Association of Breast Cancer Surgery With Quality of Life and Psychosocial Well-being in Young Breast Cancer Survivors

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IMPORTANCE Young women with breast cancer are increasingly choosing bilateral mastectomy (BM), yet little is known about short-term and long-term physical and psychosocial well-being following surgery in this population.

OBJECTIVE To evaluate the differential associations of surgery with quality of life (QOL) and psychosocial outcomes from 1 to 5 years following diagnosis.

DESIGN, SETTING, AND PARTICIPANTS Cohort study

SETTING Multicenter, including academic and community hospitals in North America

PARTICIPANTS Women age =< 40 when diagnosed with Stage 0-3 with unilateral breast cancer between 2006 and 2016 who had surgery and completed QOL and psychosocial assessments.

EXPOSURES (FOR OBSERVATIONAL STUDIES) Primary breast surgery including breast-conserving surgery (BCS), unilateral mastectomy (UM), and BM.

MAIN OUTCOMES AND MEASURES Physical functioning, body image, sexual health, anxiety and depressive symptoms were assessed in follow-up.

RESULTS Of 826 women, mean age at diagnosis was 36.1 years; most women were White non-Hispanic (86.7%). Regarding surgery, 45% had BM, 31% BCS, and 24% UM. Of women who had BM/UM, 84% had reconstruction. While physical functioning, sexuality, and body image improved over time, sexuality and body image were consistently worse (higher adjusted mean scores) among women who had BM vs BCS (body image: year 1, 1.32 vs 0.64; P < .001; year 5, 1.19 vs 0.64; P < .001; sexuality: year 1, 1.66 vs 1.20, P < .001; year 5, 1.43 vs 0.96; P < .001) or UM (body image: year 1, 1.32 vs 1.15; P = .06; year 5, 1.19 vs 0.96; P = .02; sexuality: year 1, 1.66 vs 1.41; P = .02; year 5, 1.43 vs 1.09; P = .002). Anxiety improved across groups, but adjusted mean scores remained higher among women who had BM vs BCS/UM at 1 year (BM, 7.75 vs BCS, 6.94; P = .005; BM, 7.75 vs UM, 6.58; P = .005), 2 years (BM, 7.47 vs BCS, 6.18; P < .001; BM, 7.47 vs UM, 6.07; P < .001) and 5 years (BM, 6.67 vs BCS, 5.91; P = .05; BM, 6.67 vs UM, 5.79; P = .05). There were minimal between-group differences in depression levels in follow-up.

CONCLUSIONS AND RELEVANCE While QOL improves over time, young breast cancer survivors who undergo more extensive surgery have worse body image, sexual health, and anxiety compared with women undergoing less extensive surgery. Ensuring young women are aware of the short-term and long-term effects of surgery and receive support when making surgical decisions is warranted.

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In the United States, young women diagnosed as having early-stage, unilateral breast cancer are increasingly choosing bilateral mastectomy (BM), including mastectomy to treat the affected side and contralateral prophylactic mastectomy (CPM). Contralateral prophylactic mastectomy reduces the risk of developing a contralateral breast cancer (CBC); however, in most women, this risk is estimated to be less than 5% in the 5 years following diagnosis. With the absolute risk of CBC relatively low for most patients with breast cancer (apart from those with a BRCA mutation or other risk factor such as prior mantle-field radiation) and most studies failing to demonstrate any survival improvement associated with CPM, the medical benefits of CPM are questionable. However, there are unequivocal, though small medical risks from additional surgery as well as the potential for this choice to affect short-term and long-term quality of life (QOL) and psychosocial health both positively and negatively. Among younger women, understanding the impact of BM relative to less extensive surgery on health-related and psychological health outcomes is critical given that younger women experience greater psychosocial distress at and after diagnosis.

To date, most studies of physical and psychosocial well-being in women undergoing breast cancer surgery have focused on postmenopausal women and have not explored trends over longer-term follow-up. Using a large, prospective cohort of women diagnosed as having breast cancer at 40 years and younger, we evaluated health-related QOL and psychosocial outcomes in the years following surgery. Specifically, we sought to describe changes in these outcomes from 1 to 5 years following diagnosis comparing BM vs breast-conserving surgery (BCS) and unilateral mastectomy (UM) as well as examine differences by primary surgery type, receipt of radiation, and reconstruction.

Methods
Study Participants
The Young Women’s Breast Cancer Study (YWS) is a multicenter, prospective cohort that enrolled women diagnosed as having in situ or invasive breast cancer at 40 years or younger between 2006 and 2016. Young Women’s Breast Cancer Study sites include academic and community hospitals in Massachusetts and academic sites in Colorado, Minnesota, and Toronto, Canada. Potential participants were identified systematically by pathology record and clinic list review and invited to participate by mail. Toronto participants do not complete a full version of the survey and were excluded from this analysis. Following written informed consent, women were mailed a baseline survey (median time from diagnosis to survey completion: 5 months) and then surveyed twice a year for the first 3 years following diagnosis, and annually subsequently. Because our objective was to evaluate changes following the completion of primary treatment vs acute toxicities prevalent during active treatment, our analysis was anchored at a year following diagnosis. The YWS is approved by the institutional review board at the Dana-Farber/Harvard Cancer Center and at other study sites.

Key Points

Question Among young women with breast cancer, are there differences in quality of life and psychosocial health by primary surgery type in the years after surgery?

Findings In this prospective cohort study, among women diagnosed as having breast cancer at 40 years or younger, outcomes improved over time; however, differences by surgery persisted. Women who had bilateral mastectomy experienced more sexual and body image issues, particularly among those who did not have reconstruction.

Meaning Understanding differences in quality of life and psychosocial health by surgery type may be useful to young women making preference-sensitive surgical decisions.

Measurements
Patient Characteristics
Race and ethnicity were self-reported on the baseline survey (supplemented by medical record information if these data were not available). Marital status and parity were obtained from either the baseline or the 1-year survey. Genetic testing status and results were self-reported on the 1-year survey and complemented by medical record review.

Disease and Treatment Characteristics
Stage, hormone receptor, and ERBB2 (formerly HER2) status were determined from review of pathology reports and medical records. Receipt of chemotherapy, radiation, and surgery was ascertained from the baseline and 6-month surveys in combination with medical record review. Medical record review was used to confirm self-report of recurrent disease and new primary breast or other cancer.

Primary breast cancer surgery was defined as the last procedure (BCS, UM, or BM) within the year following diagnosis. For example, a woman who initially had BCS but subsequently had BM within the year would be categorized as having BM. Among women who had either UM or BM, we used self-report of reconstruction in the first year following diagnosis and reviewed the medical record when this information was missing from the survey.

Survey Measures
Quality of Life
Physical functioning was evaluated with the Cancer Rehabilitation Evaluation System Short Form (CARES-SF), an instrument that has been validated and extensively used to evaluate QOL in cancer patients. The physical subscale includes 10 items that assess a range of functional issues, including difficulties with performing physical tasks and pain. Sexual health was assessed with the CARES-SF sexual subscale, which includes 3 items evaluating sexual attractiveness, interest, and frequency. The 3-item body image subscale from the full (139 item) CARES was also included. For each CARES item, respondents rate on a 0 to 4 scale how they have felt over the past few weeks; scores for each subscale are calculated from the mean of ratings for each individual item and range from 0 to 4, with higher scores indicative of more problems.
Anxiety and Depression
Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS). Hospital Anxiety and Depression Scale scores range from 0 to 21, with scores 0 to 7 considered “normal,” scores 8 to 10 considered “borderline abnormal,” and scores of at least 11 considered “abnormal.”14

Statistical Analysis
Primary Analysis
Frequencies and means were calculated for categorical and continuous covariates, respectively. χ² tests and 1-way analysis of variance were used to compare patient, disease, and treatment characteristics between primary breast surgery types.

Linear mixed-effects models were fit to assess changes from 1 to 5 years after diagnosis in CARES and HADS scores among the surgical groups. If CARES data were unavailable at 1 year, scores from the survey administered 6 months after baseline were used instead. Fixed effects for surgical group and time (year 1, 2, 3, 4, and 5), a group × time interaction term, and random intercepts for patients were included in each model. Least squares means (adjusted for stage, hormone receptor status, chemotherapy, and age at diagnosis) were estimated and differences compared between BM vs BCS and BM vs UM at each time. P values for pairwise comparisons of adjusted means were adjusted for multiple comparisons using the Hochberg method.15 P values of .05 or less were considered statistically significant, and all P values were 2-sided.

Secondary Analyses
Because almost all participants who underwent BCS received radiation, we were unable to adjust for radiation in the primary analysis owing to this collinearity. We therefore fit additional models, excluding women who had BCS, and compared adjusted means (P values unadjusted for multiplicity) between BM and UM, stratified by receipt of postmastectomy radiation therapy (PMRT).

To quantify the prevalence of high levels of sexual and body image concerns in both early and late survivorship, while accounting for reconstruction following mastectomy, we calculated the frequency and dichotomized responses of at least “a fair amount,” “much,” or “very much” for individual items from the CARES body image and sexual scales at 1 and 5 years, and assessed differences by surgery at both time points with the χ² test. All analyses were conducted using SAS, version 9.4 (SAS Institute Inc).

Results
Study Population Characteristics
As of the analysis cutoff date of February 5, 2019, median follow-up for the entire cohort was 6.9 years; 75% had reached at least 5 years of follow-up. Among 2162 women who were eligible and invited to participate, 1302 enrolled in the YWS (response rate: 60%). After excluding women with bilateral breast cancer (n = 17), women with de novo stage IV disease (n = 48), and women who had a recurrence or new primary (breast or other) cancer within the first 5 years (n = 125), the analytic cohort included 826 women (eFigure 1 in the Supplement). Of these, most participants were from academic sites in Massachusetts (n = 671; 81.2%), 8.2% (n = 68) were treated at community sites in Massachusetts, and 10.5% (n = 87) were enrolled at academic sites in Colorado and Minnesota. Table 1 details the study population characteristics. Most women were White non-Hispanic (86.7%). Among non-White women (n = 105), most identified as Asian (n = 41) or Black, Haitian, or African American (n = 23); 35 were Hispanic. Nearly half of women (45.4%) had BM, 30.8% BCS, and 23.8% UM. Of those who had a mastectomy, 83.6% (n = 478 of 572) had reconstruction. Almost all women (99.2%; n = 252 of 254) who underwent BCS had radiation; 52.8% (n = 104 of 197) and 39.3% (n = 147 of 375) of women who had UM and BM, respectively, underwent PMRT.

Quality of Life
All cancer-specific QOL domains, including CARES physical function (estimated change in adjusted mean scores from year 1 to 5: BCS, 0.10; UM, 0.19; BM, 0.17; all P < .001), body image (estimated change in adjusted mean scores year 1 to 5, BCS, 0.16; P = .009; UM, 0.19; P = .006; BM, 0.14; P = .007), and sexuality (estimated change in adjusted mean scores from year 1 to 5: BCS, 0.24; UM, 0.33; BM, 0.23; all P < .001), improved over follow-up for all surgery. The CARES score trajectories for each cancer-specific QOL domain are shown in Figures 1A-C. Overall change trajectories for CARES physical functioning (P = .25) and body image (P = .42) did not differ by surgery, while differences by surgical group for CARES sexual scores were statistically significant (P = .03). After multiplicity adjustment, pairwise comparisons (eTable 1 in the Supplement) demonstrated that compared with women who had BCS, women who had BM had worse physical functioning in years 1 (BM, 0.51 vs BCS, 0.39; P = .002), 2 (BM, 0.40 vs BCS, 0.27; P = .002), and 4 (BM, 0.36 vs BCS, 0.27; P = .03), and worse body image (year 1: BM, 1.32 vs BCS, 0.64; year 2: BM, 1.24 vs BCS, 0.57; year 3: BM, 1.31 vs BCS, 0.55; year 4: BM, 1.25 vs BCS, 0.51; year 5: BM, 1.19 vs BCS, 0.48; all P < .001) and sexual health (year 1, BM, 1.66 vs BCS, 1.20; P < .001; year 2, BM, 1.39 vs BCS, 1.10; P = .005; year 3, BM, 1.41 vs BCS, 1.05; P < .001; year 4, BM, 1.42 vs BCS, 1.08; P = .001; year 5, BM, 1.43 vs BCS, 0.96; P < .001) at all points. Compared with women who had UM, women who had BM had worse physical functioning in year 2 (BM, 0.40 vs. UM, 0.29; P = .01) and 4 (BM, 0.36 vs. UM, 0.25; P = .02), worse body image in year 3 (BM, 1.31 vs UM, 1.02; P = .003), year 4 (BM, 1.25 vs UM, 0.91; P = .001), and year 5 (BM, 1.19 vs UM, 0.96; P = .02), and worse sexual health at all time points (year 1, BM, 1.66 vs UM, 1.41; P = .02; year 3, BM, 1.41 vs UM, 1.09; P = .002; year 4, BM, 1.42 vs UM, 1.07; P = .001; year 5, BM, 1.43 vs UM, 1.09; P = .002) except for year 2 (BM, 1.39 vs UM, 1.30; P = .39). Further adjustment of models for marital status did not change results substantially (data not shown).

Among women who had mastectomy, change trajectories (eFigures 2-4 in the Supplement) did not differ by PMRT status for physical functioning, but did differ by surgery for body image (P = .009) and sexual health (P = .03) for women...
who had PMRT. Among women who had PMRT, physical functioning did not differ between women who had BM or UM at any point, body image was worse among women who had BM in years 3 to 5 (year 3: BM, 1.79 vs UM, 1.43; \( P = .02 \); year 4: BM, 1.74 vs UM, 1.33; \( P = .01 \); year 5: BM, 1.63 vs UM, 1.29; \( P = .04 \)), and sexual health was worse in years 3 (BM, 1.45 vs UM, 1.09; \( P = .02 \)) and 4 (BM, 1.46 vs UM, 1.11; \( P = .03 \)). Among women who did not have PMRT, women who had BM had worse physical functioning at 1 (BM, 0.57 vs UM, 0.40; \( P = .003 \)), 2 (BM, 0.48 vs UM, 0.35; \( P = .02 \)), and 4 years (BM, 0.46 vs UM, 0.32; \( P = .02 \)), worse body image at all points (year 1: BM, 1.32 vs UM, 0.96; \( P = .009 \); year 2: BM, 1.18 vs UM, 0.91; \( P = .05 \); year 3: BM, 1.24 vs UM, 0.95; \( P = .05 \); year 4: BM, 1.19 vs UM, 0.82; \( P = .01 \)) except year 5 (BM, 1.16 vs UM, 0.96; \( P = .18 \)), and worse sexual health at all points (year 1: BM, 1.69 vs UM, 1.32; \( P = .01 \); year 3: BM, 1.42 vs UM, 1.13; \( P = .04 \); year 4: BM, 1.45 vs UM, 1.07; \( P = .01 \); year 5: BM, 1.50 vs UM, 1.09; \( P = .009 \)) except year 2 (BM, 1.42 vs UM, 1.22; \( P = .16 \)).

Table 2 shows the prevalence of women reporting at least “a fair amount” of issues attributed to each CARES body image item, demonstrating differences by surgery for all domains (all \( P \leq .002 \)) at 1 and 5 years. Women who had BM (with...
and without reconstruction) frequently reported feeling at least a fair amount of discomfort with body changes, embarrassment regarding showing their body to others, and discomfort showing scars to others at both 1 and 5 years; women who had BCS reported fewer body image issues at both points.

Table 3 shows the prevalence of women reporting at least “a fair amount” of issues attributed to each CARES sexual subscale item demonstrating differences by surgery for the domains of sexual attractiveness (year 1, BM with reconstruction, 43.8%; BM without reconstruction, 56.3%; UM with reconstruction, 41.7%; UM without reconstruction, 45.0%; BCS, 29.9%; P = .002; year 5, BM with reconstruction, 34.8%; BM without reconstruction, 52.2%; UM with reconstruction, 25.0%; UM without reconstruction, 25.5%; BCS, 18.8%; P < .001) and interest (year 1, BM with reconstruction, 47.8%; BM without reconstruction, 46.9%; UM with reconstruction, 37.6%; UM without reconstruction, 36.7%; BCS, 29.1% and year 5, BM with reconstruction, 44.6%; BM without reconstruction, 60.9%; UM with reconstruction, 27.1%; UM without reconstruction, 32.6%; BCS, 28.7%; P < .001) and sexual activity frequency at 1 year (BM with reconstruction, 43.9%; BM without reconstruction, 65.2%; UM with reconstruction, 43.6%; UM without reconstruction, 36.3%; BCS, 34.3%; P = .02).

Anxiety and Depression
Anxiety was highest in year 1, with mean scores (eTable 2 in the Supplement) among women who had BM (7.75) approaching borderline abnormal levels (scores 8-10). Compared with year 1, anxiety had improved across groups at year 5 (estimated change in adjusted mean HADS scores from year 1 to 5: BCS, 1.03; P < .001; UM, 0.79; P = .007; BM, 1.07; P < .001). The overall change trajectory for anxiety (Figure 2A) differed by surgery (P = .02) with anxiety worse among women who had BM compared to both UM and BCS at 1 (BM, 7.75 vs BCS; 6.94, P = .03; BM, 7.75 vs UM, 6.58; P = .005), 2 (BM, 7.47 vs BCS, 6.18; P < .001; BM, 7.47 vs UM, 6.07; P < .001, and 5 years (BM, 6.67 vs BCS, 5.91; P = .05; BM, 6.67 vs UM, 5.79; P = .05); in year 4, anxiety also was worse among women who had BM vs UM (BM, 6.99 vs UM, 6.04; P = .04). Among women who had a mastectomy, there was a differential effect of radiation, with no significant between-group differences at any time point in women who had PMRT. Among women who did not have PMRT, anxiety was higher in those who had BM in year 1 (BM, 8.24 vs. UM, 6.30, P < .001), 2 (BM, 7.87 vs. UM, 6.12, P = .002), and 4 (BM, 7.37 vs UM, 5.78; P = .006). Change trajectories did not differ by PMRT receipt (eFigure 5 in the Supplement).

For all surgery types, depression levels (eTable 2 in the Supplement) were in the normal range (scores <8) at all points; however, scores declined over time for women who had BM (estimated change in adjusted mean scores from year 1 to year 5, 0.60; P < .001) and BCS (estimated change in adjusted mean scores from year 1 to year 5, 0.64; P < .001). The overall change trajectory for depressive scores (Figure 2B) did not differ by surgery, and pairwise comparisons demonstrated only isolated between-group differences in follow-up. Scores were similar between groups at all time points among women who had PMRT but higher among the BM group in year 1 (BM, 4.39 vs UM, 3.13; P = .003) and 4 (BM, 3.90 vs. UM, 2.76, P = .01) in women who did not. Change trajectories did not differ by PMRT receipt (eFigure 6 in the Supplement).
Further adjustment of models for marital status did not change results for anxiety or depression substantially (data not shown).

Discussion

In this prospective analysis of QOL and psychosocial well-being in young women following breast cancer surgery, it is highly reassuring that physical and psychosocial health improve over time. However, differences by surgery type persisted in the years following surgery, with women who underwent BM experiencing more sexual and body image issues both in early and later survivorship, particularly among those who did not have reconstruction. Previous studies have consistently found that women generally report satisfaction with their surgical decision many years after surgery and experience minimal decisional regret, including choosing BM.\textsuperscript{9,16-19} Despite this, many women report worse QOL following more extensive surgery. A 2017 survey\textsuperscript{9} of more than 1100 breast cancer survivors found the lowest levels of body image concerns among women who had BCS, while the highest levels were reported by women who had CPM without reconstruction. In a 2018 prospective study by Parker et al,\textsuperscript{11} women who chose CPM had more body image concerns both before surgery and at 6, 12, and 18 months after, compared with women who did not have CPM; overall QOL was also poorer at all postsurgical time points among women who had CPM.\textsuperscript{11} We previously surveyed a subset of YWS participants who had CPM and found a substantial proportion of women reported that sev-

Table 2. Proportion Experiencing at Least “a Fair Amount” of Issues for Each CARES Body Image Subscale Item

<table>
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<tr>
<th>Variable</th>
<th>Discomfort with body changes, %</th>
<th>$\chi^2$ P value</th>
<th>Embarrassment showing body, %</th>
<th>$\chi^2$ P value</th>
<th>Discomfort showing scars to others, %</th>
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Abbreviations: BCS, breast-conserving surgery; BM, bilateral mastectomy; Recon, reconstruction; UM, unilateral mastectomy. * Data limited to participants who had reached at least 5 years of follow-up/completed 5-year survey.

Table 3. Proportion Experiencing at Least “a Fair Amount” of Issues for Each CARES Sexual Subscale Item

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Abbreviations: BCS, breast-conserving surgery; BM, bilateral mastectomy; Recon, reconstruction; UM, unilateral mastectomy. * Includes only women who reported being sexually active (n = 682 at year 1, n = 518 at year 5). * Data limited to participants who had reached at least 5 years of follow-up/completed 5-year survey.
Breast Cancer Surgery and Quality of Life and Psychosocial Well-being in Young Breast Cancer Survivors

Figure 2. Trajectory of Adjusted Mean Hospital Anxiety and Depression Scale (HADS) Scores Over Follow-up

A. Anxiety scores. Higher scores indicate more symptoms. Overall group × time interaction, P = .02. B. Depression scores. Higher scores indicate more symptoms. Overall group × time interaction, P = .28. BCS indicates breast-conserving surgery; BM, bilateral mastectomy; UM, unilateral mastectomy.

Conclusions

Our study provides novel and comprehensive information about how several dimensions of QOL and psychosocial health are affected both in the short and long term among young women who undergo breast cancer surgery. Understanding how outcomes differ and change over time may be useful to newly diagnosed women making preference-sensitive surgical decisions and should be communicated by clinicians during the decision process. In addition, incorporating this information into patient-centered tools, such as decision aids, may help ensure surgical decisions are made in an informed and supportive setting.

Limitations

Our findings should be interpreted in the context of certain limitations. Because most YWS participants complete their first survey only after they have had surgery, we were unable to account for prediagnosis psychological factors and comorbidities that may not only drive surgical choice but could also affect post-surgical QOL. Additionally, this analysis only considered surgery that was performed within the first year following diagnosis and did not account for subsequent surgeries that women may have undergone (eg, women who initially had BCS or UM but had BM and/or reconstruction between years 1 and 5). However, the number of women in our cohort who have more extensive surgery later on is small and unlikely to meaningfully affect our conclusions. Because women who enrolled more recently into the YWS may not yet have reached 4 or 5 years of follow-up, the sample size for certain subgroups is small for later points, and inferences based on this data should be interpreted with caution. Our findings may be of limited generalizability given YWS participants are predominantly White non-Hispanic, with most patients treated at academic hospitals located in Massachusetts. Nonetheless, these data are some of the first to our knowledge to date describing a cohort of young survivors and their QOL prospectively over extended follow-up.

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