by surgery type depend on timing of the QOL assessments and whether physical or psychological aspects of QOL are being measured.[13,22–31] Few longitudinal studies of early-stage breast cancer patients examined QOL changes over time, but these studies did not evaluate QOL improvement in association with surgery type, chemotherapy, and the surgery–chemotherapy interaction.[13,32,33] In a large cohort

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study of same-aged women with and without breast cancer (controls), both DCIS and EIBC patients reported QOL improvements over 2-year follow-up, but DCIS patients reached QOL levels reported by controls sooner than EIBC patients.[32] Since DCIS patients do not receive chemotherapy, we hypothesized that the observed differences in QOL improvement between DCIS and EIBC patients might reflect adverse effects of chemotherapy on QOL among EIBC patients.[32,34–36] Therefore, we examined whether and to what extent improvements in QOL were affected by surgery type, chemotherapy, and their interaction.

MATERIALS AND METHODS

Patients were recruited prospectively between October 2003 and June 2007 from the Siteman Cancer Center and Saint Louis University School of Medicine, both in St. Louis, MO.[32] We included English-speaking patients who were at least 40 years old, diagnosed with first primary, pathology-confirmed stage 0–IIA breast cancers, no prior breast cancer history, had not received neoadjuvant chemotherapy, and did not demonstrate cognitive impairment on the Orientation-Memory-Concentration Test.[37]

Institutional Review Boards at both universities approved the study, and participants provided informed consent. We conducted four computer-assisted telephone interviews 4–6 weeks (Time1), 6 months (Time2), 1 year (Time3), and 2 years (Time4) following definitive surgical treatment, during which we collected demographic information and administered new and previously validated questionnaires to identify potential covariates of QOL. We collected data regarding pathological stage at diagnosis, definitive surgical treatment, and adjuvant therapies from the medical record.

At each interview, we measured QOL using the Functional Assessment of Cancer Therapy-Breast (FACT-B) Version 4.[38] FACT-B total scores range from 0 to 144, with higher scores reflecting better QOL. Based on previous work, we included the following covariates of QOL in our analysis.[32] The 19-item medical outcomes study (MOS) Social Support Survey measures perceived availability of social support; higher scores indicate greater perceived availability of social support, if needed.[39] Using a validated interview measure of comorbidity, we computed a weighted index score using the Charlson Comorbidity Index algorithm; higher scores indicate more severe comorbidity.[40,41] A history of depression was determined by an affirmative response to either, "Has a doctor ever told you that you had depression?" or "Have you ever been treated for depression with medication or psychotherapy?" We also included a validated measure of surgical side effects severity experienced in the past month, with higher mean scores indicating more severe side effects from surgery and lymph-node excision.[42,43] We also collected demographic information, including age, marital status, education, race, and height and weight to compute body mass index (BMI).

Data for receipt of adjuvant chemotherapy, radiotherapy, and hormone therapy were obtained from patients at each interview and confirmed by the medical record. Stage at diagnosis determined by surgical pathology (stages 0, I, and IIA) and type of definitive surgical treatment (BCS, mastectomy) also were collected from the medical record.

Data Analysis

Using IBM SPSS Statistics, Release 21.0.0.2 (IBM Corporation, 2012), we identified covariates of QOL at Time1, using analysis of variance (ANOVA) grouping by each demographic and clinical categorical variable and Pearson product–moment correlations between QOL and each continuous variable. We used Chi square tests to examine associations among categorical variables of interest.

Using SAS version 9.3 (SAS Institute, Cary, NC), we performed separate linear regression analyses with Time1, Time2, Time3, and Time4 data to assess the associations of surgery type and chemotherapy with QOL at each interview, controlling for covariates associated with QOL at Time1. To determine if the effect of chemotherapy on QOL differed between patients who received BCS and mastectomy, an interaction term between surgery type and chemotherapy was included in the models. We used the GENMOD procedure in SAS to fit the generalized estimating equations (GEE) to compare changes in QOL over the 2-year follow-up (Time1–Time4) according to surgery type and chemotherapy, adjusted for selected covariates. The GEE model accounts for correlations among repeated measurements from each study participant and allows for inclusion of all available data. An unstructured correlation was specified to model the correlation of responses from each participant. The interactions of surgery type and chemotherapy with time since definitive surgery were included in the model to evaluate whether QOL changed over time in a different way between patients who received BCS and mastectomy and who did and did not receive chemotherapy. We tested these interaction effects using the CONTRAST statement in PROC GENMOD. Two-sided P values $<.05$ were considered statistically significant.

RESULTS

We invited 772 early-stage breast cancer patients to participate in the parent QOL study and enrolled 549 (71 %). There were no significant differences between

TABLE 1 Patient characteristics at first interview (except as noted), by surgery type and receipt of chemotherapy

	BCS $n = 356$	Mastectomy $n = 193$	*P* value	Chemotherapy[a] $n = 136$	No chemotherapy $n = 413$	*P* value
Age, mean (SD)	59.7 (10.8)	55.9 (9.8)	<.001	53.3 (7.3)	60.0 (11.0)	<.001
Body mass index, mean (SD)[b]	28.8 (6.8)	27.8 (6.7)	.101	28.8 (6.9)	28.4 (6.7)	.513
Surgical side effects severity, mean (SD)	1.4 (0.5)	2.2 (0.8)	<.001	1.9 (0.8)	1.6 (0.7)	<.001
Comorbidity, mean (SD)	0.6 (0.9)	0.5 (1.0)	.347	0.5 (0.8)	0.6 (1.0)	.226
Social support, mean (SD)	4.5 (0.6)	4.5 (0.7)	.898	4.5 (0.7)	4.5 (0.6)	.832
Race			.102			.095
White, *n* (%)	292 (82.0)	147 (76.2)		102 (75.0)	337 (81.6)	
Nonwhite, *n* (%)	64 (18.0)	46 (23.8)		34 (25.0)	76 (18.4)	
Marital status			.040			.039
Married/member of unmarried couple, *n* (%)	203 (57.0)	130 (67.4)		82 (60.3)	251 (60.8)	
Widowed, *n* (%)	55 (15.4)	15 (7.8)		9 (6.6)	61 (14.8)	
Divorced/separated, *n* (%)	63 (17.7)	31 (16.1)		30 (22.1)	64 (15.5)	
Never been married, *n* (%)	35 (9.8)	17 (8.8)		15 (11.0)	37 (9.0)	
Education			.337			.179
<High school graduate, *n* (%)	25 (7.0)	18 (9.3)		7 (5.1)	36 (8.7)	
At least high school graduate, *n* (%)	331 (93.0)	175 (90.7)		129 (94.9)	377 (91.3)	
History of depression			.413			.845
Yes, *n* (%)	124 (34.8)	74 (38.3)		50 (36.8)	148 (35.8)	
No, *n* (%)	232 (65.2)	119 (61.7)		86 (63.2)	265 (64.2)	
Pathologic stage			<.001			<.001
0, *n* (%)	111 (31.2)	73 (37.8)		0 (0.0)	184 (44.6)	
I, *n* (%)	203 (57.0)	79 (40.9)		73 (53.7)	209 (50.6)	
IIA, *n* (%)	42 (11.8)	41 (21.2)		63 (46.3)	20 (4.8)	
Radiation therapy[c]			<.001			.498
Yes, *n* (%)	332 (93.3)	18 (9.3)		90 (66.2)	260 (63.0)	
No, *n* (%)	24 (6.7)	175 (90.7)		46 (33.8)	153 (37.0)	
Endocrine therapy[d]			<.001			<.310
Yes, *n* (%)	250 (70.2)	94 (48.7)		82 (60.3)	262 (63.4)	
No, *n* (%)	104 (29.2)	96 (49.7)		54 (39.7)	146 (35.4)	
Unknown, *n* (%)	2 (0.6)	3 (1.6)		0 (0.0)	5 (1.2)	

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

BCS breast-conserving surgery, *SD* standard deviation

[a] Numbers shown are for patients who received adjuvant chemotherapy at any time after enrollment; 59 (43.3 % of 136) early-invasive breast cancer patients reported taking chemotherapy at the first interview

[b] Body mass index was not calculated for three women lacking height and/or weight data

[c] Numbers shown are for patients who received radiation therapy at any time after enrollment; 130 patients reported receipt of radiation therapy at the first interview

[d] Numbers shown are for patients who received endocrine therapy at any time after enrollment; 96 patients reported taking endocrine therapy at the first interview

patient participants and nonparticipants by pathological stage ($P = .837$), surgery type (BCS vs mastectomy; $P = .095$), or marital status (married vs unmarried; $P = .072$). However, patient participants were younger, on average, than nonparticipants [mean (SD), 58.3 (10.6) vs. 60.6 (12.6); $P = .011$] and were more likely to be white (79.2 vs. 63.8 %; $P < .001$).

Patient characteristics by surgery type and chemotherapy are shown in Table 1. Patients completed four interviews a mean (SD) 6.1 (2.5) weeks and 6.2 (0.4), 12.3 (0.4), and 24.5 (0.5) months following definitive surgical treatment. Retention remained high with 514 patients (93.6 %) completing all four interviews, and these patients were not significantly different from those who dropped out after the first interview in terms of age, education, or race (each $P > .05$). However, a greater proportion of patients who dropped out had never been married (20.0 vs. 8.8 %, $P = .019$) and reported lower QOL at Time1-Time3 (each

$P < .01$) compared with patients who completed all 4 interviews.

At Time1, 130 of 549 patients (23.7 %) reported receiving radiotherapy and 59 (10.7 %) reported receiving chemotherapy. At Time2, 321 of 537 patients (59.8 %) reported receiving radiotherapy and 132 (24.6 %) reported receiving chemotherapy. All patients who received chemotherapy had initiated treatment by Time2; all patients who received chemotherapy and/or radiotherapy had completed these adjuvant treatments by Time3. Receipt of hormone therapy was reported by 17 % (96 of 549) of patients at Time1, 47.5 % (255 of 537) at Time2, 58.9 % (311 of 528) at Time3, and 58.0 % (298 of 514) at Time4.

Associations between QOL and factors measured at Time1 are shown in Tables 2 and 3. All variables significantly associated with QOL at Time1 were included as covariates in the multivariable regression and GEE models. We included receipt of radiation therapy and hormone therapy as covariates, because they were reported to be associated with QOL during and after treatment.[44,45]

We used linear regression models adjusted for covariates to test the differences in QOL (least squares means) by surgery type and receipt of chemotherapy at each interview (Fig. 1). At Time1, BCS (vs mastectomy; $P = .014$) and chemotherapy (vs. no chemotherapy; $P < .001$) were associated with worse QOL, but the surgery–chemotherapy interaction effect was not significant ($P = .468$). At Time2, BCS ($P < .001$) and chemotherapy ($P = .001$) were associated with worse QOL, and the adverse effect of chemotherapy on QOL was more prominent among patients who received BCS than mastectomy ($P_{\text{interaction}} = .031$). At Time3, neither surgery type nor chemotherapy was significantly associated with QOL, but at Time4, BCS was associated with worse QOL ($P = .005$).

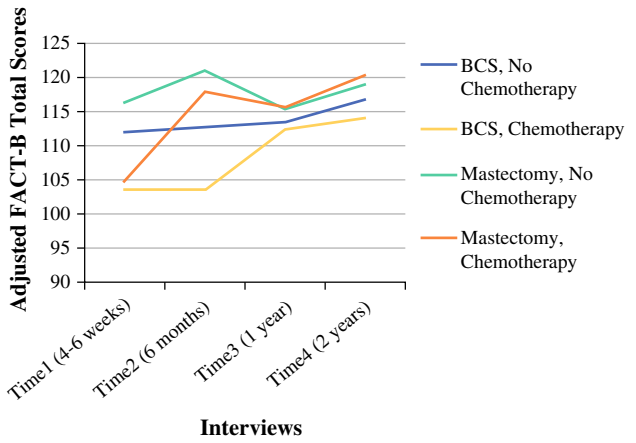

FIG. 1 Quality of life over 2-year follow-up of early-stage breast cancer patients, by surgery type [breast-conserving surgery (BCS) or mastectomy] and receipt of chemotherapy. Least squares means, shown here, were derived from four separate linear regression models (run separately for each of the 4 interviews after definitive surgical treatment). Each model was adjusted for the following covariates: age, race, education, marital status, body mass index, social support, comorbidity, history of depression, surgical side effects severity, cancer stage, and receipt of radiation and endocrine therapy

Because women with DCIS in the absence of invasive disease typically do not receive chemotherapy, we ran models without them. Results were similar to the models with DCIS patients, except that only chemotherapy was associated with worse QOL at Time1 ($P < .001$) and the surgery–chemotherapy interaction effect was attenuated at Time2 ($P_{\text{interaction}} = .215$).

We used GEE models to evaluate the trends of QOL over the 2-year follow-up by surgery type and chemotherapy. Although it appeared that QOL in patients who received BCS and chemotherapy took longer to recover compared with patients in the other 3 groups (Fig. 1), the GEE 3-way interaction (surgery type–chemotherapy–time) was not significant ($P = .86$), indicating the change in QOL over time among patients receiving chemotherapy was not modified by surgery type. In Table 4, GEE models evaluating 2-way interactions (chemotherapy–time and surgery–time) showed QOL improved among patients who received BCS and mastectomy; the improvement in each group was comparable ($P_{\text{difference}} = .440$). QOL also improved significantly in patients who received chemotherapy, but not in patients who did not receive chemotherapy. Excluding DCIS patients, the 3-way interaction in the GEE model still was not significant ($P = .96$); QOL significantly improved for patients who received chemotherapy and mastectomy but not for patients who received BCS or who did not receive chemotherapy.

DISCUSSION

Poorer QOL outcomes in EIBC patients at 2-year follow-up compared with DCIS patients were previously reported.[32] Since DCIS patients did not receive chemotherapy, we hypothesized that EIBC patients' poorer QOL might reflect adverse effects of chemotherapy on QOL among EIBC patients. Here, we ran regression models with and without DCIS patients and found similar results; however, in the model without DCIS patients, only chemotherapy was associated with worse QOL at Time1, and the surgery–chemotherapy interaction effect was attenuated at Time2. The adverse effect of chemotherapy on QOL was more prominent among patients who received BCS compared with mastectomy. These results support our hypothesis and contribute substantively to the literature regarding QOL change in association with surgical and adjuvant treatment regimens for early-stage breast cancer.

TABLE 2 Unadjusted mean (SD) FACT-B total scores at each of the 4 interviews (Time1–Time4) after definitive surgical treatment, for each demographic and clinical covariate of interest at Time1

Time1 covariates	Time1 $n = 549$	*P* value	Time2 $n = 536$[a]	*P* value	Time3 $n = 527$[b]	*P* value	Time4 $n = 514$	*P* value
Race		.024		.003		.001		<.001
White	116.2 (18.4)		119.1 (18.7)		118.9 (16.3)		122.1 (16.5)	
Nonwhite	111.5 (23.4)		112.6 (23.7)		112.4 (21.2)		113.1 (26.0)	
Marital status		<.001		<.001		<.001		<.001
Married/member of an unmarried couple	117.8 (17.0)		119.8 (17.5)		120.9 (14.6)		123.6 (15.8)	
Widowed	122.4 (15.9)		124.3 (14.3)		119.0 (17.0)		123.1 (16.0)	
Divorced/separated	105.6 (22.8)		109.0 (24.0)		108.5 (21.2)		110.3 (23.7)	
Never been married	107.7 (24.4)		111.4 (25.9)		110.8 (21.0)		112.2 (25.1)	
Education		.003		.005		.003		.001
<High school graduate	106.8 (22.0)		109.2 (24.8)		109.8 (17.7)		111.2 (23.2)	
At least high school graduate	116.0 (19.2)		118.5 (19.3)		118.3 (17.3)		121.1 (18.4)	
History of depression		<.001		<.001		<.001		<.001
Yes	106.8 (20.6)		109.9 (23.4)		112.0 (20.2)		113.4 (22.4)	
No	120.1 (17.2)		122.2 (16.1)		120.7 (15.0)		124.1 (15.7)	
Pathologic stage		<.001		<.001		.003		.006
0	117.9 (18.3)		120.0 (18.3)		119.7 (16.8)		122.5 (17.4)	
I	116.0 (18.9)		118.6 (19.3)		118.0 (16.7)		120.7 (17.6)	
IIA	107.1 (22.4)		109.9 (23.5)		111.7 (20.6)		114.2 (25.5)	
Surgery type		.001		.031		.011		.094
BCS	117.3 (18.2)		119.2 (19.0)		119.1 (15.8)		121.4 (20.0)	
Mastectomy	111.7 (21.4)		115.3 (21.3)		115.0 (20.1)		118.4 (20.8)	
Radiation therapy[c]		.136		0.324		.234		.320
Yes	116.2 (18.3)		118.4 (19.0)		118.3 (16.6)		121.0 (18.0)	
No	113.6 (21.6)		116.7 (21.4)		116.4 (18.9)		119.2 (20.8)	
Chemotherapy[c]		<.001		<.001		<.001		<.001
Yes	106.4 (21.8)		109.2 (23.5)		112.8 (20.0)		114.9 (23.1)	
No	118.2 (17.9)		120.6 (17.7)		119.2 (16.3)		122.1 (17.1)	
Endocrine therapy[d]		.200		.101		.309		.472
Yes	117.7 (15.8)		121.0 (16.2)		119.5 (13.9)		121.9 (16.2)	
No	114.9 (20.3)		117.3 (20.5)		117.5 (17.9)		120.3 (19.6)	

SD standard deviation, *FACT-B* Functional Assessment of Cancer Therapy-Breast, *Time1* first interview (4–6 weeks), *Time2* second interview (6 months), *Time3* third interview (1 year), *Time4* fourth interview (2 years), *BCS* breast-conserving surgery

[a] Although 537 women completed Time2, one participant refused to answer the FACT-B during the Time2 interview

[b] Although 528 women completed Time3, one participant had incomplete FACT-B data and could not be included in the Time3 analysis

[c] Obtained from the medical record

[d] Based on patient's self-reported receipt of adjuvant hormone therapy at each interview, confirmed by the medical record

Earlier studies indicated equivalent QOL outcomes in women who underwent BCS versus mastectomy.[22–31] However, many of these studies either did not examine the impact of adjuvant therapy on QOL or measured only anxiety and depression, which are important affective components of QOL, but do not measure other aspects of QOL that could be affected by surgery type.[22–27,29–31] Other studies reported a slight advantage in QOL outcomes in women who underwent BCS versus mastectomy; however, some studies were retrospective or cross-sectional by design, precluding examination of potential improvements in QOL over time.[31,46–49] These design differences alone could account for the discrepant results reported in the literature.

The effect of surgery type on QOL also might depend on the timing of QOL assessments following surgery.[13,47] Although we found a significant effect of surgery type on QOL 6 months following definitive surgical treatment, adjusting for demographic, psychosocial, and clinical covariates, the change pattern in QOL over time did not

TABLE 3 Pearson product-moment correlations between FACT-B total scores at each interview (Time1–Time4) after definitive surgical treatment and each covariate of interest measured at first interview (Time1)

Time1 covariates	Time1 $n = 549$	*P* value	Time2 $n = 536$[a]	*P* value	Time3 $n = 527$[b]	*P* value	Time4 $n = 514$	*P* value
Age	.300	<.001	.258	<.001	.179	<.001	.177	<.001
Body mass index[c]	−.156	<.001	−.126	.004	−.222	<.001	−.165	<.001
Surgical side effects severity	−.467	<.001	−.419	<.001	−.385	<.001	−.363	<.001
Comorbidity	−.112	.009	−.129	.003	−.134	.002	−.130	.003
Social support	.440	<.001	.427	<.001	.365	<.001	.376	<.001

FACT-B Functional Assessment of Cancer Therapy-Breast, *Time1* first interview (4–6 weeks), *Time2* second interview (6 months), *Time3* third interview (1 year), *Time4* fourth interview (2 years)

[a] Although 537 women completed Time2, one participant refused to answer the FACT-B during the interview

[b] Although 528 women completed Time3, one participant had missing FACT-B data and could not be included in the analysis at this point in time

[c] Three women lacked data to compute body mass index

TABLE 4 Generalized estimating equation (GEE) models testing differences in change in total FACT-B scores per 6 months after definitive surgical treatment over 2-year follow-up, by surgery type and receipt of chemotherapy

	Mean change (confidence limits)	*P* for trend	*P* for difference in trend
Model with DCIS patients			
Surgery type			.440
BCS	0.38 (0.01, 0.75)	.047	
Mastectomy	0.64 (0.09, 1.20)	.024	
Chemotherapy			<.001
No	0.06 (−0.28, 0.40)	.720	
Yes	2.02 (1.35, 2.70)	<.001	
Model without DCIS patients			
Surgery type			.271
BCS	0.28 (−0.20, 0.76)	.256	
Mastectomy	0.80 (0.01, 1.59)	.046	
Chemotherapy			<.001
No	−0.18 (−0.66, 0.31)	.480	
Yes	1.77 (1.07, 2.47)	<.001	

GEE models examining change in QOL by surgery type and chemotherapy were adjusted for covariates: age, race, education, marital status, BMI, social support, comorbidity, history of depression, surgical side effects severity, cancer stage, receipt of radiation therapy, and receipt of endocrine therapy

Fact-B Functional Assessment of Cancer Therapy-Breast, *BCS* breast-conserving surgery

differ by surgery type (Table 4), suggesting that QOL gains 2 years following definitive surgical treatment were equivalent between BCS and mastectomy.

We and others observed a short-term adverse effect of chemotherapy on QOL within 2 years of breast cancer surgery.[36,50] Chemotherapy also has been reported to predict impaired QOL in 5- and 10-year survivors.[51,52] QOL following specific adjuvant treatment regimens has been described in longitudinal studies with patients receiving radiation, chemotherapy, radiation and chemotherapy, and endocrine therapy.[44,45,53–60] However, unlike these studies, we included an adjuvant chemotherapy–time interaction term in our analysis—in relation to receipt of BCS or mastectomy as well—allowing us to determine if, and how, the change in QOL over time differed by receipt of chemotherapy. Women receiving chemotherapy demonstrated a significant rate of improvement in QOL within the 1st year, which was not observed in patients who did not receive chemotherapy, as women who received chemotherapy reported poorer QOL at Time1 than women who did not receive chemotherapy. In addition, this higher rate of improvement among women who received chemotherapy occurred at different times depending upon surgery type, as most women who received mastectomy had not received radiation, and most women who received BCS received radiation as standard of care.

To examine the trend of QOL over time, we adjusted the GEE model for whether or not a patient received radiation therapy over the study period. Although change in QOL over the 2-year follow-up among patients receiving chemotherapy was not modified by surgery type, we could not account for the timing of initiation or duration of radiation from the medical record to determine the potential cumulative effect of radiation for those patients who received BCS. These treatment factors, however, may not entirely explain the associations observed between QOL and either surgery type or adjuvant chemotherapy. Psychosocial factors (e.g., social support or a history of depression) might explain fluctuations in QOL over time.[26,52,61] Further research is warranted, because we controlled for these factors and yet observed small (albeit not minimally important) declines in QOL between Time2 and Time3 in both mastectomy groups but not in the BCS groups (Fig. 1).[62]

The longitudinal design and high retention of patients are study strengths. However, participation and retention rates were higher for white and for married patients—potential sources of selection bias. Generalizability of our findings might be limited by recruitment from a National Cancer Institute-designated comprehensive cancer center and another academic medical center in the same city. Our sample was representative of the racial/ethnic distribution of breast cancer patient population in our catchment area (21 %), but 95 % of nonwhite participants were black, limiting generalizability to other nonwhite racial/ethnic groups. Findings also might not be generalizable to patients with more advanced disease or patients younger than 40 years of age who are more likely to present with aggressive disease.[63]

In addition, each surgery–chemotherapy treatment interaction group yielded smaller numbers, thereby diminishing the power to detect significant differences among the various treatment combinations after completion of adjuvant treatments at Time3 and Time4. Finally, although we did not include breast reconstruction and type of lymph node biopsy (sentinel lymph node biopsy vs. axillary lymph node dissection) in the multivariate models, we controlled for surgical side effects severity to account for the negative effects of lymphedema and other surgical side effects on QOL.[42,43,64–66]

In conclusion, we demonstrated that patients who received chemotherapy reported poorer QOL in the first year after surgery, but QOL rebounded within months of treatment completion regardless of surgery type. While BCS predicted worse QOL at Time2, potentially due to the additional receipt and timing of adjuvant radiation therapy and type of chemotherapy, the pattern of change in QOL over 2-year follow-up did not differ significantly by surgery type.[36,44] The relative effects of chemotherapy and radiation on changes in QOL over time remain unknown.

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