Concurrent Prophylactic Mastectomy, Immediate Reconstruction, and Salpingo-Oophorectomy in High-Risk Patients: A Case Series

La coordination d'une double mastectomie prophylactique, d'une reconstruction immédiate et d'une salpingoovariectomie chez les patientes à haut risque : une série de cas

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Abstract

Purpose: There are limited data on coordinated breast and gynecological risk-reduction surgery for high-risk patients in Canada. Therefore, this study aims to evaluate the patient demographics, surgical details, and outcomes of prophylactic mastectomy (PM) with immediate reconstruction and bilateral salpingo-oophorectomy (BSO) in high-risk patients. **Methods:** We conducted a retrospective chart review at an academic center of patients who concurrently underwent PM with immediate reconstruction and laparoscopic BSO over a 7-year period (March 2010-February 2017) were identified. **Results:** A total of 16 patients underwent PM with immediate reconstruction and concurrent BSO. The mean age at the time of surgery was 46.2 ± 6.6 years. Thirteen (81%) patients were carriers of the BRCA1 or BRCA2 mutation. Two patients had prophylactic surgical therapy for BRCA1 mutation and 14 (87.5%) patients had prior oncological treatment. The most common type of procedures performed were skin-sparing, nipple-sparing mastectomy (56.2%) and reconstruction with acellular dermal matrix and implants (43.8%). All patients underwent laparoscopic BSO. The average combined case time was 282.5 ± 81.3 minutes with an average postoperative hospital stay of 1.3 ± 0.5 days. Six (37.5%) patients presented with 30-day postoperative complications, with higher rates in the alloplastic group. There were no gynecological complications. **Conclusions:** In conclusion, our results demonstrate that a combined multidisciplinary surgical approach did not increase length of stay or 30-day complication rates. Furthermore, concurrent risk-reducing strategies are an effective option for patients at high risk of breast or ovarian cancer.

Résumé

Objectifs : Les données sur la coordination des opérations mammaire et gynécologique de réduction des risques sont limitées chez les patientes à haut risque au Canada. La présente étude vise donc à évaluer la démographie des patientes, les détails de l'opération et les résultats cliniques d'une mastectomie prophylactique (MP) suivie d'une reconstruction immédiate et d'une salpingoovariectomie bilatérale (SOB) chez des patientes à haut risque. **Méthodologie :** Dans un centre universitaire, les chercheurs ont réalisé une analyse rétrospective des dossiers des patientes qui ont subi une MP coordonnée avec une reconstruction immédiate et une SOB par laparoscopie, et ce, sur une période de sept ans (de mars 2010 à février 2017).

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Résultats : Au total, 16 patientes, d'un âge moyen de $46,2 \pm 6,6$ ans au moment de l'opération, ont subi une MP coordonnée avec une reconstruction immédiate et une SOB. Treize d'entre elles (81 %) étaient porteuses de la mutation du gène BRCA1 ou BRCA2. Deux patientes ont subi un traitement chirurgical prophylactique à cause de la mutation du gène BRCA1 et 14 patientes (87,5 %) avaient subi un traitement oncologique auparavant. Les interventions les plus pratiquées étaient une mastectomie avec conservation de la peau et des mamelons (56,2 %) et une reconstruction par implants avec matrice dermique acellulaire (43,8 %). Toutes les patientes ont subi une SOB par laparoscopie. Les cas combinés ont duré $282,5 \pm 81,3$ minutes en moyenne et ont été associés à une hospitalisation postopératoire moyenne de $1,3 \pm 0,5$ jour. Six patientes (37,5 %) ont souffert de complications dans les 30 jours suivant l'opération, et le taux était plus élevé dans le groupe alloplastique. Aucune complication gynécologique n'a été observée. **Conclusions :** Les résultats démontrent qu'une approche chirurgicale multidisciplinaire combinée n'ont accru ni la durée de l'hospitalisation ni le taux de complications au bout de 30 jours. De plus, les stratégies coordonnées de réduction du risque constituent une option efficace pour les patientes à haut risque de cancer du sein ou des ovaires.

Keywords

BRCA, breast cancer, breast reconstruction, risk-reduction surgery

Background

Breast cancer is the most prevalent form of female malignancy worldwide.¹ Among the general population, approximately 5% to 10% of breast cancers will be hereditary while 0.1% to 0.2% of women are carriers of the BRCA mutation.^{2,3} In addition to the risk of breast cancer, those individuals identified as BRCA carriers are at increased risk of ovarian cancer. Clustering of breast and ovarian cancer within a family is highly suggestive of a BRCA1 or BRCA2 defect. These 2 genes are responsible for approximately 40% to 50% of families with hereditary breast cancer and 95% of families with both breast and ovarian cancer.⁴ Overall, women who are BRCA1 or BRCA2 carriers have a 50% to 80% chance of developing breast cancer, a 60% chance of developing cancer in the contralateral breast, and a 15% to 25% chance of developing ovarian cancer in their lifetime.⁵

In these high-risk women, it is important to inform them of options that may reduce their risk of breast and ovarian cancer. Women who are identified as being at higher risk for breast and ovarian cancer generally undergo more extensive surveillance. High-risk women include those with a known BRCA mutation, an untested first-degree relative of a known carrier, a family history consistent with a hereditary breast cancer syndrome (personal lifetime cancer risk > 25%), a high-risk marker on previous biopsy, or radiation therapy to the chest before age 30. Currently, in Ontario, strategies aimed at managing these patients involve initiating breast cancer screening at age 30 with close clinical follow-up and annual mammography and magnetic resonance imaging. Other additional screening methods include transvaginal ultrasound, serum biomarkers, chemoprevention, and prophylactic surgery.⁶

Risk-reduction surgery involving prophylactic mastectomy (PM) and bilateral salpingo-oophorectomy (BSO) has been shown to reduce the risk of breast and ovarian cancers by 90% and 95%, respectively.⁷⁻¹⁰ To date, there have been numerous concurrent breast and gynecological surgeries for breast and ovarian cancer prophylaxis, which have demonstrated success with acceptable morbidity and postoperative

complications.¹¹ There are limited data on coordinated breast and gynecological risk-reduction surgery for high-risk patients in a Canadian population. Therefore, this study aims to evaluate the patient demographics, surgical details, and outcomes of PM with immediate reconstruction and BSO in a subset of high-risk patients.

Methods

Patients at St Michael's Hospital (Toronto, Ontario, Canada) who concurrently underwent PM with immediate reconstruction and laparoscopic BSO over a 7-year period (March 2010-February 2017) were identified through a search of hospital records. Surgical procedures involved a multidisciplinary team of surgeons from General Surgery, Plastic Surgery, and Gynecology departments.

Patient risk factors, surgical indications, and treatment details were collected. Patient characteristics and risk factors included age, BRCA status, family history of breast or ovarian cancer, previous oncologic treatment, and indications for PM and BSO. For surgical details, we gathered information regarding combined length of surgical case, length of postoperative hospital stay, type of PM, type of reconstruction, and 30-day postoperative complications. This information was obtained from hospital e-records and chart hard copies.

Autogenous reconstructions were defined as reconstruction using patients' own tissues, while alloplastic involved implant-based reconstruction. Combined reconstructions included patients with a previous cancer diagnosis undergoing delayed reconstruction on a previously treated breast and concurrent immediate reconstruction on the contralateral side. These combined reconstructions also consisted of a combination of autogenous and alloplastic techniques.

Results

From March 2010 to February 2017, we identified a total of 16 patients who underwent PM with immediate reconstruction and concurrent laparoscopic BSO. The mean age at the time of surgery was 46.25 ± 6.57 years (range 31-55 years). Of these

Table 1. Patient Clinical Characteristics.^a

Personal characteristics	N (%)
Mean age at prophylactic surgery	46.25 ± 6.57
Personal history of breast cancer	14 (87.5)
Personal history of ovarian cancer	0 (0)
Family history of breast cancer	11 (68.75)
First degree relative	7 (43.75)
Family history of ovarian cancer	1 (6.25)
First degree relative	1 (6.25)
BRCA positive	13 (81.25)
BRCA1	10 (62.5)
BRCA2	3 (18.75)
Prior oncologic treatment ^b	13 (81.25)
Lumpectomy	6 (37.5)
Mastectomy	6 (37.5)
Chemotherapy and/or radiotherapy	13 (75)

^an = 16. Values expressed as average ± standard deviation.

^bTotal number of specific therapies >13 as some patients received combination therapy including any of lumpectomy, mastectomy, chemotherapy and/or radiotherapy.

women, 13 (81%) were carriers of the BRCA1 or BRCA2 mutation. Seven (43.8%) patients had a known first-degree relative with breast cancer, one of which also had a first-degree relative with ovarian cancer. Four other women (25%) had a family history of breast cancer in second-degree relatives. Fourteen (87.5%) had a personal history of breast cancer prior to surgical prophylaxis; 12 of these 14 patients had unilateral breast cancer, while 2 patients had bilateral. No patients had known ovarian cancer, but 2 patients had other gynecological indications for BSO, including ovarian cysts, abnormal uterine bleeding, and increased estrogen load. Two patients had prophylactic surgical therapy with no personal history of breast or ovarian cancer but were positive for the BRCA1 mutation. Fourteen (87.5%) patients had prior oncological treatment, which included lumpectomy, unilateral mastectomy, chemotherapy, and/or radiation therapy. Clinical characteristics are summarized in Table 1.

The type of mastectomy performed most commonly was a skin-sparing, nipple-sparing mastectomy (56.2%), followed by skin-sparing, non-nipple sparing (25%), skin-reducing, non-nipple sparing (12.5%), and nonskin-sparing, non-nipple sparing (6.2%). The type of reconstruction was most commonly acellular dermal matrix (ADM) with implants (43.8%), followed by transverse rectus abdominus muscle (TRAM) flaps (25%), latissimus dorsi flaps (18.8%), submuscular tissue expanders (6.2%), and submuscular implants (6.2%; Table 2). All patients underwent laparoscopic BSO.

The average combined case time was 282.5 ± 81.3 minutes (range 120-420 minutes) with an average postoperative hospital stay of 1.3 ± 0.5 days (range 1-2 days). Six (37.5%) patients presented with 30-day postoperative complications, including seromas, wound dehiscence, surgical site infection, and excess surgical site drainage. Surgical and postoperative details are summarized in Table 3.

Table 2. Surgical Procedures.^a

Type of surgery	N (%)
Type of mastectomy	
Skin-sparing, nipple-sparing	9 (56.25)
Skin-sparing, non-nipple sparing	4 (25)
Nonskin sparing, non-nipple sparing	1 (6.25)
Skin-reducing, non-nipple sparing	2 (12.5)
Type of reconstruction	
TRAM flap	4 (25)
Latissimus dorsi flap	1 (6.25)
ADM + implants ^b	7 (43.75)
Submuscular implants	1 (6.25)
Latissimus dorsi flap + tissue expander	2 (12.5)
Submuscular tissue expander	1 (6.25)

Abbreviation: ADM, acellular dermal matrix.

^an = 16. Values expressed as average ± standard deviation.

^bOne patient received ADM + implants with exchange of tissue expander.

Table 3. Surgical and Postoperative Details.^a

Surgical details	N (%)
Total surgical case time (minutes)	282.5 ± 81.26
Length of hospital stay (days)	1.33 ± 0.49
30-Day complications ^b	6 (37.5)
Excess surgical site drainage	3 (18.75)
Seroma	2 (12.5)
Wound dehiscence	1 (6.25)
Surgical site infection	1 (6.25)

^an = 16. Values expressed as average ± standard deviation.

^bTotal number of specific complications >6 as 1 patient exhibited both excess surgical site drainage and a seroma.

When data were analyzed based on type of reconstruction, the total surgical time was longest for combined reconstruction (345 ± 0 minutes), followed by autogenous (327 ± 81.7 minutes) then alloplastic (243.9 ± 71.8 minutes) reconstruction. The total number of days in hospital was 2 days for autogenous reconstruction and 1 day for both alloplastic and combined reconstructions. Of 9 patients, 5 (56%) in the alloplastic reconstruction group experienced 30-day complications was highest in the alloplastic reconstruction. One (20%) of 5 patients in the autogenous reconstruction group experienced a 30-day complication consisting of a small wound dehiscence at the inframammary fold. These results are summarized in Table 4.

Discussion

With increasing availability of cancer screening and genetic testing, the choice to pursue PM and BSO is increasing in high-risk women. The purpose of our study was to evaluate the feasibility and outcomes of PM and BSO in a subset of high-risk women. We identified 16 patients over a 7-year period who underwent simultaneous PM with immediate reconstruction and laparoscopic BSO. Thirteen (81%) of these patients were known carriers of the BRCA 1 or BRCA2 mutation and 14 (87.5%) had a personal history of breast cancer prior to

Table 4. Surgical and Postoperative Details According to Type of Reconstruction.^a

Type of reconstruction	N	Total surgical case time (minutes)	Length of stay (days)	30-Day complications (%)
Autogenous	5	327.00 ± 81.67	2	1 (20)
Immediate	4	338.80 ± 89.29		0
Delayed	1	280.00		1
Alloplastic	9	243.89 ± 71.80	1	5 (56)
Immediate	7	266.43 ± 59.43		3
Delayed	2	165.00 ± 63.64		2
Combined	2	345.00 ± 0	1	0

^an = 16. Total surgical time expressed as average ± standard deviation.

prophylactic surgery. Three patients, although BRCA negative, had risk-reduction surgery due to locally advanced breast cancer with or without a significant family history. Two patients had true prophylactic surgery due to high risk BRCA1 mutations with no detected cancer or prior personal history. It is important in this group of women to discuss the increased cancer risks associated with being a genetic carrier. Women of known BRCA status are at increased risk of developing a second primary breast cancer and primary ovarian cancer.¹² Numerous studies have demonstrated that these procedures are effective methods of decreasing risk of development of breast and ovarian cancer by 90% and 95%, respectively. A study by Schrag et al revealed that the greatest improvement in life expectancy from risk-reducing surgery was in young patients, in those with high penetrance mutations, and in node-negative disease.¹³

Immediate breast reconstruction remains underutilized, therefore, it is important to discuss this option with all patients undergoing PM. In Canada, only 7.7% to 7.9% of patients receiving mastectomy for breast cancer will seek breast reconstructive surgery,¹⁴ with rates as low as 3.8% to 5% in Nova Scotia.¹⁵ This low rate has previously been associated with lower socioeconomic status, geographic access to health care, non-white ethnic background, increased age, major comorbidities, and/or previous chemotherapy/radiotherapy.^{16,17} Reconstructive options include autogenous (TRAM flap, deep inferior epigastric perforator flap, latissimus dorsi flap) or alloplastic (implant-based) reconstruction. The choice of autogenous versus alloplastic reconstruction plays an important role in determining operative time and potential morbidity of the procedure. In our series, the most commonly used reconstructive technique involved ADM with implants (43.8%), followed by TRAM flaps (25%) and latissimus dorsi flaps (18.8%). Submuscular tissue expanders and implants were less commonly used. The average surgical time for autogenous reconstruction was 327 ± 81.7 minutes compared to 243.9 ± 71.8 minutes in the alloplastic group. However, 2 patients were outliers with surgical times of 410 and 420 minutes. Both of these patients received skin-sparing, nipple-sparing mastectomies, which is likely a major contributing factor to the increased operative time. Excluding these outliers, the average surgical time for all cases was 263.6 ± 67.3 minutes and 268.3 ± 20.2 minutes for autogenous reconstructions. Six (37.5%)

patients experienced 30-day postoperative complications, which included seromas, wound dehiscence, and excess surgical site drainage. The addition of gynecologic procedures did not appear to change the complication rate. One patient who received implants and ADM had a complication of true surgical site infection. An analysis of trends in breast reconstruction over 10 years demonstrated that there were significantly more complications after autogenous reconstruction compared to any other type of reconstruction.¹⁸ However, in our study, 5 of 6 patients with postoperative complications received alloplastic reconstruction.

Combined breast and gynecological surgery among multiple surgical specialties has been reported and demonstrated that the need for transfusion was the only increased complication.¹⁹ Elmi et al assessed outcomes of breast surgery with laparoscopic BSO in a large retrospective cohort analysis and found that there was no additional morbidity when surgeries were performed simultaneously.²⁰ In other similar combined breast and gynecological studies, there were no significant differences in complications and outcomes,²¹⁻²³ with acceptable morbidity.²⁴ Additionally, a large cohort study performed by University of Pennsylvania evaluated outcomes in high-risk patients undergoing free flap breast reconstruction and gynecological procedures. Their study found that compared to patients with breast surgery alone, the addition of gynecological surgery did not impact morbidity, length of stay, or operative costs.²⁵ These studies further support that concurrent risk-reduction surgery is an effective and safe option for high-risk patients with breast cancer.

In our study, the use of laparoscopic BSO as a less invasive surgical option likely reduced the likelihood of further adverse events. In multiple combined breast and gynecological studies, there have been no significant complications reported.^{21,23} However, it is important to consider underlying patient risk factors in any surgical procedure to ensure patient safety. Overall, the addition of BSO to PM with immediate reconstruction resulted in no major intraoperative surgical complications and did not increase patient morbidity at 30 days postoperatively.

Perhaps one of the most appealing aspects of this is the completion of multiple procedures during one surgery. This is beneficial to both the patient and health care system as it reduces the number of anaesthetic administrations (and accompanying risks), perioperative investigations, hospitalizations,

inhospital care, recovery time, and medications.²⁶ There may also be indirect savings by reducing the number of lost days at work, travel expenses, or cost of childcare arrangements. These savings may be even greater in countries where health care is not covered.

Notwithstanding, this study has several limitations. This was a retrospective study, which introduces the possibility of selection bias. The data collected are from a single Canadian institution, therefore due to the small sample size results may not be generalizable across other regional or national institutions. Further investigations in other Canadian institutions would be advantageous, especially in those performing free flap reconstruction. Additionally, the surgical time recorded intraoperatively did not distinguish the amount of time required by each surgical team for their respective portion of the procedure. Lastly, the type of reconstruction performed was diverse and the procedures on their own carry varying complication rates.

In conclusion, our results demonstrate, in a Canadian population, that a combined multidisciplinary surgical approach did not affect length of stay or 30-day complication rates. Furthermore, simultaneous PM with immediate breast reconstruction combined with laparoscopic BSO is an effective option for patients at high-risk of breast or ovarian cancer and should be discussed in a timely manner.

Authors' Note

This article does not contain any studies with human or animal subjects.

Declaration of Conflicting Interests

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