Surgery Open Science 18 (2024) 70–77

Contents lists available at ScienceDirect

Surgery Open Science

journal homepage: www.journals.elsevier.com/surgery-open-science

Research Paper

Contralateral prophylactic mastectomy in a rural population: A single-institution experience

Devin J. Clegg, MD [a,*], Erica N. Whiteaker, BS [b], Brett J. Salomon, MD [a], Kaylan N. Gee, MD [a], Christopher G. Porter, MD [a], Thomas W. Mazonas, MD [a], R. Eric Heidel, PhD, PStat [c], Ashton J. Brooks, MD [d], John L. Bell, MD, FACS [d], Stefanos Boukovalas, MD [e], Jillian M. Lloyd, MD, MPH, FACS [d]

[a] University of Tennessee Graduate School of Medicine, Department of Surgery, Knoxville, TN, United States of America
[b] University of Tennessee Health Science Center, College of Medicine, Memphis, TN, United States of America
[c] University of Tennessee Graduate School of Medicine, Department of Surgery, Division of Biostatistics, Knoxville, TN, United States of America
[d] University of Tennessee Graduate School of Medicine, Department of Surgery, Division of Surgical Oncology, Knoxville, TN, United States of America
[e] University of Tennessee Graduate School of Medicine, Department of Surgery, Division of Plastic & Reconstructive Surgery, Knoxville, TN, United States of America

HIGHLIGHTS

- The rate of bilateral mastectomy for unilateral breast cancer is increasing.
- Over 20 years, our rate of contralateral prophylactic mastectomy has nearly tripled.
- Most of these patients had average-risk for developing contralateral cancers.
- These patients were younger, with smaller tumors, and underwent reconstruction.
- Those with bilateral mastectomies had more wound infections.

ARTICLE INFO

Keywords:
Prophylactic mastectomy
Contralateral mastectomy
Unilateral breast cancer
Rural breast cancer
Outcomes after mastectomy
Associations with bilateral mastectomy

ABSTRACT

Background: The incidence of contralateral prophylactic mastectomy (CPM) for unilateral breast cancer (UBC) has continued to increase, despite an absent survival benefit except in populations at highest risk for developing contralateral breast cancer (CBC). CPM rates may be higher in rural populations but causes remain unclear. A study performed at our institution previously found that 21.8 % of patients with UBC underwent CPM from 2000 to 2009. This study aimed to evaluate the CPM trend at a single institution serving a rural population and identify the CPM rate in average-risk patients.

Methods: Retrospective review of patients who underwent mastectomies for UBC at our institution from 2017 to 2021 was performed. Analysis utilized frequencies and percentages, descriptive statistics, chi-square, and independent sample *t*-tests.

Results: A total of 438 patients were included, of whom 64.4 % underwent bilateral mastectomy for UBC (CPM). Patients who underwent CPM were significantly younger, underwent genetic testing, had germline pathogenic variants, had a family history of breast cancer, had smaller tumors, underwent reconstruction, and had more wound infections. Of CPM patients, 50.4 % had no identifiable factors for increased risk of developing CBC.

Conclusions: The rate of CPM in a rural population at a single institution increased from 21.8 % to 64.4 % over two decades, with an average-risk CPM rate of 50.4 %. Those that undergo CPM are more likely to undergo reconstruction and have more wound infections. Identifying characteristics of patients undergoing CPM in a rural population and the increased associated risks allows for a better understanding of this trend to guide conversations with patients.

Key message: This study demonstrates that the rate of contralateral prophylactic mastectomy for unilateral breast cancers performed at a single institution serving a largely rural population has nearly tripled over the last two decades, with half of these patients having no factors that increase the risk for developing contralateral breast

* Corresponding author at: 1924 Alcoa Highway, Box U-11, Knoxville, TN 37920, United States of America.
E-mail address: Dclegg1@utmck.edu (D.J. Clegg).

https://doi.org/10.1016/j.sopen.2024.02.007
Received 31 August 2023; Received in revised form 14 February 2024; Accepted 20 February 2024
Available online 23 February 2024

cancers. Contralateral prophylactic mastectomy was significantly associated with smaller tumors, younger age, genetic testing, germline pathogenic variants, family history of breast cancer, breast reconstruction, and increased wound infections.

Introduction

The rate of bilateral mastectomy (BLM) for unilateral breast cancer (UBC) has increased significantly over the last 20 years [1–4], often times with patients initiating the conversation about contralateral prophylactic mastectomy (CPM) rather than their surgeon [5]. This is despite evidence that CPM provides no survival benefit except in specific populations at highest risk for developing contralateral breast cancer (CBC) who undergo the procedure at an earlier age [6–8]. CPM rates may be higher in rural populations, but reasons for this are still being investigated [9–11]. A study performed at our institution from 2000 to 2009 found that 21.8 % of patients with UBC underwent BLM [12].

Previously, CPM has been associated with diagnosis at a younger age [3,6,13–17], attempts to avoid postsurgical radiation therapy and future breast cancer screening [1,18–21], lobular cancers [3,22–24], tumor size [4,14,16,22–24], White race/ethnicity [13,22,23], insurance status [13], household income [13,25], family history of breast or ovarian cancer [17,22,26], genetic testing [22,26], increased incidence of complications [2,8,27,28], and postmastectomy reconstruction (PMR) [4,22]. Risk factors for CBC development include genetic mutations such as BRCA1 and BRCA2 [8,29], and strong family histories of breast cancer without genetic testing or with negative genetic testing [30]. The CPM rate continues to increase despite the now common use of adjuvant hormonal therapy and systemic chemotherapy, which significantly decreases the risk of CBC development [6,31].

The American Society of Breast Surgeons has discouraged CPM in average-risk patients with UBC [30], and all recommendations focus on shared-decision making accounting for patient values, goals, and preferences [8,30]. There is no single-risk threshold above which CPM is clearly indicated, and it is important for treating physicians to discuss not only the risk assessment, but all available treatment strategies [8]. Despite these recommendations, more low- or average-risk patients are undergoing CPM [26,32–34]. The decision to undergo CPM is intensely personal and often influenced by a variety of factors including perceived breast cancer risk, anxiety over screening and diagnostic procedures, and the anticipated physical, emotional, cosmetic, and financial outcomes of surgery [8]. While many patients adjust well after CPM and experience reductions in cancer-related anxiety, others experience increased anxiety and distress after surgery as postmastectomy concerns with body image and sexuality are not uncommon [8]. The aim of this study was to evaluate the trend of CPM at a single institution serving a largely rural population and identify factors associated with this decision.

Material and methods

Patients that underwent mastectomies for UBC from 2017 to 2021 were retrospectively reviewed after identification within our institution's prospectively maintained tumor registry database. This study was institutional review board approved with waiver of informed consent requirement (University of Tennessee Graduate School of Medicine, Knoxville, TN, IRB reference #4810). Patients with incomplete records, male patients, and those that did not undergo mastectomy at our institution were excluded. The University of Tennessee Medical Center (UTMC) is an academic tertiary-care center with a Cancer Center of Excellence designation, offering comprehensive breast cancer care with multidisciplinary review of all patients and a survivorship program. UTMC is a primary referral center in the region for breast reconstruction, including one of the only centers in the region that offers autologous reconstruction. All patients who undergo mastectomies are offered referral to a plastic surgeon for breast reconstruction discussions.

The home ZIP Code of the patient at diagnosis was used to determine the Euclidean travel distance in miles from the patient's residence to UTMC. Median household income (MHI) was determined by the most current US Census Bureau five-year estimates per ZIP Code from 2019 and was reported in US dollars. The designation of Tennessee as a largely rural population is based on the US Census Bureau definitions of rural, mostly rural, and urban areas by population percentage [35]. CPM was defined as BLM performed for UBC. Average-risk CPM (AR-CPM) rates were calculated by sequentially removing patients who underwent BLM with risk-factors that may be associated with increased likelihood of developing CBC over their lifetime from the total study and BLM populations (Fig. 1).

The demographic and clinical characteristics of the sample were analyzed using frequencies and percentages for categorical parameters. Descriptive statistics, including means and standard deviations were used to describe interval and ratio level variables. Chi-square analyses were performed to compare independent groups on categorical outcomes, while *t*-tests were used to test for significant differences between groups on continuous outcomes. Descriptive and frequency statistics were reported for all between-subjects comparisons. All statistical analyses were performed using SPSS Version 29 (Armonk, NY: IBM Corp.) and statistical significance was assumed at an alpha value of 0.05.

Results

After review, 438 patients with unilateral breast cancer who underwent unilateral or bilateral mastectomy were included. Within this study population, 96.1 % identified as White, 100 % female, with an average age at breast cancer diagnosis of 58.5 years, average body mass index (BMI) of 29.0 kg/m^2, and average length of follow-up of 25.7 months. A total of 282 (64.4 %) patients underwent BLM while 156 (35.6 %) underwent ULM. There were no significant differences in race/ethnicity, BMI, diabetes mellitus, tobacco use, distance traveled by patients, or the median household income between groups (Table 1). Patients who underwent BLM were significantly younger than those that underwent ULM (55.5 vs. 66.0 years; $p < 0.001$). The BLM group had a significantly higher proportion of non-Medicaid/Medicare public insurance (61.3 % vs. 34.0 %; $p < 0.001$) and private insurance (2.8 % vs. 0.0 %; $p < 0.001$) than the ULM group. The ULM group had a significantly higher proportion of Medicare than the BLM group (56.4 % vs. 28.4 %; $p < 0.001$).

A significantly higher proportion of the BLM group was diagnosed at an age $\leq$ 45 years old (20.6 % vs. 4.5 %; $p < 0.001$). There were no significant differences in cancer types on final pathological review between groups (Table 2). Tumor size was significantly smaller in the BLM group (64.2 % vs. 53.2 % $\leq$2 cm; $p = 0.03$). There were no significant differences in tumor characteristics between groups (Table 2). The BLM group had a significantly higher proportion of adjuvant chemotherapy received (48.9 % vs. 37.8 %; $p = 0.03$) than the ULM group. There were no significant differences in rates of neoadjuvant treatment, adjuvant hormonal therapy, adjuvant radiation therapy, or time to final oncologic surgery between groups (Table 2).

Genetic testing was performed in a higher proportion of patients who underwent BLM (59.2 % vs. 30.1 %; $p < 0.001$), with increased rates of BRCA1 pathogenic variants (2.8 % vs. 1.3 %; $p < 0.001$) and BRCA2 pathogenic variants (4.3 % vs. 3.2 %; $p < 0.001$) in the BLM group. Non-BRCA germline pathogenic variant mutation positivity was also significantly higher in the BLM group (12.8 % vs. 4.5 %; $p < 0.001$). The overall proportion of patients with at least one germline pathogenic

variant mutation known to increase the risk of breast cancer development was significantly higher in the BLM group (18.4 % vs. 8.3 %; $p < 0.001$). The proportion of variants of unknown significance (VUS) found on genetic testing was also significantly higher in the BLM group (15.6 % vs. 8.3 %; $p < 0.001$). There were no significant differences in the proportions of patients that were adopted with unknown family history between groups (Table 3). The BLM group had significantly higher proportions of patients with a family history of breast cancer (62.1 % vs. 48.7 %; $p = 0.03$), relatives with breast cancer diagnosed under the age of 50 years (19.5 % vs. 7.9 %; $p = 0.001$), and relatives with breast cancer diagnosed over the age of 50 years (57.3 % vs. 44.7 %; $p = 0.01$). There were no significant differences in the family histories pertaining to other non-breast cancers between groups (Table 3).

Reconstruction was performed significantly more often in the BLM group (64.9 % vs. 35.3 %; $p < 0.001$), with reconstruction characteristics described in Table 4. Immediate reconstruction (59.6 % vs. 32.1 %; $p < 0.001$) and alloplastic (implant-based) reconstruction (59.2 % vs. 30.1 %; $p < 0.001$) were most common in both groups. The BLM group had significantly higher rates revision after reconstruction (31.2 % vs. 12.8 %; $p < 0.001$), implant removal (12.1 % vs. 3.8 %; $p < 0.001$), and wound infections (8.9 % vs. 3.2 %; $p = 0.03$). There were no significant differences in overall rates of complications, wound dehiscence, deep vein thrombosis (DVT), hematoma, reoperation, re-excision of margins, or lymphedema between groups (Table 5). There was no significant difference in disease status at last follow-up, with 96.8 % of the BLM and 95.5 % of the ULM group having no evidence of disease (Table 5).

The rate of BLM for UBC (CPM) was determined to be 64.4 %. Of the 282 patients that underwent BLM, patients with family histories or genetic mutations that may have increased their likelihood for developing a CBC during their lifetime were sequentially excluded until 142 patients remained (Fig. 1). We found that 50.4 % of the patients that underwent CPM had an average-risk for developing CBC (AR-CPM). Of the total study population, 32.4 % of patients underwent AR-CPM.

Table 1
Patient demographics.

	Bilateral mastectomy (n = 282)	Unilateral mastectomy (n = 156)	p-Value
Race/ethnicity			
White	273 (96.8 %)	148 (94.9 %)	
Black	7 (2.5 %)	6 (3.8 %)	
Hispanic	0 (0.0 %)	1 (0.6 %)	
Asian	2 (0.7 %)	1 (0.6 %)	0.48
Gender			
Female	282 (100.0 %)	156 (100.0 %)	
Age at diagnosis (years)[a]	55.5 (45, 65)	66.0 (59, 74)	**<0.001**
Body mass index (kg/m^2)[a]	27.4 (24, 32)	27.6 (24, 32)	0.88
Insurance status			
Medicaid	17 (6.0 %)	14 (9.0 %)	
Medicare	80 (28.4 %)	88 (56.4 %)	
Non-medicaid/ medicare public insurance	173 (61.3 %)	53 (34.0 %)	
Private insurance	8 (2.8 %)	0 (0.0 %)	
Uninsured	4 (1.4 %)	1 (0.6 %)	**<0.001**
Diabetes mellitus	31 (11.0 %)	25 (16.0 %)	0.13
Tobacco use			
Current use	31 (11.0 %)	28 (17.9 %)	
Former use	64 (22.7 %)	33 (21.2 %)	
No history of use	187 (66.3 %)	95 (60.9 %)	0.12
Travel distance[b] (miles)	16.6 (10, 28)	18.2 (10, 34)	0.14
Median household income[b] (US dollars)	$55,255.50 ($44,876, $63,009)	$51,479.00 ($43,266, $63,009)	0.13

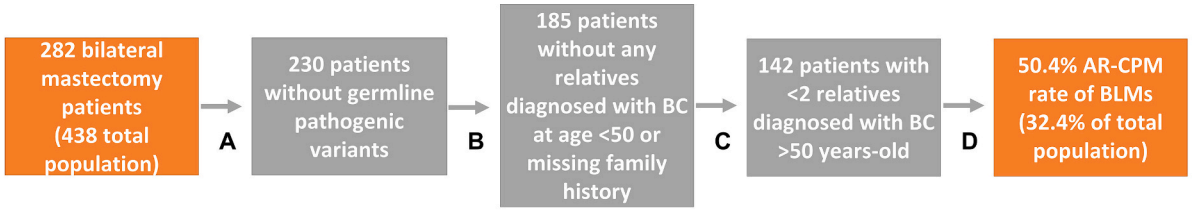
Bold indicates statistically significant, $p < 0.05$.
[a] Reported as median (25th and 75th interquartile ranges).
[b] Calculations performed using patient reported ZIP Codes and reported as medians (25th and 75th interquartile ranges).

Discussion

As CPM rates increase despite a favorable decrease in the incidence of CBC, it is critical to evaluate trends and outcomes within institutions and underrepresented populations in the literature [1–4,36,37]. The aims of this study were to evaluate the trend of CPM at a single institution serving a largely rural population and identify factors that may be contributing to this decision. We hypothesized that the rate of CPM will have increased since our last study period, specifically among younger patients and those seeking breast reconstruction, and would have a higher rate of complications than those that underwent ULM. We also hypothesized that a significant proportion of the CPM patient group would have average-risk for developing subsequent CBC (AR-CPM).

Within our study population of 438 patients with unilateral breast cancers, 64.4 % of patients underwent CPM, defined as BLM for UBC. Our study population has a higher proportion of patients who identify as White than national averages but is similar in average age at diagnosis and comorbidities to other studies. While BMI may be associated with increased risk of CBC development [38], we found no significant difference in average BMI between groups.

Studies have demonstrated that patients identifying as White are more likely to undergo CPM, which likely contributes to our high rate of CPM [13,22,23]. Notably, there was no significant difference in median household income (MHI) between BLM and ULM groups, despite previous evidence that CPM was associated with both higher and lower MHI [13,25]. Our institution serves a large twenty-one county catchment area of eastern Tennessee and portions of surrounding states, including counties with the lowest MHI and most significant health disparities in Tennessee [39]. We had previously found significant differences in MHI in patients that undergo postmastectomy reconstruction [40], but this effect does not appear to translate to the decision to undergo BLM compared to ULM. Patients who underwent BLM had significantly



A. 52 patients with at least one germline pathogenic variant mutation on genetic testing removed.
B. 40 patients with any relatives diagnosed with breast cancer <50 years-old removed. Two adopted patients and three patients with incomplete family history removed.
C. 43 patients with ≥2 relatives diagnosed with breast cancer >50 years-old removed.
D. 142 patients of 282 bilateral mastectomies (50.4%) had average risk (AR) for contralateral breast cancer development but underwent contralateral prophylactic mastectomy (CPM) for a unilateral breast cancer. 142 patients of 438 total patients underwent AR-CPM (32.4%).

Fig. 1. The calculation of the proportion of contralateral prophylactic mastectomies performed for unilateral breast cancers in average-risk patients (AR-CPM) who underwent bilateral mastectomies (BLM) and of the total study population, determined by sequentially removing patients with factors that may be associated with increased risk of developing contralateral breast cancers.

Table 2
Oncologic characteristics.

	Bilateral mastectomy (n = 282)	Unilateral mastectomy (n = 156)	p-Value
Age of diagnosis ≤45 years	58 (20.6 %)	7 (4.5 %)	**<0.001**
Cancer type			
DCIS	41 (14.5 %)	15 (9.6 %)	
IDC	69 (24.5 %)	44 (28.2 %)	
IDC + DCIS	125 (44.3 %)	62 (39.7 %)	
IDC + ILC	13 (4.6 %)	5 (3.2 %)	
IDC + LCIS	5 (1.8 %)	0 (0.0 %)	
ILC	7 (2.5 %)	12 (7.7 %)	
ILC + LCIS	18 (6.4 %)	17 (10.9 %)	
LCIS	1 (0.4 %)	0 (0.0 %)	
Inflammatory	2 (0.7 %)	1 (0.6 %)	
Other adenocarcinoma	1 (0.4 %)	0 (0.0 %)	0.06
Tumor size			
<2 cm	181 (64.2 %)	83 (53.2 %)	
>2 cm	101 (35.8 %)	73 (46.8 %)	**0.03**
Laterality			
Left	127 (45.0 %)	88 (56.4 %)	
Right	155 (55.0 %)	68 (43.6 %)	**0.02**
ER+	233 (82.6 %)	126 (80.8 %)	0.24
PR+	201 (71.3 %)	112 (71.8 %)	0.33
HER2+	36 (12.8 %)	19 (12.2 %)	0.31
Histologic grade			
Grade 1	32 (11.3 %)	15 (9.6 %)	
Grade 2	120 (42.6 %)	67 (42.9 %)	
Grade 3	99 (35.1 %)	58 (37.2 %)	
Not determined	31 (11.0 %)	16 (10.3 %)	0.78
Ki-67 percentage[a]	22.0 % (10, 44)	18.5 % (8, 40)	0.27
Neoadjuvant treatment	55 (19.5 %)	34 (21.8 %)	0.57
Adjuvant chemotherapy	138 (48.9 %)	59 (37.8 %)	**0.03**
Adjuvant hormonal therapy	201 (71.3 %)	117 (75.0 %)	0.40
Adjuvant radiation therapy	76 (27.0 %)	41 (26.3 %)	0.88
Time to final oncologic surgery[a] (days)	41.0 (27, 59)	41.0 (28, 59)	1.00

Notes. DCIS=Ductal carcinoma in-situ; IDC = Invasive ductal carcinoma; ILC = Invasive lobular carcinoma; LCIS = Lobular carcinoma in-situ; ER = Estrogen receptor; PR = Progesterone receptor, HER2 = Human epidermal growth factor receptor 2.
Bold indicates statistically significant, $p < 0.05$.
[a] Reported as median (25th and 75th interquartile ranges).

Table 3
Genetic/genomic testing and family history.

	Bilateral mastectomy (n = 282)	Unilateral mastectomy (n = 156)	p-Value
Genetic testing performed	167 (59.2 %)	47 (30.1 %)	**<0.001**
BRCA1 pathogenic variant	8 (2.8 %)	2 (1.3 %)	**<0.001**
BRCA2 pathogenic variant	12 (4.3 %)	5 (3.2 %)	**<0.001**
Other germline pathogenic variants	36 (12.8 %)	7 (4.5 %)	**<0.001**
At least one germline pathogenic variant	52 (18.4 %)	13 (8.3 %)	**<0.001**
Variant of unknown significance	44 (15.6 %)	13 (8.3 %)	**<0.001**
Genomic testing	60 (21.3 %)	34 (21.8 %)	0.90
Oncotype score[a]	15.0 (11,23)	14.0 (9, 20)	0.28
Adopted	2 (0.7 %)	3 (1.9 %)	0.35
Family history of breast cancer	175 (62.1 %)	76 (48.7 %)	**0.03**
Family history of breast cancer under age 50 years	54 (19.5 %)	12 (7.9 %)	**0.001**
Family history of breast cancer over age 50 years	157 (57.3 %)	68 (44.7 %)	**0.01**
Family history of other cancers	228 (80.9 %)	115 (73.7 %)	0.22
Family history of other cancers under age 50 years	34 (12.3 %)	14 (9.3 %)	0.35
Family history of other cancers over age 50 years	216 (81.5 %)	109 (73.2 %)	0.05

Bold indicates statistically significant, $p < 0.05$.
[a] Reported as median (25th and 75th interquartile ranges).

Table 4
Reconstruction characteristics.

	Bilateral mastectomy (n = 282)	Unilateral mastectomy (n = 156)	p-Value
Prior breast augmentation	12 (4.3 %)	7 (4.5 %)	0.91
Reconstruction performed	183 (64.9 %)	55 (35.3 %)	**<0.001**
Reconstructive timing			
Immediate reconstruction	168 (59.6 %)	50 (32.1 %)	
Delayed reconstruction	17 (6.0 %)	5 (3.2 %)	**<0.001**
Alloplastic reconstruction	167 (59.2 %)	47 (30.1 %)	**<0.001**
Type of alloplastic reconstruction			
Direct-to-implant, saline	12 (4.3 %)	2 (1.3 %)	
Direct-to-implant, silicone	39 (13.8 %)	8 (5.1 %)	
Two-stage reconstruction	119 (42.2 %)	37 (23.7 %)	**<0.001**
Final alloplastic reconstruction type			
Saline implant	47 (16.7 %)	16 (10.3 %)	
Silicone implant	87 (30.9 %)	20 (12.8 %)	**<0.001**
Autologous reconstruction	41 (14.5 %)	16 (10.3 %)	0.44

Notes. ADM = acellular dermal matrix; Alloplastic reconstruction rates include implants placed in combination with autologous reconstruction.
Bold indicates statistically significant, $p < 0.05$.

higher proportions of non-Medicaid/Medicare public insurance and private insurance than the ULM group. This is consistent with the findings of a previous study that demonstrated patients with private or managed care insurance plans were more likely to undergo CPM [13]. The ULM group also had a significantly higher proportion of Medicare than the BLM group, which was anticipated as the ULM group was significantly older.

We found no significant difference in the distance traveled by patients to the hospital between groups. A 2017 study found that increased travel distance was independently associated with increased rates of CPM for all patients, as well as increased facility-specific rates of CPM [21]. This and other studies have postulated that motivation for undergoing CPM may in part be due to desire to avoid traveling for post-surgical breast cancer screening [18–21,30]. Longer travel distances and poor access to mammography centers can deter patients from participating in mammographic screening, and patients may see CPM as an opportunity to limit the burden of continued screening [18–21]. Rural breast cancer patients tend to travel longer distances for care, and difficulties with transportation and lack of easily accessible health-care services may play a role in their breast cancer treatment decision-making [41], This is demonstrated by rural areas having lower levels of mammogram screening and less recent mammograms compared to their urban counterparts [42].

A significantly higher proportion of the BLM group were diagnosed

Table 5
Patient outcomes.

	Bilateral mastectomy ($n = 282$)	Unilateral mastectomy ($n = 156$)	p-Value
Revision after reconstruction	88 (31.2 %)	20 (12.8 %)	**<0.001**
Implant removal	34 (12.1 %)	6 (3.8 %)	**<0.001**
Any complication	105 (37.2 %)	44 (28.2 %)	0.06
Wound infection	25 (8.9 %)	5 (3.2 %)	**0.03**
Wound dehiscence	34 (12.1 %)	10 (6.4 %)	0.06
DVT	5 (1.8 %)	3 (1.9 %)	1.00
Hematoma	7 (2.5 %)	6 (3.8 %)	0.42
Reoperation	70 (24.8 %)	28 (17.9 %)	0.10
Re-excision of margins	13 (4.6 %)	10 (6.4 %)	0.42
Lymphedema	20 (7.1 %)	15 (9.6 %)	0.35
Disease status at last follow-up			
No evidence of disease	273 (96.8 %)	149 (95.5 %)	
Ongoing treatment	4 (1.4 %)	1 (0.6 %)	
Recurrence	5 (1.8 %)	6 (3.8 %)	0.32

Notes. DVT = deep vein thrombosis.
Bold indicates statistically significant, $p < 0.05$.

at an age ≤ 45 years old. This is consistent with literature demonstrating significant associations between CPM and diagnosis at a younger age [3,6,13–16]. Studies have shown that the survival benefit of CPM is most pronounced in patients with increased risk of CBC development who undergo the procedure at an earlier age [6,8,30].

Higher rates of CPM have been associated with lobular cancers [3,22–24], but our study found no significant difference in cancer types on final pathology between groups. Tumor size was significantly smaller in the BLM group, with a significantly higher proportion of patients with tumors ≤2 cm (Fig. 2). The literature on the effect of tumor size on CPM rate appears to be conflicting, as previous studies have demonstrated that less aggressive tumor pathologic features including smaller size [4,14], as well as larger tumor size [16,22–24], appear to be associated with CPM. Our study findings indicate that those patients with smaller tumors more often underwent BLM, while the proportions of specific cancer types were similar among both groups.

Most patients underwent adjuvant hormonal therapy with no significant difference between groups. The trend of increased rates of CPM is despite the now common use of adjuvant hormonal therapy. Antiestrogen medications in premenopausal women have been demonstrated to reduce the risk of CBC development by approximately 50 %, and aromatase inhibitors for postmenopausal women by 60 % [6,31]. This did not appear to significantly impact the decision to undergo BLM in our study population. We found a significantly higher proportion of BLM patients underwent adjuvant chemotherapy, which is not explained by the significantly smaller tumor size found in the BLM group, nor the similar median oncotype scores and similar tumor receptor characteristics in both groups. In addition to the risk reduction of hormonal therapies, systemic adjuvant chemotherapy reduces the risk of developing CBC by approximately 20 %, making the contemporary risk of developing CBC approximately 0.2–0.5 % per year for those undergoing adjuvant therapies [31]. Overall, these therapies have led to a favorable decrease per year of incidence of CBC development in the US [36,37]. Desire to avoid adjuvant radiation therapy has been postulated to be a potential cause for choosing CPM [1], with rural women less likely to receive adjuvant radiation therapy overall [43], but we found no significant difference between groups.

A significantly higher proportion of BLM patients underwent genetic testing, with significantly higher rates of BRCA1, BRCA2, and non-BRCA germline pathogenic variant mutation positivity (Fig. 2). These findings are consistent with the current literature and CPM recommendations [8,22,26,29]. Of the BLM group, 167 (59.2 %) patients underwent genetic testing, with 52 (18.4 %) of these patients having at least one germline pathogenic variant mutation. Therefore, despite genetic testing being negative for germline pathogenic variants in 115 (68.9 %) patients, BLM (CPM) was still performed. This may indicate that the rationale for genetic testing such as strong family history, tumor characteristics, or younger age of diagnosis, may influence the decision to undergo CPM more than the presence of germline pathogenic variant mutations alone. Recommendations have previously cited that women who test negative for BRCA whose family carries a known BRCA

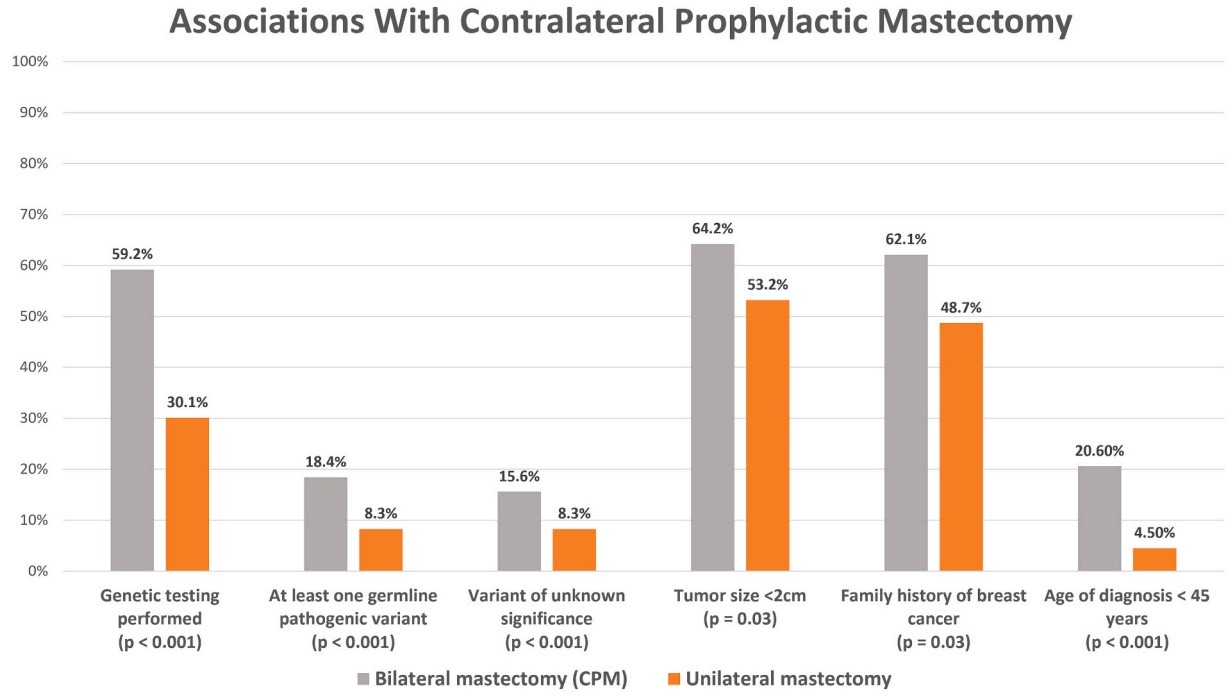


Fig. 2. The comparison of genetic testing, germline pathogenic variant mutations, variants of unknown significance, tumor size ≤2 cm, family history of breast cancer, and age of diagnosis ≤45 between patients who underwent bilateral or unilateral mastectomies for unilateral breast cancers.

mutation should be discouraged from CPM [30]. The rate of VUS was significantly higher in the BLM group, which is likely due to the greater proportion of patients that underwent genetic testing in this group.

Within our study population, a family history of breast cancer was significantly associated with BLM (Fig. 2), consistent with previous literature [22,26]. This association remained when relatives were stratified by age at diagnosis less than or greater than the age of 50 years. There was no significant difference in the family histories pertaining to other non-breast cancers between groups. It has also been recommended that younger women who have a family history of breast cancer, and those with strong family histories of breast cancer without genetic testing or with negative genetic testing, should be considered for CPM due to possible increased risk for CBC development [17,30].

Postmastectomy reconstruction (PMR) was performed significantly more often in the BLM group, with immediate and implant-based reconstruction most common. These findings are consistent with current literature [3,4,12,16,22,40,44], and it has been theorized that desire for improved reconstructed breast symmetry may influence the decision to undergo CPM [30]. This is also consistent with national trends, as the rate of overall PMR continues to increase after the passage of federal legislature for mandated insurance coverage as part of breast cancer care in 1998 [40,45–50]. PMR has been demonstrated to have numerous benefits including improved quality of life, self-esteem, psychosocial well-being, and patient satisfaction [51,52]. Our institution is the primary referral center for breast reconstruction, and one of the only in the region that offers all autologous breast reconstruction options in addition to implant-based reconstruction. In fact, there are few plastic surgeons outside of our facility that offer any breast cancer reconstruction whatsoever. This may have contributed to the proportion of patients that are referred seeking bilateral mastectomy with intent on specific reconstruction options.

The BLM group had significantly higher rates of revision after reconstruction, implant removal, and wound infections. The rates of overall complications, wound dehiscence, DVT, hematoma, reoperation, and lymphedema were not significantly different from the ULM group. Consistent with prior findings, BLM provides more opportunity for wound infections to develop with increased length of operating time, multiple surgical sites, and reconstruction more often performed [2,8,27,28].

We found no significant difference in disease status at last follow-up between groups, with an average follow-up length of 25.7 months. While this study was not designed to assess long-term recurrence or survival, our findings appear to align with current literature. CPM has not been associated with increased survival except in select patients at the highest risk of developing CBC, and may actually decrease survival in certain populations [3,13,14,53–55]. The rate of CBC development in patients diagnosed with a first-time breast cancer has historically fallen between 1.2 and 14 % [56], and recent studies demonstrate a cumulative risk of CBC in the 25-year period following first diagnosis to be 9.9 %, or 0.4 % annually [57]. This risk did not vary substantially by age at diagnosis, time from diagnosis, or by patient current age [57]. A 2016 study found that the 5-year cumulative incidence of CBC was 1.31 % for women diagnosed with a first-time breast cancer in the recent treatment era [36]. One study found that the incidence of CBC among women that did not undergo CPM was 17-fold less than the incidence of distant metastases, and seven-fold less than the incidence of locoregional recurrence [32]. This supports that prognosis is determined by the index lesion rather than by developing CBC or performing CPM [32]. The Society of Surgical Oncology Breast Disease Working Group also questioned whether the conflicting improvement in survival seen in some of the literature is due to selection bias, with CPM being performed more often on women with a better prognosis and better overall health, leading to a result that is not directly related to the CPM, as the differences in survival are generally larger than differences in CBC rates [8]. They also concluded that there is little evidence that women who do not undergo CPM and do develop a CBC are at increased risk of death from breast cancer [8].

The rate of BLM for UBC (CPM) was determined to be 64.4 % between 2017 and 2021 at our institution. Of the BLM group, 50.4 % underwent CPM with average-risk for developing CBC, and of the total study population, 32.4 % underwent AR-CPM (Fig. 1). In a previous study performed at our institution, 21.8 % of patients with UBC underwent BLM from 2000 to 2009 [12]. This study found that CPM was significantly associated with patients <50 years old, private insurance, urban residence, and PMR. Notably, it found that breast cancer stage and grade, and family history of breast cancer were not significantly associated with CPM. This study did not evaluate genetic mutations, as it was not available in the tumor registry at that time. While younger age and insurance type have remained consistent in their association with BLM at our institution, the rate of CPM has nearly tripled over the last two decades with more associated factors identified. Thus, patients at a single institution serving a largely rural population are increasingly choosing to undergo CPM in accordance with national trends.

This study is limited by its retrospective nature and homogenous study population with most patients identifying as White. Additionally, as the only regional academic institution serving a vast catchment area, our center may see higher rates of complex breast cancers, individuals seeking second opinions, and patients who seek specific reconstruction options, which may confer a higher likelihood of BLM. Future studies should include surveys and patient-reported outcome measures that would elucidate the most important factors to the individual patient in choosing to undergo CPM.

Conclusions

This study suggests that patients are increasingly choosing to undergo BLM for the treatment of UBC, with the rate of CPM increasing from 21.8 % to 64.4 % over the past two decades at one institution serving a largely rural population. This is despite the diagnosis of small tumors in younger patients and the absence of high-risk factors for the development of CBC, with 32.4 % of the total population, and 50.4 % of the BLM group, having average-risk for developing CBC but undergoing CPM. As there is no single-risk threshold above which CPM is clearly indicated, shared decision-making with patients is critically important. Identifying characteristics of patients choosing BLM in a rural population and the increased risks they face allows for a better understanding of this trend to guide these conversations with patients on their goals of breast cancer management.

Funding sources

None.

Ethical approval statement

This study is institutional review board approved, and complies with the principles outlined in the Declaration of Helsinki.

CRediT authorship contribution statement

Devin J. Clegg: Conceptualization, Data curation, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing. **Erica N. Whiteaker:** Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Brett J. Salomon:** Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Kaylan N. Gee:** Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing. **Christopher G. Porter:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Thomas W. Mazonas:** Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review &

editing. **R. Eric Heidel:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Ashton J. Brooks:** Conceptualization, Data curation, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **John L. Bell:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Stefanos Boukovalas:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Jillian M. Lloyd:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors have no declarations of interest to disclose including direct or indirect financial or personal relationships, interests, or affiliations relevant to the subject matter of the manuscript that have occurred over the last two years, or that are expected in the foreseeable future. This disclosure includes, but is not limited to, grants or funding, employment, affiliations, patents (in preparation, filed, or granted), inventions, honoraria, consultancies, royalties, stock options/ownership, or expert testimony. All authors acknowledge that the conflict of interest disclosures are complete for themselves, and their co-authors as stated above.

References

[1] Baskin AS, Wang T, Bredbeck BC, Sinco BR, Berlin NL, Dossett LA. Trends in contralateral prophylactic mastectomy utilization for small unilateral breast cancer. J Surg Res 2021;262:71–84. https://doi.org/10.1016/j.jss.2020.12.057.

[2] Kwok AC, Goodwin IA, Ying J, Agarwal JP. National trends and complication rates after bilateral mastectomy and immediate breast reconstruction from 2005 to 2012. Am J Surg 2015;210:512–6. https://doi.org/10.1016/j.amjsurg.2015.03.019.

[3] 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;265:581–9. https://doi.org/10.1097/SLA.0000000000001698.

[4] Zhang B, Coopey SB, Gadd MA, Hughes KS, Chang DC, Oseni TO. Trends in unilateral and contralateral prophylactic mastectomy use in ductal carcinoma in situ of the breast: patterns and predictors. Ann Surg Oncol 2019;26:3863–73. https://doi.org/10.1245/s10434-019-07628-w.

[5] Momoh AO, Griffith KA, Hawley ST, Morrow M, Ward KC, Hamilton AS, et al. Post-mastectomy breast reconstruction: exploring plastic surgeon practice patterns and perspectives. Plast Reconstr Surg 2020;145:865–76. https://doi.org/10.1097/PRS.0000000000006627.

[6] Bedrosian I, Hu C-Y, Chang GJ. Population-based study of contralateral prophylactic mastectomy and survival outcomes of breast cancer patients. JNCI J Natl Cancer Inst 2010;102:401–9. https://doi.org/10.1093/jnci/djq018.

[7] Boughey JC, Hoskin TL, Degnim AC, Sellers TA, Johnson JL, Kasner MJ, et al. Contralateral prophylactic mastectomy is associated with a survival advantage in high-risk women with a personal history of breast cancer. Ann Surg Oncol 2010;17:2702–9. https://doi.org/10.1245/s10434-010-1136-7.

[8] Hunt KK, Euhus DM, Boughey JC, Chagpar AB, Feldman SM, Hansen NM, et al. Society of Surgical Oncology breast disease working group statement on prophylactic (risk-reducing) mastectomy. Ann Surg Oncol 2017;24:375–97. https://doi.org/10.1245/s10434-016-5688-z.

[9] Nash R, Goodman M, Lin CC, Freedman RA, Dominici LS, Ward K, 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;152:648. https://doi.org/10.1001/jamasurg.2017.0115.

[10] Lizarraga IM, Kahl AR, Jacoby E, Charlton ME, Lynch CF, Sugg SL. Impact of age, rurality and distance in predicting contralateral prophylactic mastectomy for breast cancer in a Midwestern state: a population-based study. Breast Cancer Res Treat 2021. https://doi.org/10.1007/s10549-021-06105-x.

[11] Celaya MO, Rees JR, Gibson JJ, Riddle BL, Greenberg ER. Travel distance and season of diagnosis affect treatment choices for women with early-stage breast cancer in a predominantly rural population (United States). Cancer Causes Control 2006;17:851–6. https://doi.org/10.1007/s10552-006-0025-7.

[12] Bhat S, Orucevic A, Woody C, Heidel RE, Bell JL. Evolving trends and influencing factors in mastectomy decisions. Am Surg 2017;83:233–8. https://doi.org/10.1177/000313481708300317.

[13] Yao K, Winchester DJ, Czechura T, Huo D. Contralateral prophylactic mastectomy and survival: report from the National Cancer Data Base, 1998–2002. Breast Cancer Res Treat 2013;142:465–76. https://doi.org/10.1007/s10549-013-2745-1.

[14] Yu T-J, Liu Y-Y, Hu X, Di G-H. No survival improvement of contralateral prophylactic mastectomy among women with invasive lobular carcinoma: YU ET AL. J Surg Oncol 2018;118:928–35. https://doi.org/10.1002/jso.25221.

[15] Xiong Z, Yang L, Deng G, Huang X, Li X, Xie X, et al. Patterns of occurrence and outcomes of contralateral breast cancer: analysis of SEER data. J Clin Med 2018;7:133. https://doi.org/10.3390/jcm7060133.

[16] Arrington AK, Jarosek SL, Virnig BA, Habermann EB, Tuttle TM. Patient and surgeon characteristics associated with increased use of contralateral prophylactic mastectomy in patients with breast cancer. Ann Surg Oncol 2009;16:2697–704. https://doi.org/10.1245/s10434-009-0641-z.

[17] Reiner AS, John EM, Brooks JD, Lynch CF, Bernstein L, Mellemkjær L, et al. Risk of asynchronous contralateral breast cancer in noncarriers of *BRCA1* and *BRCA2* mutations with a family history of breast cancer: a report from the women's environmental cancer and radiation epidemiology study. J Clin Oncol 2013;31:433–9. https://doi.org/10.1200/JCO.2012.43.2013.

[18] Scheepens JCC, Van't Veer L, Esserman L, Belkora J, Mukhtar RA. Contralateral prophylactic mastectomy: a narrative review of the evidence and acceptability. The Breast 2021;56:61–9. https://doi.org/10.1016/j.breast.2021.02.003.

[19] Yao K, Sisco M, Bedrosian I. Contralateral prophylactic mastectomy: current perspectives. Int. J Womens Health 2016:213. https://doi.org/10.2147/IJWH.S82816.

[20] Pesce C, Jaffe J, Kuchta K, Yao K, Sisco M. Patient-reported outcomes among women with unilateral breast cancer undergoing breast conservation versus single or double mastectomy. Breast Cancer Res Treat 2021;185:359–69. https://doi.org/10.1007/s10549-020-05964-0.

[21] Ward EP, Unkart JT, Bryant A, Murphy J, Blair SL. Influence of distance to hospital and insurance status on the rates of contralateral prophylactic mastectomy, a National Cancer Data Base study. Ann Surg Oncol 2017;24:3038–47. https://doi.org/10.1245/s10434-017-5985-1.

[22] Yi M, Hunt KK, Arun BK, Bedrosian I, Barrera AG, Do K-A, et al. Factors affecting the decision of breast cancer patients to undergo contralateral prophylactic mastectomy. Cancer Prev Res (Phila Pa) 2010;3:1026–34. https://doi.org/10.1158/1940-6207.CAPR-09-0130.

[23] Tuttle TM, Habermann EB, Grund EH, Morris TJ, Virnig BA. Increasing use of contralateral prophylactic mastectomy for breast cancer patients: a trend toward more aggressive surgical treatment. J Clin Oncol 2007;25:5203–9. https://doi.org/10.1200/JCO.2007.12.3141.

[24] Lim DW, Metcalfe KA, Narod SA. Bilateral mastectomy in women with unilateral breast cancer: a review. JAMA Surg 2021;156:569. https://doi.org/10.1001/jamasurg.2020.6664.

[25] Baptiste DF, MacGeorge EL, Venetis MK, Mouton A, Friley LB, Pastor R, et al. Motivations for contralateral prophylactic mastectomy as a function of socioeconomic status. BMC Womens Health 2017;17:10. https://doi.org/10.1186/s12905-017-0366-2.

[26] Fu Y, Zhuang Z, Dewing M, Apple S, Chang H. Predictors for contralateral prophylactic mastectomy in breast cancer patients n.d.

[27] 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;20:3212–7. https://doi.org/10.1245/s10434-013-3116-1.

[28] Miller ME, Czechura T, Martz B, Hall ME, Pesce C, Jaskowiak N, et al. Operative risks associated with contralateral prophylactic mastectomy: a single institution experience. Ann Surg Oncol 2013;20:4113–20. https://doi.org/10.1245/s10434-013-3108-1.

[29] Kuchenbaecker KB, Hopper JL, Barnes DR, Phillips K-A, Mooij TM, Roos-Blom M-J, et al. Risks of breast, ovarian, and contralateral breast cancer for *BRCA1* and *BRCA2* mutation carriers. JAMA 2017;317:2402. https://doi.org/10.1001/jama.2017.7112.

[30] Boughey JC, Attai DJ, Chen SL, Cody HS, Dietz JR, Feldman SM, et al. Contralateral prophylactic mastectomy (CPM) consensus statement from the American Society of Breast Surgeons: data on CPM outcomes and risks. Ann Surg Oncol 2016;23:3100–5. https://doi.org/10.1245/s10434-016-5443-5.

[31] Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet Lond Engl 2005;365:1687–717. https://doi.org/10.1016/S0140-6736(05)66544-0.

[32] King TA, Sakr R, Patil S, Gurevich I, Stempel M, Sampson M, et al. Clinical management factors contribute to the decision for contralateral prophylactic mastectomy. J Clin Oncol 2011;29:2158–64. https://doi.org/10.1200/JCO.2010.29.4041.

[33] Hawley ST, Jagsi R, Morrow M, Janz NK, Hamilton A, Graff JJ, et al. Social and clinical determinants of contralateral prophylactic mastectomy. JAMA Surg 2014;149:582. https://doi.org/10.1001/jamasurg.2013.5689.

[34] Pesce CE, Liederbach E, Czechura T, Winchester DJ, Yao K. Changing surgical trends in young patients with early stage breast cancer, 2003 to 2010: a report from the National Cancer Data Base. J Am Coll Surg 2014;219:19–28. https://doi.org/10.1016/j.jamcollsurg.2014.03.043.

[35] Henderson S. Income, poverty, health insurance coverage, and education in Tennessee's 95 counties. Sycamore Inst 2020;2022:17.

[36] Ramin C, Withrow DR, Davis Lynn BC, Gierach GL, Berrington de González A. Risk of contralateral breast cancer according to first breast cancer characteristics among women in the USA, 1992–2016. Breast Cancer Res 2021;23:24. https://doi.org/10.1186/s13058-021-01400-3.

[37] Nichols HB, de González AB, Lacey JV, Rosenberg PS, Anderson WF. Declining incidence of contralateral breast cancer in the United States from 1975 to 2006. J Clin Oncol 2011;29:1564–9. https://doi.org/10.1200/JCO.2010.32.7395.
[38] Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control 2020;31:403–16. https://doi.org/10.1007/s10552-020-01284-2.
[39] Beatty K, Egen O, Dreyzehner J, Wykoff R. Poverty and health in Tennessee. South Med J 2020;113:1–7. https://doi.org/10.14423/SMJ.0000000000001055.
[40] Clegg DJ, Salomon BJ, Porter CG, Mazonas TW, Heidel RE, Chun JT, et al. The impact of travel distance and income on breast reconstruction after mastectomy in a rural population. Plast Reconstr Surg - Glob Open 2023;11:e4802. https://doi.org/10.1097/GOX.0000000000004802.
[41] Ann Bettencourt B, Schlegel RJ, Talley AE, Molix LA. The breast cancer experience of rural women: a literature review. Psychooncology 2007;16:875–87. https://doi.org/10.1002/pon.1235.
[42] Tran L, Tran P. US urban–rural disparities in breast cancer-screening practices at the national, regional, and state level, 2012–2016. Cancer Causes Control 2019;30:1045–55. https://doi.org/10.1007/s10552-019-01217-8.
[43] Schootman M, Aft R. Rural-urban differences in radiation therapy for ductal carcinoma in-situ of the breast. Breast Cancer Res Treat 2001;68:117–25. https://doi.org/10.1023/A:1011915323038.
[44] Jagsi R, Jiang J, Momoh AO, Alderman A, Giordano SH, Buchholz TA, et al. Trends and variation in use of breast reconstruction in patients with breast cancer undergoing mastectomy in the United States. J Clin Oncol 2014;32:919–26. https://doi.org/10.1200/JCO.2013.52.2284.
[45] Albornoz CR, Bach PB, Mehrara BJ, Disa JJ, Pusic AL, McCarthy CM, et al. A paradigm shift in U.S. breast reconstruction: increasing implant rates. Plast Reconstr Surg 2013;131:15–23. https://doi.org/10.1097/PRS.0b013e3182729cde.
[46] Sawyer JD, Franke J, Scaife S, Sommer NZ, Neumeister MW. Autologous breast reconstruction is associated with lower 90-day readmission rates. Plast Reconstr Surg - Glob Open 2022;10:e4112. https://doi.org/10.1097/GOX.0000000000004112.
[47] Kummerow KL, Du L, Penson DF, Shyr Y, Hooks MA. Nationwide trends in mastectomy for early-stage breast cancer. JAMA Surg 2015;150:9. https://doi.org/10.1001/jamasurg.2014.2895.
[48] Liede A, Cai M, Crouter TF, Niepel D, Callaghan F, Evans DG. Risk-reducing mastectomy rates in the US: a closer examination of the Angelina Jolie effect. Breast Cancer Res Treat 2018;171:435–42. https://doi.org/10.1007/s10549-018-4824-9.
[49] Xie Y, Tang Y, Wehby GL. Federal Health Coverage Mandates and health care utilization: the case of the women's health and cancer rights act and use of breast reconstruction surgery. J Womens Health 2002;2015(24):655–62. https://doi.org/10.1089/jwh.2014.5057.
[50] Broyles JM, Balk EM, Adam GP, Cao W, Bhuma MR, Mehta S, et al. Implant-based versus autologous reconstruction after mastectomy for breast cancer: a systematic review and meta-analysis. Plast Reconstr Surg - Glob Open 2022;10:e4180. https://doi.org/10.1097/GOX.0000000000004180.
[51] Atisha D, Alderman AK, Lowery JC, Kuhn LE, Davis J, Wilkins EG. Prospective analysis of long-term psychosocial outcomes in breast reconstruction: two-year postoperative results from the Michigan breast reconstruction outcomes study. Ann Surg 2008;247:1019–28. https://doi.org/10.1097/SLA.0b013e3181728a5c.
[52] Guyomard V, Leinster S, Wilkinson M. Systematic review of studies of patients' satisfaction with breast reconstruction after mastectomy. The Breast 2007;16:547–67. https://doi.org/10.1016/j.breast.2007.04.004.
[53] Fayanju OM, Stoll CRT, Fowler S, Colditz GA, Margenthaler JA. Contralateral prophylactic mastectomy after unilateral breast cancer: a systematic review and meta-analysis. Ann Surg 2014;260:1000–10. https://doi.org/10.1097/SLA.0000000000000769.
[54] Rebbeck TR, Friebel T, Lynch HT, Neuhausen SL, van't Veer L, Garber JE, et al. Bilateral prophylactic mastectomy reduces breast cancer risk in *BRCA1* and *BRCA2* mutation carriers: the PROSE study group. J Clin Oncol 2004;22:1055–62. https://doi.org/10.1200/JCO.2004.04.188.
[55] Carbine NE, Lostumbo L, Wallace J, Ko H. Risk-reducing mastectomy for the prevention of primary breast cancer. Cochrane Database Syst Rev 2018;2019. https://doi.org/10.1002/14651858.CD002748.pub4.
[56] Gao X, Fisher SG, Emami B. Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: a population-based study. Int J Radiat Oncol 2003;56:1038–45. https://doi.org/10.1016/S0360-3016(03)00203-7.
[57] Giannakeas V, Lim DW, Narod SA. The risk of contralateral breast cancer: a SEER-based analysis. Br J Cancer 2021;125:601–10. https://doi.org/10.1038/s41416-021-01417-7.