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Breast Cancer Occurrence After Risk-reducing Mastectomies in 274 Cases: A Single Center With More Than 42 Years of Experience

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Introduction: Carriers of genetic mutations with a high risk of developing breast cancer have a lifetime risk of this cancer of up to 70%. To reduce the risk, patients have the option of a risk-reducing mastectomy. There is limited data with only short follow-ups on its safety. The aim of the study was to determine the long-term incidence of breast cancer in healthy patients with no previous surgery, who underwent bilateral risk-reducing mastectomies (BRRMs).

Methods: We retrospectively reviewed 274 patients from our facility with no previous breast surgery, who underwent BRRM from 1981 to 2022, due to genetic mutations, a strong family history, or having very dense mammary glands. We approached these patients during their checkups, by phone call or email, and we asked them if they had developed breast cancer after their procedures. We recorded the patients' demographic factors, their genetic mutation types, and the mastectomy methods carried out.

Results: A total of 274 patients had BRRMs with a mean follow-up after 76 months; 208 patients had undergone nipple-sparing mastectomies, 39 patients had undergone skin-sparing mastectomies, and 27 patients had skin-reducing mastectomies. One BRCA1+ patient developed breast cancer 21 months after undergoing the risk-reducing skin-sparing mastectomy procedure. None of the patients died of breast cancer.

Conclusions: The incidence of breast cancer in the monitored patients is comparable to the results of the other related studies. The study result confirms that risk-reducing mastectomies reduce the risk of breast cancer in high-risk populations, regardless of the type of mastectomy performed. *(Plast Reconstr Surg Glob Open 2025; 13:e6526; doi: 10.1097/GOX.0000000000006526; Published online 10 February 2025.)*

INTRODUCTION

Compared with the general population, women carrying the BRCA1, BRCA2, PALB2, CHECK2, ATM, and TP53 germline mutations, or with a positive family history of breast carcinoma, face a higher lifetime risk of developing breast cancer.[1] Upon confirmation of the diagnosis, these mutation carriers are offered various risk management options, such as surveillance regimens—utilizing imaging methods and clinical breast examinations. The National Comprehensive Cancer Network recommends a monthly breast self-examination, a semiannual clinical breast examination, an annual mammogram, and an annual breast magnetic resonance imaging (MRI) scan.[2] Warner et al[3] found that annual MRIs reduce the risk of stage II to IV breast cancers by up to 1.9% at 6 years in women with BRCA mutations compared with 6.6% with conventional screenings. Conversely, MRIs are quite time-consuming and expensive. The other option is a bilateral risk-reducing mastectomy (BRRM).[4]

A BRRM can be performed as a skin-sparing mastectomy (SSM) from an elliptical incision around the nipple–areola complex (NAC), by involving the removal of breast tissue, including the NAC.[5] In patients with large breasts, the skin-reducing mastectomy (SRM) can be performed by using a Wise pattern incision.[6] This procedure includes the removal of the mammary gland, excessive skin, and the NAC. Finally, a nipple-sparing mastectomy (NSM) leaves the NAC intact and is considered to offer the most

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aesthetically pleasing outcome.[7] NSMs can be performed with a mastopexy, with an incision from the inframammary fold, or with a periareolar incision. For mastectomy patients, reconstruction options can be offered, considering both the timing (immediate or delayed) and the type of reconstruction (implant-based, autologous tissue-based, or a combination of both).[8,9]

The number of risk-reducing mastectomies (RRMs) around the world has been increasing every year since Angelina Jolie revealed her own surgery.[10,11] In recent years also, the accessibility of genetic testing has significantly increased, with commercial markets offering these services at much more affordable prices.[12] Not only are positive genetic mutations an indication for RRM procedures, but these procedures are also offered to patients with a strong family history—a significant occurrence of breast cancer among mainly the female family members.[13] Before genetic testing, another indication for RRMs was also the presence of nontransparent mammary glands on the radiological scans. This indication is now obsolete.

Research findings indicate that individuals carrying BRCA1 mutations face a lifetime risk of around 57%–72% for breast cancer and 39%–44% for ovarian cancer. On the other hand, BRCA2 mutation carriers have an estimated 45%–69% risk of breast cancer and an 11%–18% risk of ovarian cancer.[14]

Studies have demonstrated that a BRRM procedure can reduce the lifetime risk of breast cancer by more than 90% in high-risk populations. Additionally, in certain patients with genetic mutations, BRRMs have been associated with reduced mortalities compared with surveillance-only approaches.[15,16] However, most of the studies have low-quality heterogeneous data and short follow-ups.[17] Skytte et al[18] suggest that the reductions in risk are not as dramatic as have been suggested by previous studies. Our study aimed to determine the long-term incidence of breast cancer in patients with healthy, surgery-free breasts who underwent BRRMs.

PATIENTS AND METHODS

This retrospective cohort study examined the long-term outcomes of BRRMs in patients without any prior breast surgery. We identified 274 patients who underwent BRRMs at our institution between 1981 and 2023, due to having known genetic predispositions, a strong family history of breast cancer, or having very dense mammary glands. Patients with therapeutic mastectomies for confirmed or suspected malignancies were excluded, whereas those with malignancies identified in BRRM specimens were included. We divided patients into 4 study groups based on the type of mastectomy done: NSM with mastopexy, NSM from an inframammary fold incision, SSM, and SRM. Before surgery, all patients received counseling on reconstructive options. They were also informed about the potential risks to the residual breast tissue following a mastectomy. Data collection, including age, body mass index (BMI), surgical history, indication for BRRMs, and the methods of reconstruction, was conducted by using an institutional database. In November 2023, our research team performed a telephone and email follow-up to ascertain any new breast cancer diagnoses (primary end point) and mortalities (secondary end point). The follow-up duration for each patient commenced from the date of the BRRM and concluded upon a successful contact with our team. We had 100% success in contacting the patients. Descriptive statistics, generated using Microsoft Excel 365 (version 2021), were used to characterize the demographic, surgical, and oncological features of the cohort.

Takeaways

Question: Does prophylactic mastectomy reduce the risk of breast cancer in the long term?

Findings: Based on checkups in 274 patients after mastectomy, only 1 case of breast cancer occurred.

Meaning: Prophylactic mastectomy reduces the risk of breast cancer in the long term.

RESULTS

We performed a total of 274 BRRMs. The mean follow-up period was 76 months with a median of 60 months (range 30–510 mo). The standard deviation was 57.7, and the modus was 42 months. The average age at the time of the RRM was 42.3 ± 9.2 years; the average age at the time of the survey was 49.1 ± 10.3 years. The mean BMI was 24.3 kg/m^2 (range 18.3–35.7 kg/m^2). No patient had a history of any previous breast surgery. Almost a third of the patients (31%) were current smokers or had a history of smoking at the time of the mastectomy (Table 1).

We documented known genetic predispositions in 237 patients. The BRCA1 mutation was present in 155 (56.6.2%) patients, the BRCA2 mutation in 59 (21.5%) patients, the combined mutations of BRCA1 and BRCA2 in 1 (0.4%) patient, PALB2 in 10 (3.6%) patients, CHEK2 in 6 (2.2%) patients, ATM in 2 (0.7%) patients, and the combined mutations of BRCA1 and ATM in 2 (0.7%) patients. We also found 2 patients with the RAD51C mutation and 1 with the ERCC2 mutation. For patients without a known genetic predisposition, the reasons for RRMs were either the presence of a strong family history, 9 (3.3%) patients, or very dense mammary glands on the radiological scans, 28 (10.2%) patients. The data are all summed up in Table 2. In all cases, oncologists indicated a patient for a mastectomy. We performed several types of mastectomies. The most common type was an NSM with a mastopexy in 44.4% of the patients, then an NSM from an inframammary incision in 29.6% of the patients. We also performed SRMs in 9.8% of the patients

Table 1. Patient Characteristics

	Mean	SD
Age at the time of surgery	42.3	9.2
Age at the time of survey	48.1	10.0
BMI	24.3	5.3
Smoker	38	
Ex-smoker	47	
Nonsmoker	189	

and SSMs in 14.2% of the patients. The most common type of reconstruction was an implant-based reconstruction performed on 213 (77.7%) patients. Two women (0.7%) underwent reconstruction with lipofilling, and 59 (21.5%) patients opted not to undergo any breast reconstruction. The types of mastectomies are summed up in Table 3.

Our study identified 1 case of breast cancer following surgery from a group of 274 women. The tumor occurred in the right breast of a BRCA1+ patient who underwent SSMs in 2019. The tumor site was in the residual axillary tail, and the patient found the mass 21 months after having an RRM. The biopsy revealed a low-grade triple negative (invasive carcinoma of no special type) carcinoma. The patient underwent extirpation of the mass with a sentinel lymph node biopsy and adjuvant chemotherapy, which finished in March 2022, and since then, the patient has been tumor-free.

DISCUSSION

Breast cancer is the most common malignancy diagnosed in women worldwide.[19] It is a huge burden for the patients and also for the healthcare systems across the world. Besides screening programs, which usually include regular mammographies, breast ultrasound, and MRI scans, there is also genetic testing of selected patients for genetic mutations in several genes, mainly BRCA1 and BRCA2. The panel of genetic testing is quickly expanding, and indications for RRMs are constantly evolving. RRMs have gained popularity since Angelina Jolie, in 2013, shared with the world that she underwent a bilateral mastectomy because of her BRCA1 positivity.[20,21] During the past years, several techniques of mastectomies were introduced, and since then, researchers across the world have started to assess the effectiveness of these techniques in reducing the risk of the onset of malignant tumors of the breasts. One of the oldest studies is the work of Horton et al,[22] who in 1978, found no incidence of breast cancer after SSMs in 104 patients with high risk of developing breast cancer. The follow-up, however, was for only 3.1 years. A study with similar follow-up was conducted by Meijers-Heijboer et al,[23] who in 2001, found no incidence of breast cancer after SSMs in 139 BRCA mutation carriers. Pennisi et al[24] published in 1989 a statistical analysis of 1500 patients with a mean follow-up of 9 years, however, with only a 70% response rate. In this analysis, only 6 patients developed breast cancer after subcutaneous mastectomy. Another big study was published by Mutter et al,[25] who reported breast cancer occurrence after RRM in 1065 patients after bilateral procedures and in 1643 patients after contralateral mastectomy with a median follow-up of more than 22 years. The limitations of the study are a lack of information on BRCA1/2 status for the majority of patients and incomplete tumor information. Jakub et al[26] in 2018, published a retrospective study with 364 BRCA-positive patients with a 56-month follow-up and reported no onset of cancer after an RRM. The study, however, was found to have several major limitations. It is a multicentric study with almost half of the patients undergoing only unilateral mastectomies with a short follow-up.[26] Rebbeck et al[20] conducted a Prevention and Observation of Surgical Endpoints study with 105 BRCA-positive patients with a 6.4-year follow-up and described 2 cases of breast cancer after a subcutaneous mastectomy. In our study, 86.5% of the patients were found to have positive genetic mutations. The rest of the patients had either a positive family history or on radiological examinations, very dense mammary glands with the oncologists deciding to carry out preventive mastectomies because of the near impossibility of any successful radiological screenings.

Our outcomes are consistent with the previous studies on this topic. In our cohort, only 1 patient developed breast cancer following an RRM. The patient was BRCA1+ and underwent an SSM, which is surprising for us because an SSM is considered to be a more effective technique than an NSM considering that the NSM leaves a small amount of gland tissue in the nipple.[27] The incidence rate of breast cancer following RRMs was 0.4%, which is little bit lower than the numbers we found in the literature. Berkeš et al[28] reported the incidence of breast cancer after RRMs at 0.99% in 201 patients with a 5-year follow-up. Boyd et al,[16] in their heterogenous cohort study of patients who underwent NSMs, reported only a 0.16% incidence. In our NSM group, the incidence was 0%; however, this was in a group of 208 patients in comparison to the Boyd group of 641 patients.

To the best of our knowledge, this is a straight homogenous cohort study with the longest follow-up. We enrolled only healthy patients without any previous breast surgery because patients with a history of breast cancer do not carry the same risk of breast carcinoma.[16] Our study is also unique with a 100% response rate from our patients, and we still

Table 2. Indications for Mastectomy

	n	%
BRCA1+	155	56.6
BRCA2+	59	21.5
BRCA1+ ATM+	1	0.4
BRCA1,2+	1	0.4
ATM	2	0.7
CHEK2	6	2.2
PALB2+	10	3.6
RAD51C	2	0.7
ERCC2+	1	0.4
Nontransparent mammary gland	28	10.2
Strong family history	9	3.3

Table 3. Types of Mastectomy and Tumor Occurrence

	n	%	No. Carcinomas	%
SPM	39	14.2	1	2.6
SRM	27	9.8	0	0
NSM—inframammary fold incision	81	29.6	0	0
NSM with mastopexy	127	44.4	0	0
Total	274	100	1	0.4

keep the follow-up ongoing. The limitations of our study are that it was a single-institution cohort, and the extraction of information was performed manually, which could lead to an error. We believe that in the future our study can be a part of an international meta-analysis like the Cochrane review from 2018.[29] The strengths of our study are the large sample size and long follow-ups, including several cases performed 41 years ago.

CONCLUSIONS

RRMs are reliable surgical techniques used to minimize the risk of breast cancer in patients with confirmed genetic mutations, strong positive family histories, and the presence of very dense mammary glands for a long time period.

As far as we know, this study has the longest follow-up of all published homogenous studies on this topic. There was no significant difference in the type of mastectomy carried out. However, this is a single-center study, and a meta-analysis is necessary for a higher level of evidence.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

DECLARATION OF HELSINKI

The study protocol was designed according to the Declaration of Helsinki.

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