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Survival Outcomes in Women with Unilateral, Triple-Negative, Breast Cancer Correlated with Contralateral Prophylactic Mastectomy

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ABSTRACT

Background. Despite increased utilization of contralateral prophylactic mastectomy (CPM), there is insufficient evidence that it improves survival in average-risk women with unilateral breast cancer. CPM may be of heightened interest to patients with triple negative breast cancer (TNBC) because these patients are more likely to have BRCA1 mutation-associated disease and are not candidates for the chemoprevention benefits of adjuvant endocrine therapy.

Methods. Survival and recurrence outcomes were evaluated for all TNBC patients from a multi-institutional database (1999–2018) at two academic cancer programs in two metropolitan cities of the Northeast and Midwest. Median follow-up time was 3.7 years.

Results. Seven hundred and nighty six TNBC patients were evaluated and 15.45% underwent CPM. Women undergoing CPM were more likely to be white ($p < 0.001$), younger ($p < 0.001$), and underwent genetic testing ($p < 0.001$). A borderline survival benefit was observed for TNBC patients undergoing CPM (5-year overall survival 95.1% vs. 85.0%; $p = 0.05$). There was no difference in survival when BRCA mutation carriers were excluded (5-year overall survival 94.1% vs. 85.2%; $p = 0.12$). For BRCA mutation carriers, a numeric trend was observed for improved survival for patients undergoing CPM (5-year overall survival 97.2% vs. 84.1%; $p = 0.35$). Among patients not undergoing CPM, the rate of developing a new primary breast cancer was 2.2% (15/673). Among these 15 patients, 20% (3/15) were known BRCA mutation carriers.

Conclusions. Our data demonstrate no survival benefit for TNBC patients without BRCA1/2 mutations undergoing CPM.

Rates of contralateral prophylactic mastectomy (CPM) surgery have increased in the United States from less than 2% in 1998–30% in 2012 among women diagnosed with a unilateral breast cancer.[1,2] This increase has occurred despite insufficient evidence that CPM confers a survival advantage.[3,4] Additionally, the incidence of developing a contralateral breast cancer for most patients is low, at a rate of 0.25–1% per year.[5,6] The American Society of Breast Surgeons therefore discourages routine use of CPM.[7] However, patient preferences regarding the value of risk-reducing surgery and chest wall symmetry must be considered and the risks versus benefits of more extensive surgery conveyed in a shared decision-making process.[8]

Triple-negative breast cancer (TNBC) represents a biologically aggressive phenotype associated with higher risk of locoregional as well as distant recurrence compared to non-TNBC, and women with TNBC also are more likely to be BRCA1 mutation carriers.[9] Additionally, due to the lack of the estrogen and progesterone receptor, TNBC patients are not candidates for adjuvant systemic endocrine therapy. Ineligibility to receive the chemoprevention benefits of endocrine therapy, coupled with the higher likelihood of harboring hereditary susceptibility for breast cancer might

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motivate these patients to pursue CPM surgery. This patient-level interest must be balanced against the facts that CPM will not completely eliminate risk of new primary breast cancer, and it increases surgical complication rates.[10] Survival endpoints are prioritized in oncology, and although large population-based datasets have investigated the impact of CPM on women with estrogen receptor-negative disease, data are sparse regarding the impact of CPM on TNBC patients. In this study, we evaluated the survival impact of CPM on a large population of TNBC patients.

MATERIALS AND METHODS

Patient Population

The study design and data collection methods were approved by the Weill Cornell Medicine (WCM) and Henry Ford Health System (HFHS) Institutional Review Boards, located in New York City, New York, and Detroit, Michigan respectively. Reconsenting of patients was not required given the nature of the study. We reviewed the electronic medical records of TNBC patients seen at WCM and HFHS from 1999 to 2018. Patients meeting inclusion criteria for this study were those with pathologically confirmed invasive TNBC defined as estrogen receptor $< 1\%$, progesterone receptor $< 1\%$, and HER2/neu immunohistochemistry (IHC) 1+ or 0+, 2+ cases of HER2/neu were included if they were negative for amplification by fluorescence in situ hybridization (FISH) according to the guidelines of the American Society of Clinical Oncology.[11] Racial/ethnic information was based on self-reported identity documented in the electronic medical record.

New primary breast cancers were identified as those detected in a different quadrant compared with the initial/index cancer, those that were detected in the contralateral breast, those that had a non-TNBC phenotype, and those that developed more than 5 years following diagnosis of the initial/index cancer. Patient treatment records were reviewed to gather information regarding demographics, mode of detection, and treatment. Patients with unknown or unverified hormone receptor and/or HER2 status, an incomplete clinical record or those in whom type of surgery could not be confirmed were excluded. Patient, disease, and treatment characteristics were retrospectively reviewed and entered into a RedCap database.

Statistical Analysis

The statistical programming language R version 3.6.1 (R Foundation for Statistical Computing) was used. Chi-squared tests assessed association between categorical variables; Student's *t*-tests were used to compare differences of continuous variables within groups. Bonferroni correction was used to adjust the *p*-values for multiple comparisons. The primary endpoints were overall survival, local recurrence-free survival, and distant recurrence-free survival. The Kaplan-Meier plot and the 5-year survival probability was evaluated. Log-rank test was used to assess the survival difference between patients who did and did not undergo CPM. To evaluate for survival differences among patients undergoing breast-conserving surgery, unilateral mastectomy, and CPM, Cox proportional hazards modeling was performed to adjust for clinical nodal status, age, and high-grade disease.

RESULTS

A total of 796 TNBC patients were evaluated. The median follow-up time was 3.7 (mean 4.5) years. The median age at diagnosis was 57 (range 24–92) years. Overall, 15.5% (123/796) patients underwent CPM.

Characteristics of TNBC Patients with CPM

Table 1 demonstrates characteristics of the study population stratified by receipt of CPM. Differences were seen with respect to site, race, age at diagnosis, presence of lymphovascular invasion, type of surgery, receipt of adjuvant radiation, and genetic testing. Patients who had mammography-detected disease were less likely to have CPM compared with patients who presented symptomatically (11.9% vs. 17.6%; $p = 0.8$), although this difference was not statistically significant. In total, 603 patients received chemotherapy (75.8% of total study sample), of whom 173 (28.7%) received neoadjuvant treatment and 430 (71.3%) received adjuvant chemotherapy. Sequence of treatment was not significantly associated with choice of CPM surgery. Of the patients treated with neoadjuvant therapy, 33 (19.1%) chose to undergo CPM ($p = 1.0$) compared with 70 (16.3%) of the patients who had adjuvant therapy ($p = 1.0$). Among 101 CPM patients in which it was known whether neoadjuvant or adjuvant chemotherapy was delivered, 14 (13.9%) patients did not receive any chemotherapy. The no CPM patients ($n = 673$) include 327 (48.6%) patients who received adjuvant breast radiation after lumpectomy for the index cancer. Patients undergoing genetic testing were significantly more likely to undergo CPM surgery ($p < 0.001$). No significant differences were seen regarding CPM surgery related to *T* stage of disease ($p = 1.0$) or node-negativity ($p = 1.0$) (Table 1).

TABLE 1 Characteristics of the study population (n = 796) stratified by receipt of contralateral prophylactic mastectomy (CPM)

Variable		No CPM (n = 673)	CPM (n = 123)	p
Site	Midwest (n = 190)	178 (93.7%)	12 (6.3%)	0.002
	Northeast (n = 606)	495 (81.7%)	111 (18.3%)	
Race	African American/black (n = 193)	184 (95.3%)	9 (4.7%)	< 0.001
	White (n = 486)	387 (79.6%)	99 (20.4%)	
	Unknown (n = 117)	102 (87.2%)	15 (12.8%)	
Median age		59	46	< 0.001
Histology	Invasive ductal (n = 686)	572 (83.4%)	114 (16.6%)	0.8
	Invasive ductal/invasive lobular (n = 27)	24 (88.9%)	3 (11.1%)	
	Invasive lobular (n = 18)	18 (100%)	0 (0%)	
	Metaplastic (n = 12)	10 (83.3%)	2 (16.7%)	
	Other (n = 28)	28 (100%)	0 (0%)	
	Unknown (n = 25)	21 (84.0%)	4 (16.0%)	
High grade	No (n = 107)	94 (87.8%)	13 (12.1%)	1.0
	Yes (n = 643)	537 (83.5%)	106 (16.5%)	
	Unknown (n = 46)	42 (91.3%)	4 (8.7%)	
Lymphovascular invasion	No (n = 457)	399 (87.3%)	58 (12.7%)	0.016
	Yes (n = 135)	102 (75.5%)	33 (24.4%)	
	Unknown (n = 204)	172 (84.3%)	32 (15.7%)	
Mammography screen-detected	No (n = 387)	319 (82.4%)	68 (17.6%)	0.8
	Yes (n = 311)	274 (88.1%)	37 (11.9%)	
	Unknown (n = 98)	80 (81.6%)	18 (18.4%)	
Attempt at lumpectomy	No (n = 279)	192 (68.8%)	87 (31.2%)	< 0.001
	Yes (n = 488)	458 (93.8%)	30 (6.1%)	
	Unknown (n = 29)	23 (79.3%)	6 (20.7%)	
Neoadjuvant chemotherapy	No (n = 578)	495 (85.6%)	83 (14.3%)	1.0
	Yes (n = 173)	140 (80.9%)	33 (19.1%)	
	Unknown (n = 45)	38 (84.4%)	7 (15.5%)	
Adjuvant chemotherapy	No (n = 226)	194 (87.0%)	32 (14.1%)	1.0
	Yes (n = 430)	360 (83.7%)	70 (16.3%)	
	Unknown (n = 140)	119 (85%)	21 (15%)	
Adjuvant radiation therapy	Breast (n = 342)	330 (96.53%)	12 (3.5%)	< 0.001
	Breast/regional (n = 68)	56 (82.3%)	12 (17.6%)	
	None (n = 201)	138 (68.6%)	63 (31.3%)	
	Postmastectomy radiation (n = 50)	39 (78.0%)	11 (22.0%)	
	Unknown (n = 135)	110 (81.5%)	25 (18.5%)	
T stage	T1 (n = 375)	318 (84.8%)	57 (15.2%)	1.0
	T2 (n = 206)	175 (85.0%)	31 (15.0%)	
	T3 (n = 37)	31 (83.8%)	6 (16.2%)	
	T4 (n = 43)	41 (95.3%)	2 (4.7%)	
	Unknown (n = 135)	108 (80.0%)	27 (20.0%)	
N stage	N0 (n = 502)	428 (85.3%)	74 (14.7%)	1.0
	N1 (n = 110)	93 (84.5%)	17 (15.4%)	
	N2 (n = 23)	21 (91.3%)	2 (8.7%)	
	N3 (n = 21)	18 (85.7%)	3 (14.3%)	
	Unknown (n = 140)	113 (80.7%)	27 (19.3%)	
Genetic testing performed	No (n = 345)	320 (92.7%)	25 (7.2%)	< 0.001
	Yes (n = 290)	210 (72.4%)	80 (27.6%)	
	Unknown (n = 161)	143 (88.8%)	18 (11.2%)	
Follow-up time (yr)		3.77	3.62	1.0

Survival Outcomes of CPM in TNBC

A borderline improvement in 5-year unadjusted overall survival was noted for patients undergoing CPM (5-year overall survival 95.1% for CPM vs. 85.0% for no CPM; $p = 0.05$). However, no significant improvement was observed for local recurrence-free survival (5-year survival 80.1% for CPM vs. 78.0% for no CPM; $p = 0.40$) or distant recurrence-free survival (5-year survival 82.7% for CPM vs. 79.9% for no CPM; $p = 0.37$; Fig. 1). Among the 363 patients undergoing breast-conserving surgery, 5-year overall survival was 93.3%, local recurrence-free survival was 85.7%, and distant recurrence-free survival was 88.6%. Among the 191 patients undergoing unilateral mastectomy without CPM, these rates were 79.6%, 69.9%, and 71.3%, respectively. The survival advantage for breast-conserving surgery was eliminated when other treatment variables, including clinical nodal status, age, and high-grade disease were accounted for (Table 2).

Development of New Primary Breast Cancer

None of the CPM patients developed a new primary breast cancer compared with 2.2% (15/673) of patients in the no CPM group (median follow-up 3.7 years). Among these 15 patients, 20.0% (3/15) were known BRCA 1 or 2 mutation carriers. As shown in Table 3, all 15 of the new primary breast cancers were detected as contralateral tumors. One patient who underwent breast-conserving surgery for the initial index cancer developed contralateral ductal carcinoma in situ 1 year later, as well as a new hormone receptor-positive/HER2-negative cancer ipsilateral to her original index cancer 14 years later. Only 4 of these 15 patients (26.7%) developed a new/contralateral TNBC; all the others except for one triple-positive tumor were hormone receptor-positive and HER2-negative.

Subset Analysis of TNBC Patients Excluding BRCA Mutation Carriers

Among 703 non-BRCA mutation carriers, 79 (11.2%) underwent CPM. No significant difference in 5-year overall survival was observed for patients undergoing CPM versus those not undergoing CPM (94.1% vs. 85.2%, respectively; $p = 0.12$). No significant difference in local recurrence-free survival (5-year survival 77.1% for CPM vs. 78.2% for no CPM; $p = 0.51$) or distant recurrence-free survival was observed (5-year survival 81.2% for CPM vs. 80.3% for no CPM; $p = 0.64$; Fig. 2).

Subset Analysis of BRCA Mutation Carriers Undergoing CPM

Among the 93 genetic mutation carriers, 44 (47.3%) underwent CPM. Numeric trends were observed for improved outcomes among the BRCA mutation carriers undergoing CPM. Five-year overall survival was 97.2% for CPM versus 84.1% for no CPM ($p = 0.35$). Five-year local

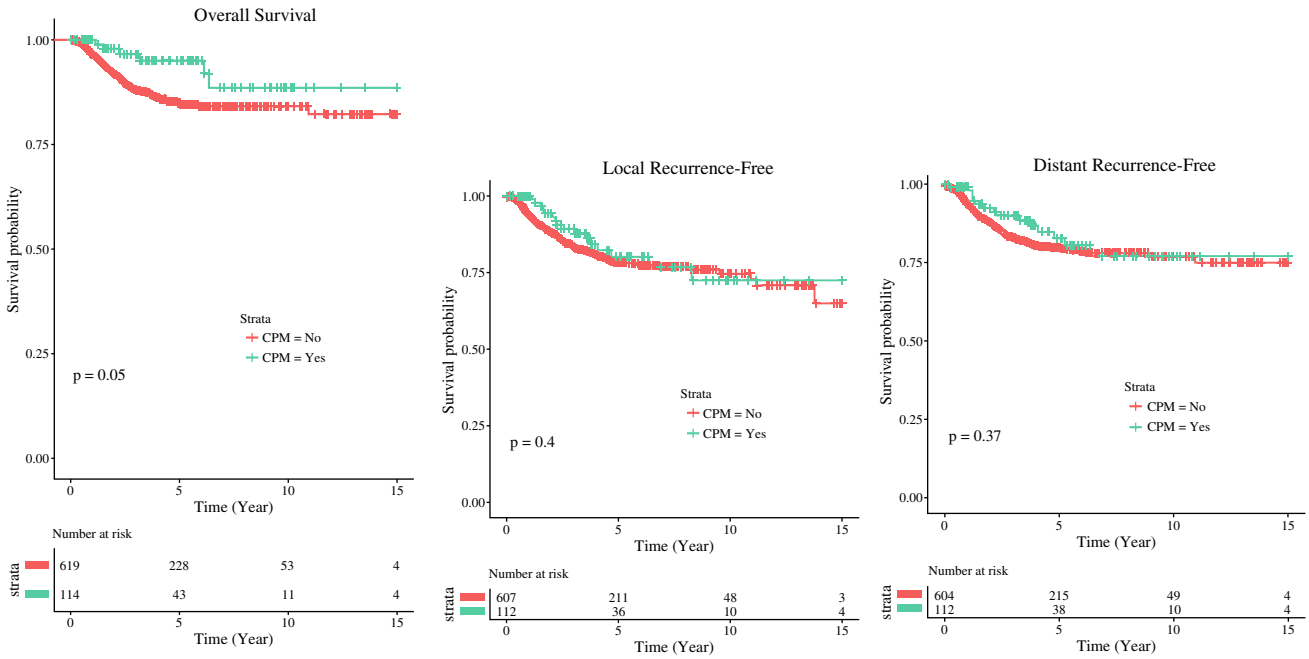

FIG. 1 Five-year overall, local recurrence-free, and distant recurrence-free survival of triple-negative breast cancer patients undergoing contralateral prophylactic mastectomy (CPM) versus those not undergoing CPM

TABLE 2 Survival outcomes for patients undergoing breast-conserving surgery and unilateral mastectomy

	Breast-conserving surgery (n = 363) (%)	Unilateral mastectomy (n = 191) (%)
5-year overall survival	93.3	79.6
Local recurrence-free survival	85.7	69.9
Distant recurrence-free survival	88.6	71.3

The survival advantage seen among the breast-conserving surgery patients was eliminated after adjusting for other treatment variables, such as clinical nodal status, age, and high-grade disease

TABLE 3 Characteristics of the 15 no-CPM patients who developed a new primary breast cancer

ID	Year of initial diagnosis	Laterality of initial TNBC	Stage of initial TNBC	Treatment	Date of diagnosis of new primary	Laterality of new primary	Stage of new primary	Phenotype of new primary	Genetic mutation status
1	2009	Right	T1bN0	BCT	2010	Left	T2N0	ER+/PR−/HER2−	Unknown
2	2008	Left	T1cN0	BCT + CTX	2011	Right	T2N3	ER+/PR+/HER2−	Unknown
3	2010	Right	T2N0	NACT + BCT	2013	Left	T3N1	ER+/PR+/HER2+	Unknown
4	2010	Right	T1cN0	BCT	2011	Left	T1cNx	ER+/PR−/HER2−	Unknown
5	2004	Right	T2N0	BCT + CTX	2017	Left	T1aN0	ER+/PR+/HER2−	Unknown
6	2004	Left	T1aN0	UM	2016	Right	T1bN0	ER+/PR+/HER2−	Negative
7	2016	Left	T2N0	UM + CTX	2019	Right	T1cN0	ER+/PR+/HER2−	Unknown
8	1/2012	Left	T2N0	BCT	9/2012	Right	T1cN0	ER−/PR−/HER2−	Unknown
9	2007	Right	T1bN0	BCT	2016	Left	T1bN0	ER−/PR−/HER2−	BRCA1 positive
10	2008	Left	T1cN0	BCT + CTX	2018	Right	T1cN0	ER−/PR−/HER2−	BRCA1 positive
11	2011	Right	T1bN0	UM	2014	Left	T1cN1	ER+/PR+/HER2−	Unknown
12	2007	Left	T1cN0	BCT	2012	Right	T1bN0	ER+/PR+/HER2−	Negative
13	2005	Right	T1cN0	BCT	2006	Left	TisNx	Unknown	Negative
					2019	Right	T1bN0	ER+/PR+/HER2−	
14	2011	Right	T1bN0	BCT	2013	Left	T1cN0	ER+/PR+/HER2−	Unknown
15	2004	Left	T1bN0	BCT	2006	Right	T1bN0	ER−/PR−/HER2−	BRCA2 positive

CPM contralateral prophylactic mastectomy, *TNBC* triple-negative breast cancer, *BCT* breast-conservation therapy, *CTX* adjuvant chemotherapy, *NACT* neoadjuvant chemotherapy, *UM* unilateral mastectomy, *ER* estrogen receptor, *PR* progesterone receptor, *HER2* HER2/neu receptor

recurrence-free survival was 86.8% for CPM versus 76.6% for no CPM (p = 0.56) and 5-year distant recurrence-free survival was 86.3% for CPM versus 76.5% for no CPM (p = 0.53) (Fig. 3).

DISCUSSION

In this study of TNBC patients undergoing CPM during a nearly 20-year period, our data demonstrate a borderline survival advantage for women with TNBC and no survival

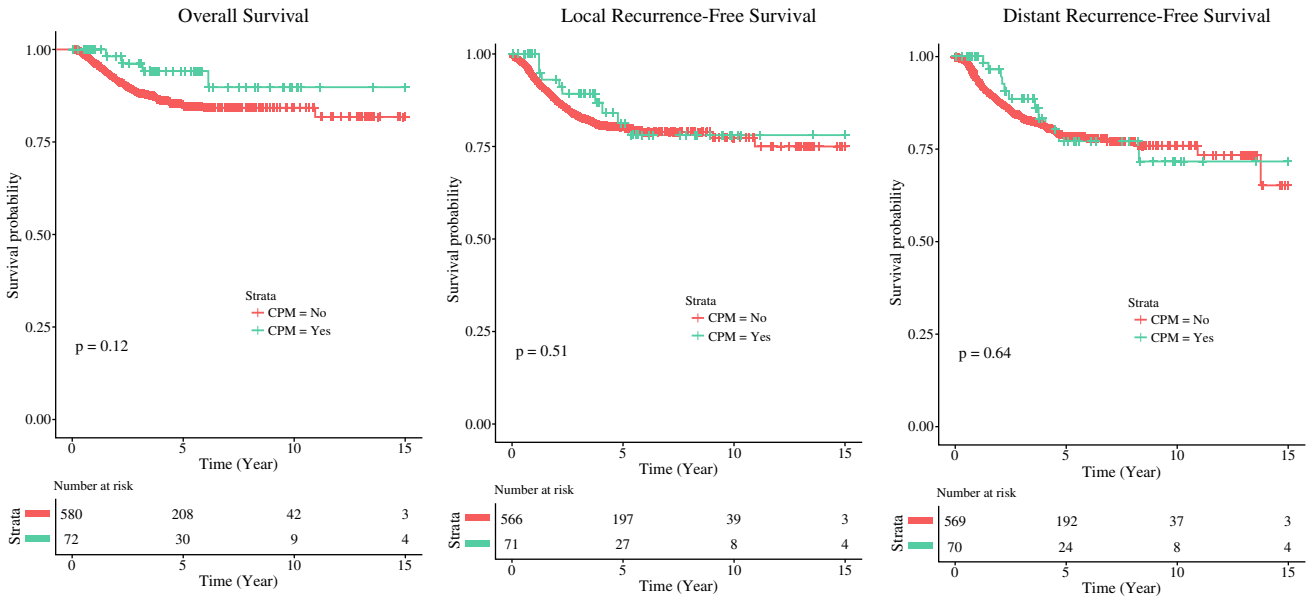

FIG. 2 Five-year overall, local recurrence-free, and distant recurrence-free survival of triple-negative breast cancer patients without BRCA mutations undergoing contralateral prophylactic mastectomy (CPM) versus those not undergoing CPM

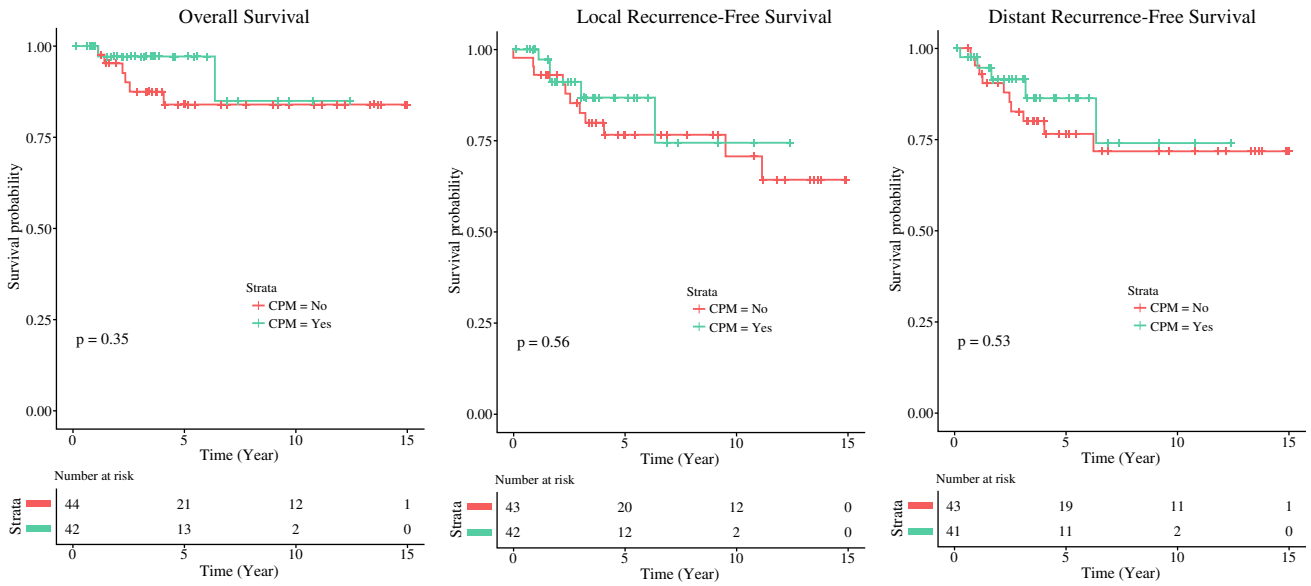

FIG. 3 Five-year overall, local recurrence-free, and distant recurrence-free survival of triple-negative breast cancer patients with BRCA mutations undergoing contralateral prophylactic mastectomy (CPM) versus those not undergoing CPM

advantage for women with unilateral breast cancer undergoing CPM without BRCA1/2 mutations. We also found that the rate of developing a new CBC was low (2.2%) among unilateral mastectomy patients and that among those developing a new CBC, 20% were BRCA 1 or 2 mutation carriers. These data are consistent with large population-based studies that have investigated the impact of CPM on women with unilateral breast cancer.[4,12,13]

For example, one large study of more than 14,000 mastectomy patients with stage I and II breast cancer from the National Cancer Database found that patients undergoing CPM and patients not undergoing CPM had equivalent outcomes (hazard ratio [HR] 0.93; $p = 0.39$). Furthermore, subset analysis of women with estrogen receptor-negative tumors found that overall survival was not improved for women undergoing CPM compared with

those having unilateral mastectomy (HR = 1.12, $p = 0.32$).[3] Another smaller study of 355 patients with stage 0–III unilateral breast cancer found that at a median follow-up of 61 months, CPM did not improve overall, disease-free, or distant metastases-free survival.[14] Analysis of breast cancer patients aged ≤40 years from 1980 to 2010, Zeichner and colleagues found that CPM did provide a survival advantage regardless of tumor characteristics, but the effect was only seen after 10 years of follow-up.[15] Surveillance, Epidemiology, and End Results data of mastectomy patients from 1998 to 2003 found that CPM was associated with only a small improvement in 5-year, breast cancer-specific survival, mainly in women with early-stage, estrogen receptor-negative disease.[16]

Survival for most women with invasive breast cancer is driven by the metastatic risk of the primary tumor.[17,18] For most patients, this risk is already established as distant organ micrometastatic disease at the time of initial cancer diagnosis, but contemporary systemic therapy regimens are usually successful in eradicating these micrometastases. Any patient with one primary breast cancer is at risk for developing a new primary breast cancer, but the overall survival rates continue to be most closely related to the aggressiveness of the first breast cancer, at least in part because of lead-time advantage in establishing micro metastases.[19] This context would explain the failure of CPM to impact overall survival rates of women with a unilateral breast cancer. However, as systemic therapies for breast cancer continue to improve, one can argue that there is an enlarging pool of patients that have been "cured" from their first cancer, and for these patients the metastatic risk of a new primary breast cancer is theoretically more relevant. This rationale in support of CPM as a strategy that can reduce the risk of new primary breast cancer must be balanced against the data demonstrating that incidence of contralateral breast cancer has been declining over time, likely because of the chemoprevention benefits of systemic therapy (especially relevant in the setting of endocrine therapy delivered for hormone receptor-positive breast cancer).[5] Potential CPM benefit should be analyzed more precisely by accounting for intrinsic breast tumor biology, endocrine therapy delivered, and inherent higher likelihood of developing a second primary breast cancer.

Our study therefore adds unique data to the existing literature on CPM surgery, by focusing on women with TNBC as a biologically aggressive tumor subtype and by including data on genetic testing with documented hereditary susceptibility for breast cancer. Similar to data reported by Chung et al. that examined patients with a variety of tumor phenotypes, our TNBC patients with BRCA mutations were more likely to undergo CPM surgery.[14] We did not demonstrate any statistically significant survival difference between the CPM versus no CPM surgery patients, regardless of whether a BRCA mutation was present. In contrast, previous data had demonstrated an improvement in survival for BRCA mutation carriers who undergo CPM.[20,21] Additionally, a recent 2016 meta-analysis also found that CPM reduces all-cause mortality for BRCA mutation carriers (HR 0.512; 95% CI 0.368–0.714).[22] The nonsignificant numeric trends of improved outcomes seen for the BRCA mutation carriers that underwent CPM surgery indicates that this subset warrants further study.

We also found that women with TNBC undergoing genetic testing were more likely to pursue CPM surgery, regardless of the results. This contrasts to previous work that found that the uptake of CPM for women who were planning on CPM before genetic testing was reduced after receiving a negative BRCA1/2 genetic test result.[23] Utilization of genetic testing is influenced by several factors, including resource availability, whether the provider offers genetic testing, and personal patient preference.[24,25] Despite these diverse issues, women motivated to evaluate their germline genetic risk for cancer likely represent a subset of patients with a heightened level of apprehension regarding their personal predisposition for developing breast cancer, and this may account for our findings.

In our series, patients with TNBC whose cancers were detected by either symptoms or another nonmammographic screening modality also were more likely to pursue CPM surgery, although this difference was not statistically significant. This may reflect the patient's reflex loss of confidence in mammography screening to detect a new breast cancer.

Very few ($n = 15$, 2.2%) of the no CPM patients developed a second primary breast cancer. Interestingly, however, nearly three-quarters of these new cancers were hormone receptor-positive. Brown et al. reported a 61.3% phenotype concordance rate among women with TNBC who developed a second primary breast cancer.[26] Patients with TNBC are not candidates for therapeutic endocrine treatment, but our findings prompt the question of whether these patients can reasonably consider chemoprevention to reduce the subsequent incidence of new primary hormone receptor-positive breast cancer.

Decisions regarding surgical management of the breast are complex. Interactions of individual preferences for treatment, including lumpectomy, radiation, and reconstruction, combined with fear regarding the possibly of another breast cancer influence decisions.[27] Patients need to reconcile these personal factors with the clinical factors that are presented to them by surgical breast oncologists.

The shared decision-making process therefore must include a discussion of lumpectomy eligibility and likelihood of breast asymmetry. The importance of ongoing surveillance to detect a local recurrence and/or a new primary breast cancer must be emphasized. Patients considering CPM surgery also must be offered plastic surgery consultation to discuss reconstruction options as well as risks, recognizing that some patients may opt for no reconstruction. Providers are obligated to ensure that patients understand that although bilateral mastectomy surgery provides the largest magnitude reduction in risk of developing a new primary breast cancer, it does not eliminate this risk. Ongoing clinical monitoring to detect a new breast cancer therefore remains necessary even if bilateral mastectomy surgery is performed. Most importantly, providers must clearly state that the CPM approach does not confer any definitive survival advantage. Lastly, patients should be reassured regarding flexibility in the timing of prophylactic mastectomy decisions; treatment of the index cancer is the highest priority, and risk-reducing surgery can be reconsidered months or even years after the acute cancer treatment has been completed.

Limitations

Our study is limited by a relatively short follow-up, and the time to develop a new contralateral breast cancer is not known to be over a shortened timeframe for patients with TNBC; however most recurrences in patients with TNBC occur within the first 5 years of diagnosis.[28] It also should be noted that our study included patients diagnosed over a 20-year period. Many of these women were therefore diagnosed before the Supreme Court 2013 ruling that resulted in expanded commercial availability of genetic testing by placing a ban on DNA gene patents.[29] It is therefore possible that a subset of patients in the older cohort failed to have their BRCA mutation status identified because of the more limited genetic testing options in that timeframe. This misclassification of hereditary susceptibility status might have resulted in loss of statistical power to detect outcome advantages associated with CPM in the subset of BRCA mutation carriers.

CONCLUSIONS

While many studies have evaluated the utility of CPM for women with unilateral breast cancer, data are sparse regarding the impact on patients with TNBC. Our data suggest that even among this high-risk subgroup, CPM does not confer a survival advantage. However, larger studies are needed to evaluate the potential benefit of CPM among TNBC patients with BRCA1/2 mutations.

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