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Surgical Decision Making and Management of CHEK2 and PALB2 Breast Cancer Mutation Carriers

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ABSTRACT

Background: Next-generation genetic sequencing has increasingly identified carriers of breast cancer susceptibility genes *CHEK2* and *PALB2*. Despite the growing population of non-*BRCA* mutation carriers, literature on surgical decision-making in this cohort remains limited.

Methods: A retrospective cross-sectional study was conducted on patients diagnosed with *CHEK2* or *PALB2* genetic mutations between 2016 and 2024 at a breast clinic at a tertiary-care hospital. Demographics, surgical interventions, and complications were analyzed.

Results: Of over 4000 patients who were tested for a full breast cancer genetic panel, 132 *CHEK2* and/or *PALB2* positive patients were included. Overall, 74.2% had a personal history of breast cancer, and 25.8% were tested as part of screening. Genetic diagnosis awareness significantly impacted surgical choices, with 36.7% of patients aware of their diagnosis choosing a mastectomy over breast-conserving therapy, compared to 15.7% of patients unaware of their diagnosis. There was a 23.0% conversion rate from BCT to mastectomy. Also, 12 patients had autologous breast reconstruction and 28 had implant-based reconstruction. The major complication rate was 7.5%, and the minor complication rate was 12.5%.

Conclusion: Patients with *CHEK2* or *PALB2* genetic diagnoses have a lifetime breast cancer risk of up to 40%, high rates of cancer recurrence, and are 6 times more likely to convert to a mastectomy after BCT compared to the general population. It is imperative that *CHEK2*/*PALB2* carriers are informed about all surgical options—including contralateral prophylactic mastectomy, bilateral risk-reducing mastectomy, and breast reconstruction. Breast reconstruction is safe in this patient population, and early consultations are important for optimizing reconstructive outcomes.

INTRODUCTION

Breast cancer is the leading cause of cancer-related death for women in the United States and Europe. The prevalence of breast cancer in the United States is increasing, with over 260,000 new cases diagnosed and over 42,000 women dying from the disease each year.[1] About 5% to 10% of new breast cancer diagnoses can be attributed to a pathogenic variation (PV) in a breast cancer susceptibility gene.[2,3] Genetic testing for high-penetrance breast cancer predisposition genes, including *BRCA1/2*, has become the standard of care in patients with breast cancer. Breast cancer genetic testing has a significant impact on clinical decision making, with one study

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showing greater than 70% of *BRCA* mutation carriers altering their surgical plan after genetic diagnosis.[4]

New advances in genetic testing, such as next-generation sequencing, have allowed patients to be screened with multigene panels for a variety of known breast cancer susceptibility genes of varying degrees of penetrance. As these tests become commercially available and genetic testing is increasingly utilized for patients with a personal and/or family history of breast cancer, the population of patients diagnosed with non-*BRCA* breast cancer susceptibility genes has been increasing. Checkpoint Kinase 2 (*CHEK2*) and Partner and Localizer of *BRCA2* (*PALB2*) are 2 important breast cancer genes associated with DNA repair.

CHEK2 is considered a moderate penetrance breast susceptibility gene. Multiple mutations have been found in *CHEK2*, conferring an overall breast cancer risk of 20% to 40% and a 10-year cumulative contralateral breast cancer risk of 6% to 8% according to the latest 2024 National Comprehensive Cancer Network (NCCN) guidelines version 3.[5] The best characterized mutation within the *CHEK2* gene, the *CHEK2**1100delC mutation, confers a higher risk of breast cancer, earlier metastatic spread, and worse distant metastasis-free survival and disease-free survival. Women with *CHEK2* pathogenic variants are recommended to begin annual breast MRIs as early as age 30–35, adding yearly mammograms at age 40. Risk-reducing surgery remains an individualized choice influenced by family history.[10]

PALB2, a tumor suppressor gene interacting with both *BRCA1/2*, was previously classified as moderate risk, but is now recognized as a high-penetrant gene, with a 44-63% lifetime breast cancer risk and a 10-year contralateral risk of 5-8%.[11,14] The American College of Medical Genetics and Genomics (ACMG) recommends *BRCA1/2*-equivalent surveillance for *PALB2* heterozygotes, with consideration of risk-reducing mastectomy based on personalized risk assessment.[15] NCCN guidelines recommend annual breast MRI and mammogram starting at 30 for *PALB2* carriers, compared to *BRCA1/2* carriers, who begin MRI at 25 and add mammography at 30.[5]

As non-*BRCA1/2* breast cancer susceptibility genes become better characterized and testing becomes more accessible, patients diagnosed with germline mutations in these breast cancer susceptibility genes represent a growing part of the breast cancer patient population for all members of the treatment team. However, we lack important information regarding decision-making for oncologic surgery and breast reconstruction in this patient population. In this study of patients diagnosed with a *PALB2* or *CHEK2* mutation at our institution, we aim to understand and highlight specific considerations for surgical treatment and reconstruction of this particular group of breast cancer patients. It is important to understand the nuances of these patients' risk profile and outcomes such that all members of the multidisciplinary team—including geneticists and genetic counselors, medical oncologists, breast surgeons, and plastic surgeons—may effectively and specifically counsel these patients to their unique needs.

METHODS

Patient Identification and Retrospective Review

Patients were selected using a convenience sampling approach. The head of the hereditary breast clinic at Weill Cornell Medicine, a board-certified cancer genetic counselor, queried all patients tested for non-syndromic cancer genes between 2016 and 2024 and identified patients positive for *CHEK2* and/or *PALB2* mutations. Patients were tested by one of the following genetic labs: Invitae, Counsyl, Ambry, Myriad, and GeneDx. All these labs tested for genes associated with breast cancer predisposition, including *BRCA1/2*, *CHEK2*, *PALB2*, and others.

Electronic medical records were retrospectively reviewed for patients' demographics, medical history, family history, and oncologic history. Surgical and medical treatments, including the postoperative course and follow-up, were recorded. Postoperative complications reviewed included infection, skin necrosis, dehiscence, bleeding/hematoma, seroma, and flap congestion. These were classified as major if they necessitated an operative intervention or minor if they were treated nonoperatively.

Male patients were excluded from the analysis. While *CHEK2* and *PALB2* mutations increase breast cancer risk in men, their absolute risk remains significantly lower than that of female carriers. Surgical considerations in male breast cancer patients differ from those in female patients, and current guidelines for male carriers are less well-defined. Additionally, patients who pursued treatment at a different institution and patients lost to follow-up were excluded. In screening patients opting for high-risk surveillance, follow-up was based on NCCN imaging guidelines.[5] Patients with and without breast cancer who underwent surgery had standard follow-up care with their breast and/or plastic surgeon(s) postoperatively. All reporting followed the Committee on Publication Ethics (COPE) guidelines.[16]

Statistical Analysis

The `tableone` package of R statistical software version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. Fisher exact tests were used to compare

categorical variables, *t* tests were used to compare normally distributed continuous variables, and Wilcoxon rank-sum tests were used to compare non-normally distributed continuous variables. A predetermined alpha level of 0.05 was used as the criterion for statistical significance.

RESULTS

Between 2016 and 2024, over 4000 patients were tested by a full breast cancer genetic panel at a breast clinic at a large, tertiary-care hospital in New York City, where 121 patients tested positive for a *CHEK2* mutation, and 30 patients tested positive for a *PALB2* mutation. One patient tested positive for a mutation in both of these genes. Twenty patients were excluded from this study: 2 male patients and 18 female patients who were lost to follow-up or pursued care at another institution (Figure 1).

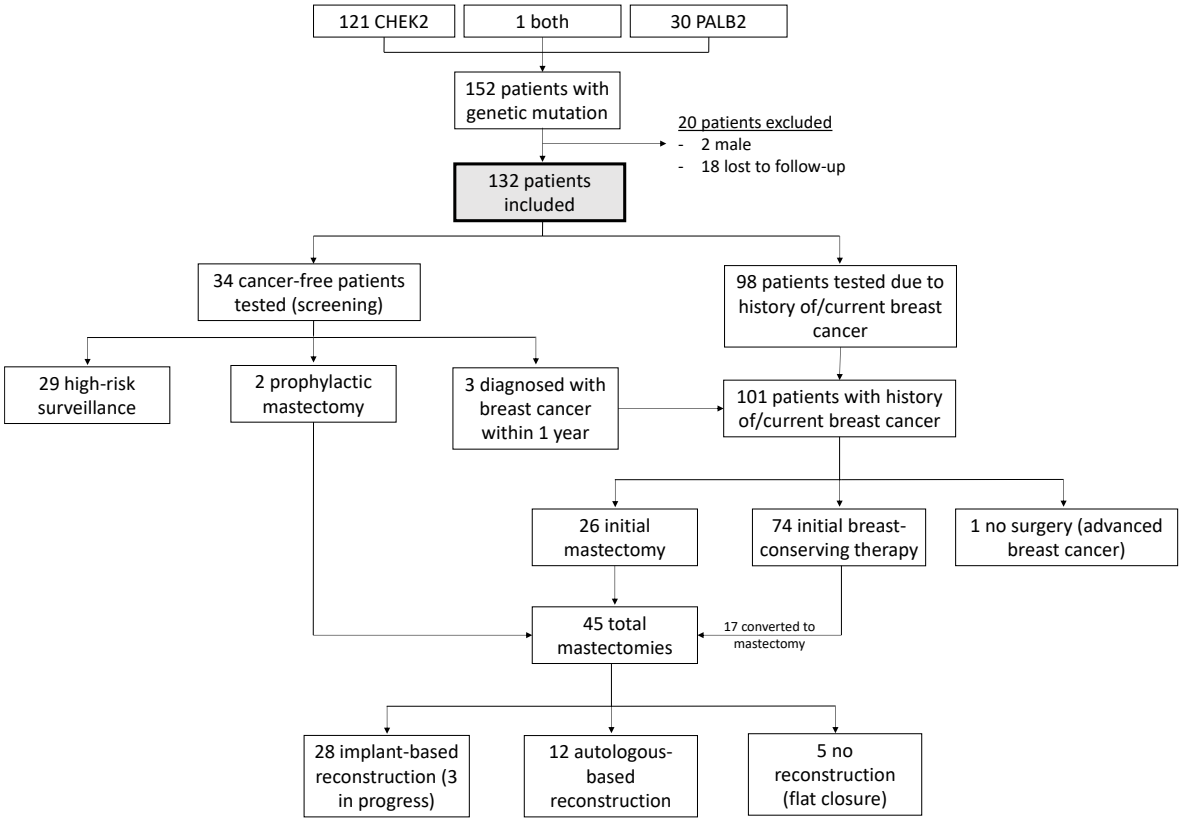

Figure 1. Flow Chart of Study Selection, Oncologic Status, and Surgical Decision-Making

Of 132 patients included in this study, the median age of *CHEK2* and/or *PALB2* PV diagnosis was 57 (IQR, 24.5–26) years old. At the time of the genetic diagnosis, 77 (72.6%) of *CHEK2* patients and 21 (80.8%) of PALB2 patients had a history or current diagnosis of breast cancer or a breast tumor, while the remainder were tested as part of screening (Table 1).

Table 1. Patient Cohort Genetic Mutation Details

Patient characteristics	Total	*CHEK2*	*PALB2*
Total patients included, n	132	106	26
Age at genetic diagnosis, y (median [IQR])	57 [45–69]	57 [44.25–68.75]	57 [46.75–72.75]
Reason for genetic testing			
History of, or current, breast cancer diagnosis, n (%)	98 (74.2)	77 (72.6)	21 (80.8)
Screening, n (%)	34 (25.8)	29 (27.4)	5 (19.2)
Genetic mutation			
CHEK2, n (%)	106 (80.3)		
PALB2, n (%)	26 (19.7)		

Descriptive statistics are reported as frequencies and percentages for categorical variables and as median with interquartile range (IQR) for non-normally distributed continuous variables.

Patients who were tested as part of screening were considerably younger compared to patients with a personal history of cancer (47 [IQR, 22] vs 59 [IQR, 22.75]; P=0.001).

Of 34 patients who were tested as part of screening, one had ductal carcinoma in situ (DCIS) detected by a breast MRI due to the specific clinical recommendation given after her genetic diagnosis. Two additional patients were diagnosed with breast cancer within one year of getting their genetic test results. Two cancer-free patients opted for prophylactic bilateral mastectomies, and the remainder of the patients opted for high-risk breast surveillance following NCCN imaging guidelines.[5]

Seventy-eight patients tested due to a new diagnosis of breast cancer (first or recurrent) received their genetic diagnosis a median of 35.5 (IQR: 48.5) days after their new cancer diagnosis. Also, 19 patients were in remission and having updated testing, receiving their genetic diagnosis a median of 2159 (IQR: 5546.5) days after their prior breast cancer diagnosis.

Characteristics of the 101 patients with breast cancer—including cases diagnosed after genetic testing—are presented in Table 2.

All patients with breast cancer—except one with advanced-stage cancer—had surgery. In addition, 74 (73.3%) patients initially underwent breast-conserving therapy (BCT), and 26 (25.7%) patients underwent complete mastectomy. Details of surgical lymph node management are summarized in Table 3.

Seventeen patients who initially underwent BCT (23.0%) converted to a complete mastectomy a median of 281 days (IQR, 1496) after their BCT: 12 had a cancer recurrence, 2 changed their minds after learning of their genetic diagnosis, 1 decided she did not want to undergo radiotherapy, and 2 had narrow margins on the lumpectomy specimen (Table 4). Of patients who had a cancer recurrence, completion mastectomy occurred a median of 735 days (IQR, 1606) after initial BCT.

Fifty-five (74.3%) patients with initial BCT also had neoadjuvant or adjuvant radiation therapy to the breast, while only 9 (34.6%) patients with mastectomy received concurrent radiation. Recurrence rates were expectedly higher in BCT patients (23.3%) compared to mastectomy patients (7.7%).

Table 2. Cancer Characteristics in *CHEK2*/*PALB2*+ Variants

Patient characteristics	Total
Total patients with breast cancer, n	101
Age of first breast cancer diagnosis, y (median [IQR])	59 [48–71]
Type of cancer	
DCIS, n (%)	13 (12.9)
IDC, n (%)	64 (63.4)
ILC, n (%)	11 (10.9)
IDC and ILC, n (%)	6 (5.9)
Inflammatory, n (%)	2 (2.0)
Mucinous, n (%)	1 (1.0)
Phyllodes, n (%)	1 (1.0)
N/A, n (%)	3 (3.0)
Clinical stage	
0, n (%)	13 (12.9)
I, n (%)	60 (59.4)
II, n (%)	17 (16.8)
III, n (%)	7 (6.9)
IV, n (%)	3 (3.0)
N/A, n (%)	1 (1.0)
Tumor size, cm (median [IQR])	1.32 [0.70–2.02]
Nodal Status	
Positive lymph nodes, n (%)	77 (76.2)
At least 1 positive lymph node, n (%)	24 (23.8)
Laterality	
Unilateral, n (%)	88 (87.1)
Bilateral, n (%)	13 (12.9)
Oncologic Treatment	
Neoadjuvant chemotherapy, n (%)	17 (16.8)
Adjuvant chemotherapy, n (%)	28 (27.7)
Neoadjuvant radiotherapy, n (%)	7 (6.9)
Adjuvant radiotherapy, n (%)	59 (58.4)
Hormone therapy, n (%)	66 (65.3)
Initial Surgical Treatment	
Breast-conserving therapy, n (%)	74 (73.3)
Mastectomy, n (%)	26 (25.7)
No surgery, n (%)	1 (1.0)

Descriptive statistics are reported as frequencies and percentages for categorical variables and as median with IQR for non-normally distributed continuous variables. DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IQR, interquartile range; N/A, not applicable.

Table 3. Lymph Node Management in Patients With Early-Stage and Late-Stage Breast Cancer

	Early-stage cancer (n=90)	Late-stage cancer (n=10)
Node management		
Sentinel lymph node biopsy, n (%)	77 (85.6)	9 (90.0)
Axillary dissection, n (%)	5 (5.6)	7 (70.0)
No nodal surgery/no nodes identified, n (%)	12 (13.3)	1 (10.0)
Nodal status, if tested		
No positive lymph nodes, n (%)	62 (79.4)	0 (0.0)
At least 1 positive lymph node, n (%)	16 (17.6)	9 (100.0)

Descriptive statistics are reported as frequencies and percentages for categorical variables.

Table 4. First-Line Surgical Intervention

Patient characteristics	Breast-conserving therapy (n=74)	Complete mastectomy (n=26)	P-value
Age at first oncologic surgery, y (median [IQR])	59 [46.5–69]	54.5 [43–65]	0.089
Knew of genetic diagnosis before surgery, n (%)	31 (41.9)	18 (69.2)	0.030
Radiation therapy, n (%)	55 (74.3)	9 (34.6)	0.001
Follow-up			
Breast cancer recurrence, n (%)	17 (23.3)	2 (7.7)	0.149
Eventual mastectomy,n (%)	17 (23.0)	N/A	
Total number of lumpectomies, mean (SD)	1.23 (SD 0.45)	N/A	

Categorical variables are reported as frequencies and percentages with Fisher's exact tests for statistical comparison. Normally distributed continuous variables are reported as mean with standard deviation, with *t-tests* for statistical comparison. Non-normally distributed continuous variables are reported as median with IQR, with Wilcoxon signed-rank tests for statistical comparison. IQR, interquartile range; N/A, not applicable; SD, standard deviation.

One unilateral mastectomy patient had another breast cancer occurrence in the contralateral breast, and one bilateral mastectomy patient had a recurrence in the chest wall.

At the time of their first surgery, 51 patients (51%) were unaware of their genetic diagnosis, and 49 patients (49%) knew about their genetic diagnosis, determined by a positive result and chart documentation that it was communicated to the patient. Patients who were aware of their genetic diagnosis were more likely to choose a mastectomy as their first-line surgical option than BCT (36.7% vs 15.7%, P=0.030). Additionally, patients who were unaware were more likely to convert from BCT to a complete mastectomy later, either during a subsequent breast cancer occurrence or prophylactically (29.6% vs 4.1%, P=0.002). These patients also underwent more lumpectomies compared to patients who did not know their diagnosis (1.16 [SD, 0.67] vs 0.67 [SD, 0.55]; P<0.001) (Table 5). In this study, 45 patients underwent a mastectomy: 10 unilateral (22.2%) and 35 bilateral (77.8%). Five women had a flat closure, 28 had implant-based breast reconstruction, and 12 had autologous breast reconstruction. Among autologous cases, one deep inferior epigastric perforator (DIEP) flap required reoperation for hematoma, and another developed infection with skin necrosis and dehiscence, necessitating washout. Minor complications included non-operative seromas and wound-healing issues, which were treated with local wound care. Among implant-based cases, one required washout and tissue expander removal for infected seroma; minor complications included partial-thickness skin necrosis and nonoperative hematoma. Three patients with planned alloplastic reconstruction were undergoing adjuvant chemoradiotherapy with tissue expanders inserted, with no complications at the latest follow-up appointment (Table 6).

Table 5. Decision Making With and Without Genetic Diagnosis

Diagnosis	Unaware of genetics (n=51)	Knew genetic diagnosis (n=49)	P-value
Initial surgical intervention			0.030
Mastectomy, n (%)	8 (15.7)	18 (36.7)	
Breast-conserving treatment, n (%)	43 (84.3)	31 (63.3)	
Total number of lumpectomies, mean (SD)	1.16 (0.67)	0.67 (0.55)	<0.001
Lumpectomy → Mastectomy, n (%)	15 (29.4)	2 (4.1)	0.002

Note: Categorical variables are reported as frequencies and percentages with Fisher exact tests for statistical comparison. Normally distributed continuous variables are reported as mean with standard deviation with t-tests for statistical comparison.

DISCUSSION

Breast cancer genetics is a rapidly changing field; with improving affordability, accessibility, and turnaround times of multigene sequencing, more patients are learning of their carrier status of non-*BRCA1/2* breast cancer susceptibility genes. Non-*BRCA1/2* pathogenic variants have been identified in 2-3% of women with breast cancer and in approximately 1% of the general population. In comparison, *BRCA1/2* mutations occur in 5-10% of women with breast cancer, 0.2% of the general population, and 2.5% of the general Ashkenazi Jewish population.[17,18]

Identification of these mutations, along with increased molecular-based and population-based studies, has allowed for a greater understanding of the specific risk profiles of PV carriers. Carriers of mutations in *CHEK2* are now understood to have an

overall breast cancer risk of up to 40%, with a contralateral breast cancer risk of 6% to 8%. *PALB2* mutations confer an overall breast cancer risk up to 60% and a contralateral breast cancer risk of 5% to 8%.[18,19] Recommendations for breast cancer screening in *CHEK2* and *PALB2* PV carriers have recently been updated to recommend the start of screening at age 30 for *PALB2* PV carriers and 30-35 for *CHEK2* PV carriers, in contrast to *BRCA1/2* carriers, who begin screening at 25.[5] As more patients are diagnosed as PV carriers and greater information is known about cancers driven by these variants, it becomes imperative to define appropriate management of these patients.

Table 6. Reconstruction Details and Complications

Patient characteristics	Alloplastic (n=28)	Autologous (n=12)
Age at surgery, y (median [IQR])	51.50 [42.75–66.25]	54.50 [34.25–59]
BMI (median [IQR])	23.56 [21.55–26.59]	26.24 [24.47–31.31]
Medical history		
Hypertension, n (%)	6 (21.4)	1 (8.3)
Hyperlipidemia, n (%)	5 (17.9)	1 (8.3)
Diabetes, n (%)	0 (0.0)	0 (0.0)
Smoking history		
Active, n (%)	2 (7.1)	0 (0.0)
Former, n (%)	5 (17.9)	2 (16.7)
Bilateral reconstruction, n (%)	25 (89.3)	8 (66.7)
Major Complications		
Infection, n (%)	1 (3.6)	1 (8.3)
Skin necrosis, n (%)	1 (3.6)	1 (8.3)
Dehiscence, n (%)	0 (0.0)	1 (8.3)
Bleeding/hematoma, n (%)	0 (0.0)	1 (8.3)
Seroma, n (%)	1 (3.6)	0 (0.0)
Flap congestion, n (%)	N/A	0 (0.0)
Minor Complications		
Infection, n (%)	1 (3.6)	0 (0.0)
Skin necrosis, n (%)	1 (3.6)	1 (8.3)
Dehiscence, n (%)	0 (0.0)	0 (0.0)
Bleeding/hematoma, n (%)	1 (3.6)	0 (0.0)
Seroma, n (%)	0 (0.0)	2 (16.7)
Flap congestion, n (%)	N/A	0 (0.0)

Descriptive statistics are reported as frequencies and percentages for categorical variables, as mean with standard deviation for normally distributed continuous variables, and as median with IQR for non-normally distributed variables. BMI, body mass index; N/A, not applicable.

In our study of 132 patients diagnosed with *CHEK2* or *PALB2* PVs, most patients received genetic testing in the setting of prior or current breast cancer. Patients who had genetic testing as part of screening were younger than those who had breast cancer. With greater availability of multigene testing, this subset of younger, high-risk women represents the greatest potential influx of new patients seeking medical guidance on appropriate follow-up and management. Only two unaffected patients in our cohort sought to undergo prophylactic bilateral mastectomy and reconstruction after their genetic diagnosis, but 3 patients (8.8%) received new breast cancer diagnoses within one year of genetic diagnosis, highlighting the elevated risk of these PVs. This highlights the urgency of early discussions about risk-reducing options for these high-risk patients.

The decision to undergo risk-reducing mastectomies is multifaceted and patient-specific, influenced not only by an individual's cancer risk but also by personal, psychological, and social factors. Patients often weigh concerns of sexuality, body image, and quality of life against perceived cancer risk. Moreover, risks of surgery must be considered against potential psychological distress and anxiety associated with high-risk surveillance programs.[20] Early and frequent engagements with oncologic and reconstructive surgeons are essential in helping patients make informed decisions. Patients opting for surveillance undergo yearly imaging, which provides regular opportunities to revisit discussions about

surgical risk reduction. These annual touchpoints allow providers to reassess a patient's evolving risk perception and reinforce education on surgical and reconstructive outcomes.

Awareness of genetic status notably impacts patients' surgical decisions. Our data showed individuals informed of their mutation status opted for more definitive surgical measures, akin to the decision-making trajectory observed in carriers of known *BRCA1/2* mutations.[3,4] Patients aware of their mutation status more often chose mastectomy as their initial surgical approach compared to those unaware of their mutation status, who underwent significantly more lumpectomies. The conversion rate from BCT to mastectomy was also significantly higher among patients unaware of their mutation status. The overall conversion rate from BCT to mastectomy in this cohort was 23.0%, nearly 6 times higher than the general breast cancer population, with conversion rates of 4%.[21] Many of these conversions were secondary to breast cancer recurrences. Breast cancer recurrences occurred in about one-fourth of the patients who did not have completion surgery, including one patient who had a unilateral mastectomy for her initial breast cancer occurrence, who later developed breast cancer in the contralateral breast. As more is understood about the risks of breast cancer occurrence and recurrence in this population, it is imperative to engage carriers in a comprehensive discussion about all surgical options—including contralateral prophylactic mastectomy and bilateral risk-reducing mastectomy—upfront.[21]

For those considering reconstruction, early consultation optimizes planning, particularly in cases where prior lumpectomy or radiation may affect reconstructive options. While radiation plays a pivotal role in breast cancer treatment, irradiated patients are at a greater risk of mastectomy flap skin necrosis and reconstruction complications.[22,23] Even if they are leaning toward BCT, patients should be informed about the potential impacts of radiation on the aesthetic and functional results of reconstructive surgery, due to the significant proportion of these patients who later need salvage mastectomy. These early, big-picture discussions may help with patients' surgical decision-making.

Advances in breast surgery and reconstructive surgery have made nipple-sparing and skin-sparing mastectomies with alloplastic or autologous breast reconstruction safe, reproducible, and with good patient satisfaction. Of 40 patients in our cohort with postmastectomy reconstruction, major complications were rare and successfully managed with a return to the operating room or an in-clinic washout. Minor complications, such as seromas and wound-healing issues, were also uncommon and managed non-operatively. Given the safety and viability of postmastectomy reconstruction for PV carriers, prompt referral for plastic surgery consultation at the time of diagnosis is an important step in the care pathway for *CHEK2* or *PALB2* PV carriers.

The incidence of positive sentinel lymph node biopsies in our early-stage patients brings forth the question of the utility of routine sentinel lymph node biopsies in PV carriers. Routine sentinel lymph node biopsy in clinically node-negative stage I and early-stage II invasive breast cancer is widely practiced, but its use in non-invasive breast cancer or during prophylactic mastectomies is controversial.[24] While there are no formal recommendations for this patient population, a pathologic study by the Breast Cancer Association Consortium found that tumors associated with PVs in *BRCA2*, *CHEK2*, and *PALB2* were associated with lymph node involvement, even after adjusting for intrinsic tumor subtypes.[7] Based on this data, the routine use of sentinel lymph node biopsy is our preferred management of patients with known *CHEK2* or *PALB2* mutations and early-stage breast cancer, whether invasive or not. Data remains limited regarding occult invasive malignancy during risk-reducing mastectomies for patients with non-*BRCA* PVs, but knowing that these PVs are associated with tumors of higher grade, higher stage at diagnosis, and lymph node involvement, it is reasonable to also biopsy the sentinel nodes at the time of a risk-reducing mastectomy.

Limitations

As a single-center, retrospective cross-sectional study, our findings may have limited generalizability and causal inference. Additionally, our sample size, particularly for *PALB2* mutation carriers, was relatively small. We grouped carriers of *CHEK2* and *PALB2* together, which may mask potential differences in cancer characteristics or decision-making between carriers of the two mutations. Larger-scale studies are needed to validate our results and provide a more comprehensive understanding of the surgical and oncological outcomes for this population.

CONCLUSION

Patients with *CHEK2* or *PALB2* genetic diagnoses have a lifetime breast cancer risk of up to 40%, high rates of cancer recurrence, and are 6 times more likely to convert to a full mastectomy after a lumpectomy compared to the general population. It is imperative that *CHEK2*/*PALB2* carriers are informed about all surgical options, including contralateral prophylactic mastectomy and bilateral risk-reducing mastectomy. Breast reconstruction is safe in this

patient population, and early consultations are important for optimizing reconstructive outcomes.

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None

CONFLICTS OF INTEREST
The authors do not have any conflicts of interest to report.

ETHICAL CONSIDERATIONS
This study was approved by the Weill Cornell Medicine Institutional Review Board (IRB #23-07026281) with waiver of patient consent for research of existing data/records. All research methods complied with the Declaration of Helsinki.

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DATA AVAILABILITY
The data for this article is available upon reasonable request.

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