

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

Shoshana M. Rosenberg, ScD, MPH; Laura S. Dominici, MD; Shari Gelber, MS, MSW; Philip D. Poorvu, MD; Kathryn J. Ruddy, MD, MPH; Julia S. Wong, MD; Rulla M. Tamimi, ScD; Lidia Schapira, MD; Steven Come, MD; Jeffrey M. Peppercorn, MD, MPH; Virginia F. Borges, MD, MMSc; Ann H. Partridge, MD, MPH

 Supplemental content

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 0.48; $P < .001$; 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.

Author Affiliations: Dana-Farber Cancer Institute, Boston, Massachusetts (Rosenberg, Gelber, Poorvu, Wong, Partridge); Brigham and Women's Hospital, Boston, Massachusetts (Dominici, Tamimi); Mayo Clinic, Rochester, Minnesota (Ruddy); Stanford University, Stanford, California (Schapira); Beth Israel Deaconess, Boston, Massachusetts (Come); Massachusetts General Hospital, Boston, Massachusetts (Peppercorn); University of Colorado Cancer Center, Denver (Borges).

Corresponding Author: Shoshana M. Rosenberg, ScD, MPH, 450 Brookline Ave, Dana 1160, Boston, MA 02215 (shoshana_rosenberg@dfci.harvard.edu).

JAMA Surg. doi:10.1001/jamasurg.2020.3325
Published online September 16, 2020.

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).¹⁻³ 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.⁴ 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.^{1,2} However, there are unequivocal, though small medical risks from additional surgery^{5,6} 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.⁷ 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.⁸

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.⁹⁻¹¹ 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.¹² 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.¹³ 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. χ^2 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 \times 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 χ^2 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 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

Table 1. Study Population Characteristics (N = 826)

Characteristic	No. (%)			P value
	Breast-conserving surgery (n = 254)	Unilateral mastectomy (n = 197)	Bilateral mastectomy (n = 375)	
Mean age at diagnosis, y	35.9	36.4	36.1	.35
Stage				
0	17 (6.7)	13 (6.6)	42 (11.2)	<.001
1	123 (48.4)	59 (30.0)	127 (33.9)	
2	104 (40.9)	81 (41.1)	154 (41.1)	
3	10 (3.9)	44 (22.3)	52 (13.9)	
HR status				
ER+ or PR+	195 (76.8)	153 (77.7)	271 (72.7)	.32
ER-/PR-	59 (23.2)	44 (22.3)	102 (27.4)	
Missing			2	
ERBB2 status				
ERBB2+/indeterminate	52 (21.3)	82 (43.2)	106 (30.4)	<.001
ERBB2-	192 (78.7)	108 (56.8)	243 (69.6)	
Missing	10	7	26	
Chemotherapy				
Yes	169 (66.5)	155 (79.1)	282 (75.2)	.007
No	85 (33.5)	41 (20.9)	93 (24.8)	
Missing		1		
Radiation				
Yes	252 (99.2)	104 (52.8)	147 (39.3)	<.001
No	2 (0.8)	93 (47.2)	227 (60.7)	
Missing			1	
Race/ethnicity				
WNH	219 (86.2)	169 (86.7)	329 (88.2)	.74
Non-WNH	35 (13.8)	26 (14.2)	44 (12.3)	
Unknown ^a		2	2	
BRCA 1/2 or TP53				
Tested/+	8 (3.2)	4 (2.1)	75 (20.1)	<.001
Tested/-	214 (84.6)	154 (79.4)	265 (71.1)	
Not tested/unsure	31 (12.3)	36 (18.6)	33 (8.9)	
Missing	1	3	2	
Married/living as married				
Yes	182 (71.7)	165 (84.2)	305 (81.3)	.002
No	72 (28.4)	31 (15.8)	70 (18.7)	
Missing		1		
Children before or since diagnosis				
Yes	125 (51.2)	126 (67.4)	249 (70.9)	<.001
No	119 (48.8)	61 (32.6)	102 (29.1)	
Missing	10	10	24	

Abbreviations: ER, estrogen receptor; HR, hormone receptor; PR, progesterone receptor; WNH, White non-Hispanic.

^a Includes patients where race was documented as other/unknown and ethnicity was non-Hispanic. Patients who identified as White where ethnicity was unknown were classified as WNH.

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, 1.11; $P = .04$; 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.

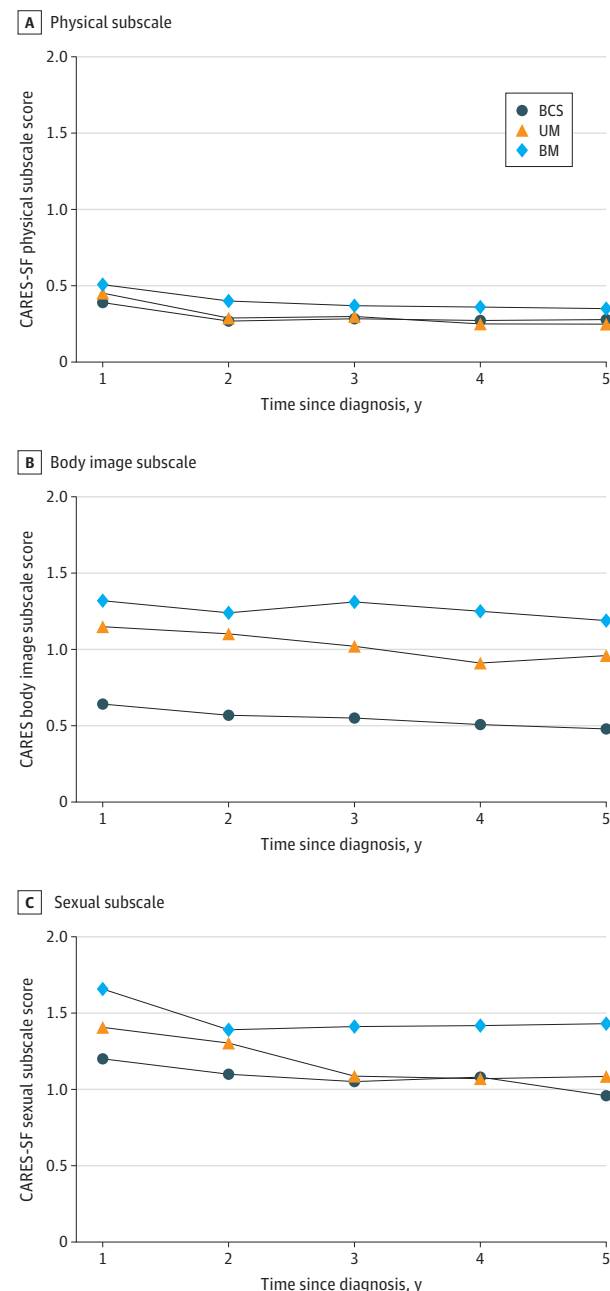
Table 3 shows the prevalence of women reporting at least “a fair amount” of issues attributed to each CARES sexual subscale item demonstrating differences by surgery for the domains of sexual attractiveness (year 1, BM with reconstruction, 43.8%; BM without reconstruction, 56.3%; UM with reconstruction, 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

Figure 1. Trajectory of Adjusted Mean Cancer Rehabilitation Evaluation System (CARES) Scores Over Follow-up Physical Subscale Scores Over Follow-up



A, Physical subscale scores. Higher scores indicate poorer QOL. Overall group \times time interaction, $P = .25$. B, Body image subscale scores. Higher scores indicate poorer QOL. Overall group \times time interaction, $P = .42$. C, Sexual subscale scores. Higher scores indicate poorer QOL. Overall group \times time interaction, $P = .03$. BCS indicates breast-conserving surgery; BM, bilateral mastectomy; CARES-SF, Cancer Rehabilitation Evaluation System Short Form; UM, unilateral mastectomy.

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).

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

	Discomfort with body changes, %	χ^2 P value	Embarrassment showing body, %	χ^2 P value	Discomfort showing scars to others, %	χ^2 P value
Year 1 (n = 826)						
BM/recon	40.6	.002	33.7	<.001	36.0	<.001
BM/no recon	43.8		43.8		50.0	
UM/recon	34.6		24.1		27.8	
UM/no recon	28.3		30.0		28.3	
BCS	25.2		12.0		9.6	
Missing, No.	11		13		12	
Year 5 (n = 599)^a						
BM/recon	27.0	.002	30.5	<.001	34.6	<.001
BM/no recon	52.2		52.2		52.2	
UM/recon	21.9		22.9		29.2	
UM/no recon	31.9		23.4		21.3	
BCS	17.9		9.7		9.7	
Missing, No.			1			

Abbreviations: BCS, breast-conserving surgery; BM, bilateral mastectomy; Recon, reconstruction; UM, unilateral mastectomy.

^a 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

Variable	Perceived sexual unattractiveness, %	χ^2 P value	Disinterest in sex, %	χ^2 P value	Decreased sexual activity frequency, % ^a	χ^2 P value
Year 1 (n = 826)						
BM/Recon	43.8		47.8		43.9	
BM/No Recon	56.3		46.9		65.2	
UM/Recon	41.7	.002	37.6	<.001	43.6	.02
UM/No Recon	45.0		36.7		36.3	
BCS	29.9		29.1		34.3	
Missing, No.	11		11		2	
Year 5 (n = 599)^b						
BM/Recon	34.8	<.001	44.6	<.001	41.8	.36
BM/No Recon	52.2		60.9		63.2	
UM/Recon	25.0		27.1		39.1	
UM/No Recon	25.5		32.6		39.0	
BCS	18.8		28.7		39.1	
Missing, No.	5		9		8	

Abbreviations: BCS, breast-conserving surgery; BM, bilateral mastectomy; Recon, reconstruction; UM, unilateral mastectomy.

n = 518 at year 5).

^b Data limited to participants who had reached at least 5 years of follow-up/completed 5-year survey.

^a Includes only women who reported being sexually active (n = 682 at year 1,

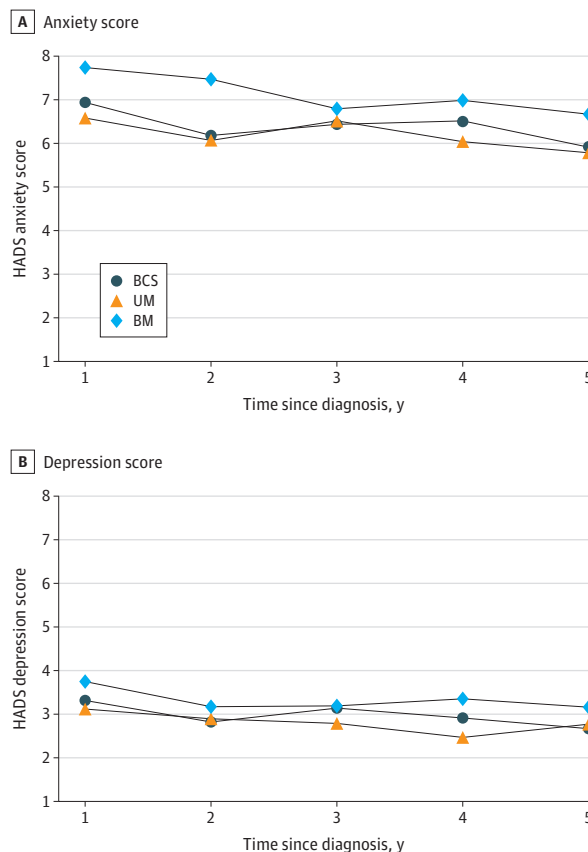
Further adjustment of models for marital status did not change results for anxiety or depression substantially (data not shown).

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 undergo 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 con-

sistently found that women generally report satisfaction with their surgical decision many years after surgery and experience minimal decisional regret, including choosing BM.^{9,16-19} Despite this, many women report worse QOL following more extensive surgery. A 2017 survey⁹ 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,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 post-surgical time points among women who had CPM.¹¹ We previously surveyed a subset of YWS participants who had CPM and found a substantial proportion of women reported that sev-

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

eral domains of physical and psychosocial health were worse than they had expected.²⁰ Regarding QOL, 42% said that their sense of sexuality was worse than expected, while 31% reported that self-consciousness about their appearance was worse than expected.²⁰

We have previously described the association between undergoing BM and higher levels of generalized anxiety.²¹ In our study, while anxiety decreased over time, women who had BM continued to have more anxiety relative to women who had BCS or UM up to 5 years after diagnosis. Given our observational design, it is important to consider that women who choose BM are likely different than those who undergo UM or BCS, and their surgical choices may be affected by distress ex-

perienced before or at diagnosis. In addition to body image concerns, Parker et al¹¹ reported greater cancer distress and worry prior to surgery among women who had CPM compared to those who did not.¹¹ The fact that in the years following surgery some women with more extensive surgery in our study continue to experience anxiety, as well as more sexual and body image issues compared to women who undergo less surgery, underscores the importance of presurgical counseling around expectations regarding post-surgical psychosocial health.

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 postsurgical 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.

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.

ARTICLE INFORMATION

Accepted for Publication: May 6, 2020.

Published Online: September 16, 2020.
doi:10.1001/jamasurg.2020.3325

Author Contributions: Dr Rosenberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Rosenberg, Gelber, Poorvu, Schapira, Partridge.

Acquisition, analysis, or interpretation of data: Rosenberg, Domini, Poorvu, Ruddy, Wong, Tamimi, Schapira, Come, Peppercorn, Borges, Partridge.

Drafting of the manuscript: Rosenberg, Poorvu.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Rosenberg, Tamimi.

Obtained funding: Rosenberg, Partridge.

Administrative, technical, or material support: Come, Partridge.

Supervision: Gelber, Partridge.

Conflict of Interest Disclosures: Dr Rosenberg reported grants from Agency for Healthcare Research and Quality, Susan G Komen, and Breast Cancer Research Foundation during the conduct of

the study. Dr Poorvu reported personal fees from WebMD outside the submitted work. Dr Peppercorn reported personal fees from GlaxoSmithKline and Athenex and grants from Pfizer outside the submitted work. No other disclosures were reported.

Funding/Support: This project was supported by grant K01HS023680 (Dr Rosenberg) from the Agency for Healthcare Research and Quality. Dr Partridge is supported by grants for research efforts focused on young women with breast cancer from Susan G. Komen (SAC1000008) and the Breast Cancer Research Foundation (BCRF17-121).

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

Meeting Presentation: Preliminary data from this manuscript were presented in abstract form at the 40th Annual San Antonio Breast Cancer Symposium; December 6, 2018; San Antonio, Texas.

Additional Contributions: We thank all the young women enrolled in the YWS. We thank Patricia Ganz, MD, Jonsson Comprehensive Cancer Center, University of California at Los Angeles, and Laura Petersen, MS, Jonsson Comprehensive Cancer Center, University of California at Los Angeles, for their generous assistance and analytic advice, and Kaitlyn Bifolck, BA, Dana-Farber Cancer Institute, for her assistance with manuscript submission.

REFERENCES

- Wong SM, Freedman RA, Sagara Y, Aydogan F, Barry WT, Golshan M. Growing use of contralateral prophylactic mastectomy despite no improvement in long-term survival for invasive breast cancer. *Ann Surg*. 2017;265(3):581-589. doi:10.1097/SLA.0000000000001698
- Kurian AW, Lichtensztajn DY, Keegan TH, Nelson DO, Clarke CA, Gomez SL. Use of and mortality after bilateral mastectomy compared with other surgical treatments for breast cancer in California, 1998-2011. *JAMA*. 2014;312(9):902-914. doi:10.1001/jama.2014.10707
- Nash R, Goodman M, Lin CC, et al. State variation in the receipt of a contralateral prophylactic mastectomy among women who received a diagnosis of invasive unilateral early-stage breast cancer in the United States, 2004-2012. *JAMA Surg*. 2017;152(7):648-657. doi:10.1001/jamasurg.2017.0115
- Murphy JA, Milner TD, O'Donoghue JM. Contralateral risk-reducing mastectomy in sporadic breast cancer: a single institution experience. *Ann Surg Oncol*. 2013;14(7):e262-e269. doi:10.1016/S1470-2045(13)70047-0
- Miller ME, Czechura T, Martz B, et al. Operative risks associated with contralateral prophylactic mastectomy: a single institution experience. *Ann Surg Oncol*. 2013;20(13):4113-4120. doi:10.1245/s10434-013-3108-1
- Osman F, Saleh F, Jackson TD, Corrigan MA, Cil T. Increased postoperative complications in bilateral mastectomy patients compared to unilateral mastectomy: an analysis of the NSQIP database. *Ann Surg Oncol*. 2013;20(10):3212-3217. doi:10.1245/s10434-013-3116-1
- Tracy MS, Rosenberg SM, Dominici L, Partridge AH. Contralateral prophylactic mastectomy in women with breast cancer: trends, predictors, and areas for future research. *Breast Cancer Res Treat*. 2013;140(3):447-452. doi:10.1007/s10549-013-2643-6
- Howard-Anderson J, Ganz PA, Bower JE, Stanton AL. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. *J Natl Cancer Inst*. 2012;104(5):386-405. doi:10.1093/jnci/djr541
- Anderson C, Islam JY, Elizabeth Hodgson M, et al. Long-term satisfaction and body image after contralateral prophylactic mastectomy. *Ann Surg Oncol*. 2017;24(6):1499-1506. doi:10.1245/s10434-016-5753-7
- Hwang ES, Locklear TD, Rushing CN, et al. Patient-reported outcomes after choice for contralateral prophylactic mastectomy. *J Clin Oncol*. 2016;34(13):1518-1527. doi:10.1200/JCO.2015.61.5427
- Parker PA, Peterson SK, Shen Y, et al. Prospective study of psychosocial outcomes of having contralateral prophylactic mastectomy among women with nonhereditary breast cancer. *J Clin Oncol*. 2018;36(25):2630-2638. doi:10.1200/JCO.2018.78.6442
- Schag CA, Ganz PA, Heinrich RL. Cancer Rehabilitation Evaluation System--short form (CARES-SF): a cancer-specific rehabilitation and quality of life instrument. *Cancer*. 1991;68(6):1406-1413. doi:10.1002/1097-0142(19910915)68:6<1406::AID-CNCR2820680638>3.0.CO;2-2
- Schag CA, Heinrich, R.L. Cancer Rehabilitation Evaluation System (CARES) Manual. CARES Consultants;1988.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370. doi:10.1111/j.1600-0447.1983.tb09716.x
- Dmitrienko A, Tamhane AC, Bretz F. *Multiple Testing Problems in Pharmaceutical Statistics*. Boca Raton, FL: Chapman & Hall/CRC; 2010.
- Montgomery LL, Tran KN, Heelan MC, et al. Issues of regret in women with contralateral prophylactic mastectomies. *Ann Surg Oncol*. 1999;6(6):546-552. doi:10.1007/s10434-999-0542-1
- Frost MH, Slezak JM, Tran NV, et al. Satisfaction after contralateral prophylactic mastectomy: the significance of mastectomy type, reconstructive complications, and body appearance. *J Clin Oncol*. 2005;23(31):7849-7856. doi:10.1200/JCO.2005.09.233
- Bloom DL, Chapman BM, Wheeler SB, et al. Reframing the conversation about contralateral prophylactic mastectomy: Preparing women for postsurgical realities. *Psychooncology*. 2019;28(2):394-400. doi:10.1002/pon.4955
- Geiger AM, West CN, Nekhyudov L, et al. Contentment with quality of life among breast cancer survivors with and without contralateral prophylactic mastectomy. *J Clin Oncol*. 2006;24(9):1350-1356. doi:10.1200/JCO.2005.01.9901
- Rosenberg SM, Tracy MS, Meyer ME, et al. Perceptions, knowledge, and satisfaction with contralateral prophylactic mastectomy among young women with breast cancer: a cross-sectional survey. *Ann Intern Med*. 2013;159(6):373-381. doi:10.7326/0003-4819-159-6-201309170-00003
- Rosenberg SM, Sepucha K, Ruddy KJ, et al. Local therapy decision-making and contralateral prophylactic mastectomy in young women with early-stage breast cancer. *Ann Surg Oncol*. 2015;22(12):3809-3815. doi:10.1245/s10434-015-4572-6