HHS Public Access

Author manuscript

JAMA Oncol. Author manuscript; available in PMC 2023 January 20.

Published in final edited form as:

JAMA Oncol. 2023 January 01; 9(1): 143–145. doi:10.1001/jamaoncol.2022.5162.

Receipt of Bilateral Mastectomy Among Women With Hereditary Breast Cancer

Sonya Reid, MD,

Mya L. Roberson, PhD,

Kenna Koehler, MD,

Tiana Shah,

Anne Weidner, MPH,

Jennifer G. Whisenant, PhD,

Tuya Pal, MD

Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, Tennessee (Reid, Roberson, Pal); Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee (Reid, Koehler, Shah, Weidner, Whisenant, Pal); Department of Health Policy, Vanderbilt University School of Medicine, Nashville, Tennessee (Roberson).

The 5% to 10% of breast cancers due to hereditary breast cancer (HBC) genes include pathogenic or likely pathogenic (P/LP) variants in genes with high (eg, *BRCA1*, *BRCA2*, *PALB2*) or moderate (eg, *ATM*, *CHEK2*) penetrance, with lifetime breast cancer risk of more than 40% and 25% to 30%, respectively.[1,2] Risk-reducing mastectomy is a consideration in female *BRCA1*, *BRCA2*, and *PALB2* heterozygotes, in contrast with *ATM* and *CHEK2* heterozygotes, per current national practice guidelines.[3] The objective of this study was to evaluate differences in surgical treatment across high- and moderate-penetrance breast cancer genes with differing clinical recommendations.

Methods |

This case series study was conducted from June 2021 to April 2022. Through the Inherited Cancer Registry (ICARE),[4] a registry of individuals with or at risk for inherited cancer

Corresponding Author: Tuya Pal, MD, Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, 1500 21st Ave S, Ste 2810, Nashville, TN 37212 (tuya.pal@vumc.org).

Author Contributions: Drs Reid and Pal had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Reid, Roberson, Koehler, Pal.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: Reid, Roberson, Koehler, Weidner.
Statistical analysis: Reid, Roberson, Shah, Pal.
Obtained funding: Pal.
Administrative, technical, or material support: Weidner, Whisenant.
Supervision: Reid, Weidner, Pal
Additional Contributions: Lindsay Venton, BSc (Vanderbilt University Medical Center), provided assistance with data collection and curation. She was not compensated beyond her regular employment.

Conflict of Interest Disclosures: Dr Reid reported being a consultant for Novartis, AstraZeneca, and Daiichi Sankyo outside the submitted work. No other disclosures were reported.

predisposition, we identified adult females with invasive breast cancer who had a P/LP variant in *BRCA1*, *BRCA2*, *PALB2*, *ATM*, or *CHEK2*. Participants with stage IV disease at initial diagnosis or with missing surgery data were excluded. Data were collected using surveys and medical records. Type of surgical treatment (lumpectomy, mastectomy, or bilateral mastectomy) and family history of breast cancer were compared across the 5 genes using χ^2 tests. Genetic testing was categorized as done before surgery (year of surgery or earlier) or after surgery. Crude and multivariable adjusted logistic regression was used to assess factors associated with receipt of bilateral mastectomy. Models to calculate the adjusted odds ratio (AOR) included age (<50 years, ≥50 years), timing of genetic testing, family history of breast cancer, and gene. Data were analyzed using SAS Studio, version 9.4; 2-sided $P < .05$ was significant. The study was approved by Vanderbilt University; participants provided written informed consent. We followed the reporting guideline for case series.

Results |

We identified 684 adult females with breast cancer and a confirmed P/LP variant in *BRCA1* (235 participants), *BRCA2* (217), *PALB2* (121), *ATM* (50), or *CHEK2* (61) in the ICARE registry who met inclusion criteria. Mean age at diagnosis was 53 years (range, 23–83 years.) Participants were predominantly White (623 [91%]), college educated (396 of 580 with available data [68%]), and privately insured (455 [67%]). Family history of breast cancer was similar across all 5 genes (Table 1), with no association between receipt of bilateral mastectomy and family history of breast cancer (Table 2). Bilateral mastectomy was associated with breast cancer diagnosed before age 50 years (AOR, 2.21; 95% CI, 1.44–3.40) and genetic testing before surgery (AOR, 5.79; 95% CI, 3.83–8.76). There were no significant differences in bilateral mastectomy rates across participants with *BRCA1* (42%), *BRCA2* (44%), *PALB2* (45%), *ATM* (55%) and *CHEK2* (43%) P/LP variants ($P = .73$; Table 1) or in participants with P/LP variants in high-penetrance (*BRCA1*, *BRCA2*, *PALB2*) vs moderate-penetrance (*ATM*, *CHEK2*) genes (191 of 573 participants [33%] vs 40 of 111 [36%]; $P = .47$). Multivariate logistic regression analysis revealed no association between receipt of bilateral mastectomy and the gene in which the P/LP variant was detected, after adjustment for potential confounders (Table 2).

Discussion |

Our findings indicated similar rates of bilateral mastectomy across high- and moderate-penetrance genes. These results are consistent with findings from single-institution and state cancer registry studies that reported identification of P/LP variants in both high- and moderate-penetrance genes was associated with risk-reducing mastectomy.[5,6] Although we included a large sample of participants with HBC P/LP variants and robust survey and medical records data, a limitation of our study is that the results may underestimate true deviation of care from practice guidelines, given that our study sample chose to participate in a registry study. It remains important to evaluate this information across diverse populations and health care settings. Similar rates of bilateral mastectomy across all 5 genes of varied penetrance are concerning, given that prophylactic contralateral mastectomy for risk reduction is considered only for high-penetrance genes, per national practice guidelines.

These findings warrant further evaluation to explore possible overtreatment among patients with breast cancer who have *ATM* and *CHEK2* P/LP variants.

Funding/Support:

This study was supported by grant 2K12CA090625-22A1 from the National Cancer Institute, National Institutes of Health (Dr Reid), grant SAC210105 from the Susan G. Komen Foundation (Dr Pal), and a Career Development Award (2021CDA-540627204) from the American Society of Clinical Oncology (Dr Reid).

Role of the Funder/Sponsor:

The funders 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.

References

1. Dorling L, Carvalho S, Allen J, et al. ; Breast Cancer Association Consortium. Breast cancer risk genes—association analysis in more than 113,000 women. N Engl J Med. 2021;384(5):428–439. doi:10.1056/NEJMoa1913948 [PubMed: 33471991]
2. Hu C, Hart SN, Gnanaolivu R, et al. A population-based study of genes previously implicated in breast cancer. N Engl J Med. 2021;384(5):440–451. doi: 10.1056/NEJMoa2005936 [PubMed: 33471974]
3. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 1.2023. National Comprehensive Cancer Network; September 7, 2022. Accessed June 24, 2022. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf
4. Pal T, Radford C, Weidner A, Tezak AL, Cragun D, Wiesner GL. The Inherited Cancer Registry (ICARE) initiative: an academic-community partnership for patients and providers. Oncology Issues. 2018;33(6):54–63. doi:10.1080/10463356.2018.1525993
5. Dettwyler SA, Thull DL, McAuliffe PF, et al. Timely cancer genetic counseling and testing for young women with breast cancer: impact on surgical decision-making for contralateral risk-reducing mastectomy. Breast Cancer Res Treat. 2022;194(2):393–401. doi:10.1007/s10549-022-06619-y [PubMed: 35596825]
6. Bergstrom C, Pence C, Berg J, et al. Clinicopathological features and outcomes in individuals with breast cancer and ATM, CHEK2, or PALB2 mutations. Ann Surg Oncol. 2021;28(6):3383–3393. doi:10.1245/s10434-020-09158-2 [PubMed: 32996020]

Table 1.

Characteristics of the Study Population

	Gene with variant, No. (%) of participants						
Characteristic	**All (N = 684)**	***BRCA1* (n = 235)**	***BRCA2* (n = 217)**	***PALB2* (n = 121)**	***ATM* (n = 50)**	***CHEK2* (n = 61)**	***P* value**
Age at first breast cancer diagnosis, mean (range), y	53 (23–83)	50 (23–74)	54 (27–82)	54 (23–83)	58 (36–76)	57 (28–77)	NA
Race and ethnicity[a]							
Asian	4 (1)	1 (0)	1 (1)	2 (2)	0	0	.47
Black	32 (5)	16 (7)	9 (4)	6 (5)	1 (2)	0	
White	623 (91)	210 (89)	203 (94)	106 (88)	46 (92)	58 (95)	
Other	3 (0)	1 (0)	1 (1)	1 (1)	0	0	
Unknown	22 (3)	7 (3)	3 (1)	6 (5)	3 (6)	3 (5)	
First breast cancer surgery							
Lumpectomy	203/524 (39)	72/182 (40)	60/167 (36)	37/91 (41)	10/31 (32)	24/53 (45)	.73
Mastectomy	90/524 (17)	33/182 (18)	34/167 (20)	13/91 (14)	4/31 (13)	6/53 (11)	
Bilateral mastectomy	231/524 (44)	77/182 (42)	73/167 (44)	41/91 (45)	17/31 (55)	23/53 (43)	
Data missing	160/684 (23)	53/235 (23)	50/217 (23)	30/121 (25)	19/50 (38)	8/61 (13)	
Received radiotherapy	260 (38)	95 (40)	79 (36)	48 (40)	14 (28)	24 (39)	.60
Relatives with breast cancer[b]							
family history	122 (18)	39 (17)	32 (15)	27 (22)	9 (18)	15 (25)	.46
First degree	321 (47)	105 (45)	114 (53)	52 (43)	26 (52)	24 (39)	
Second degree	189 (28)	69 (29)	58 (27)	35 (29)	12 (24)	15 (25)	
Third degree	52 (8)	22 (9)	13 (6)	7 (6)	3 (6)	7 (11)	

[a]Self-reported on the survey. The Inherited Cancer Registry is open to individuals of all races and ethnicities; these data were included to show the demographic characteristics of the study population. The 3 participants who selected “Other” were prompted to write their race in a text box and indicated Eastern Indian, Mestizo, and Pakistani.

[b]Categorized into 4 mutually exclusive categories based on the closest relative with a history of breast cancer: (1) at least 1 first-degree relative, (2) at least 1 second-degree relative, (3) at least 1 third-degree relative, and (4) no first-, second-, or third-degree relatives (ie, no family history).

Table 2.

Multivariate Logistic Regression for Bilateral Mastectomy

	OR (95% CI)	
Variable	**Unadjusted**	**Adjusted**
Age at first breast cancer diagnosis, y		
<50	2.97 (2.03–4.35)	2.21 (1.44–3.40)
≥50	1 [Reference]	1 [Reference]
Timing of genetic testing		
Before surgery	6.65 (4.45–9.92)	5.79 (3.83–8.76)
After surgery	1 [Reference]	1 [Reference]
Family history of breast cancer		
No family history	1 [Reference]	1 [Reference]
First-degree relative	0.89 (0.53–1.48)	1.03 (0.57–1.87)
Second-degree relative	1.05 (0.59–1.84)	0.99 (0.52–1.88)
Third-degree relative	0.58 (0.26–1.28)	0.63 (0.25–1.56)
Gene with variant		
BRCA1 or *BRCA2*	1 [Reference]	1 [Reference]
ATM	1.45 (0.66–3.18)	1.62 (0.66–3.95)
CHEK2	0.97 (0.53–1.78)	1.23 (0.63–2.42)
PALB2	1.03 (0.63–1.67)	1.32 (0.76–2.29)

Abbreviation: OR, odds ratio.