



Delayed Contralateral Prophylactic Mastectomy: A Tertiary Centre Experience

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Abstract

Introduction: Reasons for requesting CPM include prevention of recurrence, peace of mind and moving on after breast cancer. Some women seek CPM as a delayed procedure but factors influencing this are poorly understood. There are challenges for Breast Reconstruction (BR) after delayed CPM relating to previous ipsilateral reconstructive procedures, adjuvant therapies such as radiotherapy, and comorbidities.

Methods: A retrospective analysis examined breast cancer patients undergoing CPM with or without BR at a single tertiary referral center between January 2009 and December 2019. Patients undergoing delayed CPM were identified. Data were collected on demographics, timing and type of surgery, neoadjuvant/adjuvant treatments and complications based on the Clavien-Dindo classification. A cross-sectional survey based on validated questionnaires (5-point Likert scale) explored patients' decision-making process in terms of timing of CPM and any BR.

Results: A total of 123 patients with unilateral breast cancer underwent CPM with 39 (32.5%) of them as delayed procedures (with respect to therapeutic mastectomy) with or without BR. Of these 39 delayed CPM patients 12 (31%) had immediate BR at the time of cognate mastectomy, 22 (56%) had bilateral BR simultaneously with the delayed CPM, 3 (8%) had bilateral delayed BR following CPM whilst 2 (5%) had no reconstruction at all. Mean patient age was 52 years (range 24-73) and the average interval between initial and delayed mastectomy was 2.67 years (range 0-22). The majority of reconstructions where patients had underwent implant-based (n=28) rather than exclusively autologous reconstruction (n=9). Complications (major) occurred in 8 patients with unilateral BR compared with 5 of patients with bilateral immediate BR and 3 of patients undergoing bilateral delayed BR.

The response rate amongst patients receiving questionnaires (n=33) was 22/33 (66%). The most common reason for delayed CPM was to complete all cancer treatments (including radiotherapy) before surgery on the unaffected breast (score 2.91).

Conclusion: Factors for delayed CPM are patient-driven with few women spontaneously changing their mind having initially decided against immediate CPM for reasons also including surgical duration. CPM should be offered as a potentially delayed option with informed discussion of risks and benefits.

Keywords: Contralateral prophylactic mastectomy; Risk-reducing mastectomy; Immediate breast reconstruction; Delayed breast reconstruction; Patient reported outcomes; Implant reconstruction; Autologous reconstruction; Trends in CPM; Trends in breast reconstruction

Introduction

Contralateral Prophylactic Mastectomy (CPM) refers to surgical removal of the opposite disease-free breast in a patient diagnosed with invasive or non-invasive unilateral breast cancer [1,2]. There has been a notable increase in rates of CPM since the beginning of the millennium with an early study from Tuttle and colleagues revealing an increase of approximately 150% in rates of CPM for the period 1998-2003 [3]. This trend for 'big surgery' has continued with a doubling in rates of CPM performed for both invasive and non-invasive disease over the past 15 years in

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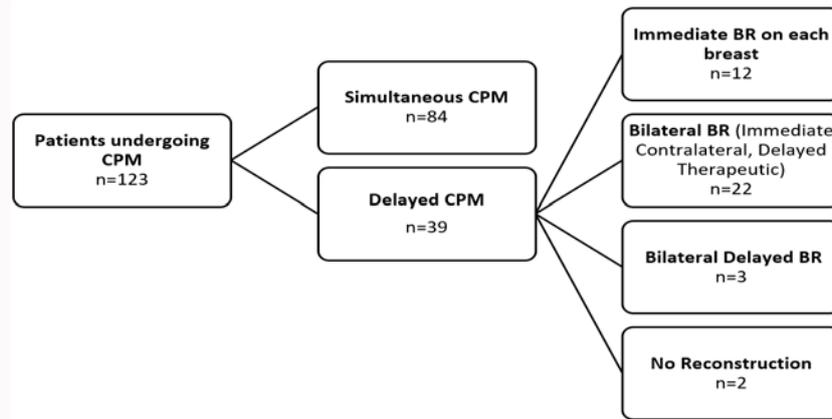


Figure 1: Flowchart depicting the cohorts of contralateral prophylactic mastectomy patients who had undergone breast reconstruction stratified by its timing.

<i>Implant and ADM reconstruction</i>	<i>Combined Latissimus Dorsi (LD) flap and implant reconstruction</i>	<i>Autologous Reconstruction</i>
<ul style="list-style-type: none"> •16/37 patients had bilateral implants and ADM. (Image 6) •2/37 had implant and ADM on the CPM and a LD with implant on the therapeutic side 	<ul style="list-style-type: none"> •9/37 Bilateral LD flap and implant. (Image 2,3) •1/37 LD flap and implant on CPM and DIEP on therapeutic side. 	<ul style="list-style-type: none"> •8/37 bilateral DIEPs (Image 3,4,5) •1/37 bilateral IGAPs

Figure 2: Types of Reconstruction. Table schematic of patient cohort reconstruction choices.

the United States [4,3]. Contralateral prophylactic mastectomy can be undertaken simultaneously with a therapeutic mastectomy or as a delayed procedure at a later date. Furthermore, breast reconstruction following CPM can be performed either at the time of mastectomy (immediate) or months or years later (delayed). There is, however, scant literature specifically addressing the issue of surgical timing of CPM with or without breast reconstruction. Single institution reports suggest CPM is less likely to be carried out as a delayed procedure than at the same time as therapeutic mastectomy [5]. A study of 241 patients from MD Anderson Cancer Centre found that only 23% of women (55/241) underwent delayed CPM compared with a majority opting for immediate CPM [6].

The reasons for this increase in rates of CPM are poorly understood but this trend for choosing maximal surgery is most evident amongst younger women under 40 years of age and those with lower-risk disease (stage I invasive and ductal carcinoma-*in-situ*) [4]. Limited research suggests that often patients over-estimate their personal risk of developing future contralateral disease after being diagnosed with a unilateral cancer and fail to appreciate that CPM does not improve breast cancer specific survival. The latter will be determined by the ipsilateral cancer and not a subsequent contralateral cancer that usually has a better prognosis from detection at an earlier stage due to annual surveillance. Patient decision-making and surgeon interaction can be dominated by ‘fear of recurrence’ and ‘avoidance of decisional regret’ with healthcare professionals feeling pressurized to accede to demands in the wider context of patient-centered care [7-9]. Most women diagnosed with a unilateral breast cancer without any genetic predisposition have a relatively modest risk of contralateral

malignancy with an average estimate of approximately 0.2% to 0.5% per annum [10] and a commonly cited figure of 0.4% per annum [11]. For patients with carriage of a pathogenic mutation in BRCA1 or BRCA2, these lifetime estimates for contralateral breast cancer are several-fold higher (2% to 5%) [12].

There are several key issues to address for women who have made a decision to proceed with CPM. Firstly, whether this is done as an immediate or delayed procedure (with respect to therapeutic mastectomy) and secondly how patients should be counselled on reconstructive options in terms of the timing and type of reconstruction. This paper primarily explores the reasons for seeking a delayed CPM and the potential challenges with reconstruction of the breast irrespective of whether immediate reconstruction was done at the time of the initial therapeutic mastectomy. Secondary aims include evaluation of outcomes and complications of reconstruction in the context of CPM along with patient reported outcomes using validated instruments.

Methods

A retrospective analysis examined patients undergoing Contralateral Prophylactic Mastectomy (CPM) as either an immediate or delayed procedure with or without breast reconstruction at a single tertiary referral center between January 2009 and December 2019. Clinical information was extracted from a prospectively maintained database with details collected on patient demographics, timing and type of surgery, previous adjuvant treatments and complications. A cross-sectional survey was undertaken that was compiled and based on validated questionnaires and responses to defined

Table 1: Data were extracted from an electronic patient records system and manually from paper records of Delayed CPM patients.

1. I wanted a delayed CPM as this would not have affected my life expectancy compared to an immediate CPM
2. My decision to undergo CPM was dependent on results of genetic testing and these were not available at the time of my therapeutic mastectomy for breast cancer
3. I made a decision to have CPM after my original therapeutic mastectomy due to a recent change in my family history of breast cancer
4. I needed a delayed CPM because I changed my mind about wanting CPM after my initial therapeutic mastectomy for breast cancer
5. I preferred to undergo delayed CPM due to concerns about an excessively long operating time with a simultaneous procedure
6. I preferred to undergo CPM as a delayed procedure to allow a shorter recovery time from my initial surgery for breast cancer (time in hospital and recuperation at home)
7. I preferred to undergo CPM as a delayed procedure in order to get back to work as soon as possible after my initial surgery for breast cancer
8. I requested a delayed CPM (with reconstruction) in order to maximize the chances of achieving symmetrical/matching breasts following my initial therapeutic mastectomy (with immediate reconstruction) for breast cancer
9. I wanted to have CPM as a delayed procedure as I was concerned that any complications from more extensive surgery might delay the start of non-surgical treatments such as chemotherapy or radiotherapy
10. I wanted to have CPM as a delayed procedure in order to complete all treatments for my breast cancer (including post-mastectomy radiotherapy) before having surgery on the opposite non-affected breast

Table 2: Clinical details of patients undergoing delayed CPM.

Clinical details of patients undergoing delayed CPM (n = 39)
Age: 52 years (24-73)
Time from therapeutic to contralateral prophylactic mastectomy: 2.67 years (0-22)
Co-morbidities:
• Diabetes: 2
• Hypertension: 6
• Smokers (Current and Ex): 6
• BMI: 26 (18.1-36.8)
Cancer Details:
• Tumour Size: 38mm (6-130)
• Node Positive Average (If Positive): 16%
• Neoadjuvant Chemotherapy: 24
• Radiotherapy: 33

statements generated using a 5-point Likert-type scale (1= strongly disagree to 5= strongly agree). This questionnaire explored patients' decision-making process in terms of timing of CPM and any breast reconstruction and was supported by subjective free-text boxes to gauge both qualitative and quantitative aspects of the patient-related decision-making process. All delayed CPM patients were contacted *via* e-mail and provided with written information about the study; those who consented to participate in the survey (n=33) were sent an online questionnaire. Details of these individual statements relating to CPM are listed in Figure 1, 2. In addition to patient-related factors, the questionnaire contained a section on pre-surgical discussion and whether the surgeon's opinion influenced decisions not only for CPM but also immediate breast reconstruction.

For purposes of addressing surgical outcomes and complications, patients having delayed CPM were stratified based on whether or not breast reconstruction was undertaken and timing thereof. Patients undergoing delayed contralateral surgery were therefore categorized as follows: 1) Immediate reconstruction at time of delayed CPM (previous immediate breast reconstruction with therapeutic mastectomy). 2) Bilateral breast reconstruction at the time of delayed CPM (immediate on contralateral side; delayed on therapeutic side). 3) Delayed reconstruction after delayed CPM and, 4) no reconstruction. Delayed CPM patients were analyzed as 3 groups depending on whether breast reconstruction was done as an immediate procedure (n=12), a delayed procedure (n=25) or not performed (n=2). Complications were categorized based on the Clavien-Dindo system that employs a scale of 1 to 5 to grade adverse events following surgical procedures. Major complications included wound infection necessitating hospital admission for intravenous antibiotics or drainage and minor complications related predominantly to seromas. Postoperative complications were classified as early (within 30 days) or late (more than 30 days) and analysis excluded patients with missing follow up data (n=2). Despite

small numbers, complications were analyzed for any discernible differences in relation to therapeutic and contralateral prophylactic mastectomy together with type and timing of breast reconstruction.

A modified version of the BREAST-Q instrument for measuring patient reported outcomes was distributed *via* an online survey platform. This survey contains domains for breast satisfaction as well as assessing psychosocial and sexual well-being. Patient reported outcomes were collected using a Likert-type scale and analyzed in relation to type and timing of reconstruction.

Data were extracted from an electronic patient records system (EPIC Systems Corporation, Wisconsin, Michigan) and manually from paper records or electronic medical records for those cases that pre-dated instigation of the EPIC system. The study was registered with the hospital's Audit Department and designated a service improvement project for which Ethical Committee approval was not required (Table 1).

Results

A total of 123 patients underwent Contralateral Prophylactic Mastectomy (CPM) over the time period of this study amongst whom 39 (32%) had CPM sequential to therapeutic mastectomy (delayed CPM).

Patient characteristics

The mean patient age for the delayed CPM group was 52 years (range 24-73) with a mean body mass index of 26 kg/m² (range 18.1-36.8). The average interval between initial therapeutic mastectomy and delayed CPM was 2.67 years (range 0-2). There were few significant co-morbidities with 6 patients recorded as either current or ex-smokers (Table 2) whilst and over half of the group (24/39) had received neoadjuvant chemotherapy as primary breast cancer management. This is consistent with a mean tumor size at presentation of 38 mm (range 6-130) and a node positivity rate of 16%. Moreover,



Image 1: This 48-year-old woman underwent a left risk-reducing, nipple-sparing Wise pattern mastectomy and immediate breast reconstruction with an expandable implant, SurgiMend ADM and an inferior dermal sling. She had a simultaneous delayed right breast reconstruction with a latissimus dorsi myocutaneous flap and an expandable implant for a failed implant reconstruction. 7 years prior to the reconstruction she had a bilateral Wise pattern augmentation-mastopexy with subpectoral implants (which had been replaced 3 years earlier). The middle images were taken 11 months following bilateral reconstruction but prior to nipple reconstruction and tattooing. The right most images show her one year following nipple reconstruction and tattooing; 14 months after the bilateral breast mound reconstruction.

33 patients (85%) had received post-mastectomy radiotherapy on the (therapeutic) side prior to CPM (\pm reconstruction).

Timing of reconstruction

Of 39 patients who underwent delayed CPM, 95% (37/39) had either immediate (n=34) or delayed breast reconstruction (n=3). Twelve patients had immediate breast reconstruction at the time of delayed CPM having undergone immediate reconstruction at the time of initial therapeutic mastectomy. By contrast, 22 patients had bilateral breast reconstruction at the time of CPM that constituted a delayed reconstructive procedure on the ipsilateral (cancer) side and immediate reconstruction on the delayed CPM side. The remaining three patients had bilateral simultaneous delayed reconstructions subsequent to delayed CPM. Finally, there were just two patients who chose not to undergo reconstruction of either breast at any time point (Figure 1).

Type of reconstruction

Amongst patients with delayed CPM almost three-quarters of reconstructions were implant-based (28/37; 76%) comprising either an implant-Acellular Dermal Matrix (ADM) procedure (n=18) or an implant-assisted latissimus dorsi flap (n=10) (Image 1). Only 9 patients underwent an exclusively autologous tissue reconstruction with either a deep inferior epigastric artery perforator flap (12) (n=8) (Image 2) or Inferior Gluteal Artery Perforator flap (IGAP) (n=1). The majority of patients undergoing reconstruction after delayed CPM had a similar type of reconstruction to the ipsilateral side;

thus 16 patients had bilateral implant-ADM reconstruction whilst 9 patients underwent bilateral implant-assisted LD flap reconstruction. One patient had an implant-assisted LD flap reconstruction after delayed CPM having undergone a DIEP flap on the therapeutic side [because the DIEP flap had already been used]. There were no patients with a totally autologous LD flap reconstruction in the series. Hence amongst this cohort of 37 reconstructions for delayed CPM, the majority (34/37; 92%) had the same type of reconstruction on both sides with only 3 patients having a different type of reconstruction on the ipsilateral (therapeutic) and contralateral (prophylactic) sides (Figure 2, 3).

Reasons for seeking delayed CPM

Amongst this cohort of 39 delayed CPM patients, there were 6 decliners who did not participate in the questionnaire study and therefore questionnaires were issued to only 33 patients. The response rate for the questionnaire was 67% (22/33). Table 3 lists potential reasons for seeking delayed CPM along with the mean Likert scores and standard deviations. The highest mean Likert score [2.91; SD 1.0] indicated that the strongest reason for requesting CPM as a delayed procedure was to allow completion of oncological treatments without risk of delay in commencing adjuvant treatment consequent to potential complications of reconstructive surgery. The second most important reason for women seeking a delayed CPM was due to unavailability of genetic test results at the time of therapeutic mastectomy [mean score 2.64; SD 1.4]. A total of 17 patients in this cohort were found to have a pathogenic mutation (BRCA1/2=14;

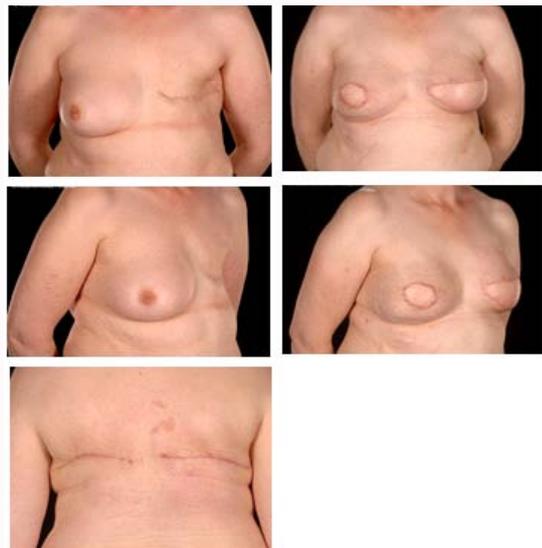


Image 2: Pre and postoperative appearances of a 48-year-old woman following bilateral breast reconstruction with Latissimus Dorsi (LD) flaps with expandable implants, right immediate at the time of prophylactic mastectomy and the left delayed (having had a mastectomy 3 years earlier). She declined nipple reconstruction.

MYBPC3, PALB2, TP53=3) and some patients had genetic testing prompted by a change in family history after their personal breast cancer diagnosis [mean score 2.55; SD 2.7]. Several patients cited a shorter recovery time as a strong reason for requesting CPM as a delayed procedure. These patients wanted to recover as soon as possible from their cancer surgery with minimization of time spent in hospital and recuperating at home. A related reason for choosing delayed CPM were concerns about an excessively long operating time when CPM (with reconstruction) was done at the same surgical sitting as the therapeutic mastectomy [mean score 2.5; SD 3.4]. An interesting theme that has emerged recently is attainment of better symmetry with bilateral breast reconstruction compared with attempts to match the natural breast with reconstruction after therapeutic mastectomy alone. This was reflected in a mean Likert score of 2.32 [SD 2.4]. It is noteworthy that some patients may have chosen delayed CPM in the knowledge that an immediate CPM does not prolong overall survival and delayed CPM does not compromise life expectancy [mean score 2.5; SD 4.1] (Figure 4).

Complications

A total of 16 patients developed complications within 30 days of surgery on the contralateral side. Major complications (CD score ≥ 2) occurred in 3/12 patients having unilateral immediate reconstruction after delayed CPM and 5/22 patients undergoing bilateral simultaneous breast reconstruction at the time of delayed CPM. Moreover, 2 out of 3 patients having delayed bilateral breast reconstruction on both therapeutic and prophylactic sides experienced major complications but numbers are small for this group. Rates of complications overall were 8/12 (66.6%) for patients having unilateral breast reconstruction, 5/22 (%) for bilateral reconstruction at the time of delayed CPM and 3/3 (100%) for those with delayed bilateral breast reconstruction. The small numbers of patients and various confounding factors limited any robust statistical analysis but a Fisher's exact test revealed no statistically significant differences between these groups when comparing immediate or delayed reconstruction for delayed CPM patients. Moreover, complication rates appeared higher



Image 3: This 61-year-old lady had bilateral delayed breast reconstructions with bilateral hemi-DIEP flaps. She was diagnosed with left breast cancer 12 years earlier (in 1998) for which she had a mastectomy and immediate breast reconstruction with an expandable implant followed by adjuvant chemotherapy and radiotherapy.

She developed a late peri-implant infection five years later which resulted in implant loss.

Two years later she had a right risk-reducing (Wise-pattern) skin-reducing mastectomy with no reconstruction. She then presented 11 years later for bilateral delayed reconstructions with autologous tissue which was performed with bilateral hemi-DIEP flaps. The postoperative appearances are at 4 months. She declined nipple reconstruction.

when immediate reconstruction was performed after delayed CPM compared with therapeutic mastectomy. Amongst the group of 12 patients with unilateral reconstruction after delayed CPM, 4 patients developed complications on the prophylactic side only (Table 4).

Radiotherapy

The majority of patients in this cohort of delayed CPM had received PMRT following primary chemotherapy and subsequent therapeutic mastectomy. Neoadjuvant chemotherapy patients are more likely to have larger tumors at presentation (>5 cm) and to be node positive. The mean tumor size for pre-treatment was 38 mm and 20% of patients had core biopsy-proven nodal metastases at presentation or sentinel lymph node positivity. Administration of prior irradiation to the ipsilateral chest wall should not affect complication rates for delayed CPM surgery (minimal scatter effects). Nonetheless, there are long term effects of PMRT such as capsular contracture and this may lead to implant exchange on the therapeutic side at the time of reconstruction after delayed CPM. Amongst non-irradiated patients (n=6), there were documented complications from initial therapeutic surgery including cellulitis requiring intravenous antibiotics, venous congestion (surgical exploration and re-anastomosis), fat necrosis and wound dehiscence (donor LD flap site).

Patient reported outcomes

Half of those patients issued with the BREAST-Q questionnaire (11/22) provided feedback on surgical outcomes. The principal domains assessed were satisfaction with the breasts and physical well-being. Question 1 evaluated breast reconstruction after risk-reducing surgery by assessing levels of satisfaction in terms of size, shape and comfort. Question 2 related to satisfaction with the cosmetic

Immediate BR on each breast n=12 patients	Bilateral BR (Immediate - Contralateral, Delayed - Therapeutic) n=22 patients	Bilateral Delayed BR n=3 patients
<ul style="list-style-type: none"> • 5/12 patients had implants with ADM • 4/12 patients had bilateral LD flaps with implants • 1 patient had LD-implant on therapeutic side, and implant-ADM on CPM side • 1 patient had bilateral DIEPs with implant exchange on the therapeutic side • 1 patient had a DIEP on therapeutic side and LD-implant on CPM side - because the DIEP had already been used 	<ul style="list-style-type: none"> • 10/22 had bilateral implants with ADM. • 5/22 had bilateral LD flaps with implants • 6/22 had bilateral DIEPs. • 1 had bilateral IGAPs. 	<ul style="list-style-type: none"> • 1 had bilateral DIEP • 1 had bilateral implants with ADM • 1 had LD with implant on therapeutic side, and implant-ADM on CPM side.

Figure 3: Types of Reconstruction undergone by patient by type of reconstruction scenario.
ADM: Acellular Dermal Matrix; LD: Latissimus Dorsi; CPM: Contralateral Prophylactic Mastectomy; DIEP: Deep Inferior Epigastric Pedicle; IGAP: Inferior Gastric Artery Pedicle

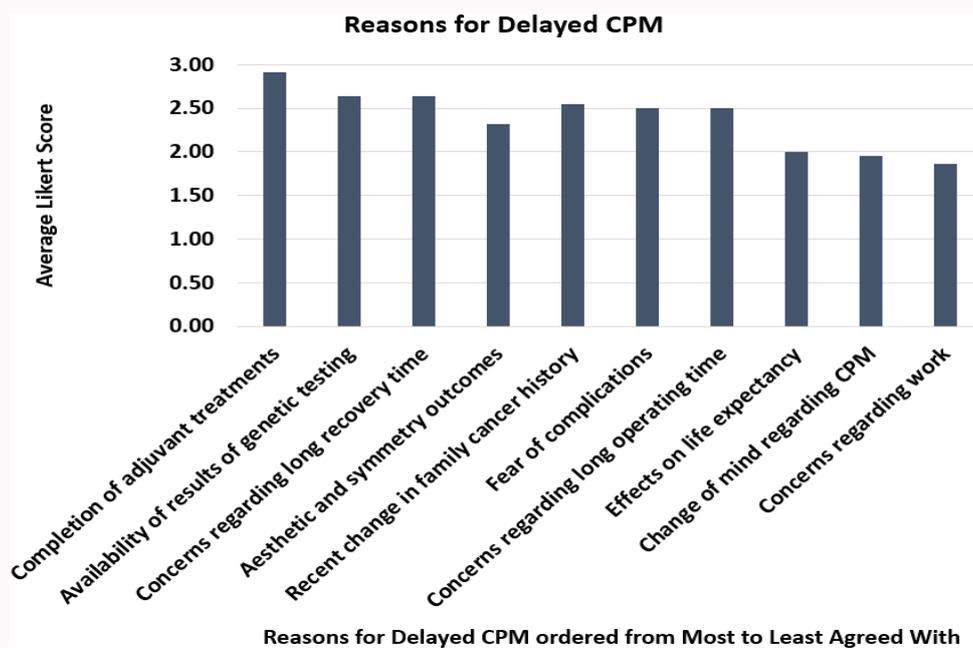


Figure 4: A bar chart demonstrating patient decision making for delayed CPM in descending order of frequency of 'agree'.

appearance of the breasts and factors such as comfort and selection of bras/clothing. Question 3 focused on symptoms of pain, tightness and lymphoedema. For questions 1 and 2, a higher score correlated with higher levels of satisfaction whilst for question 3 a lower score indicated more favorable physical well-being.

Levels of satisfaction across all domains were highest for bilateral simultaneous breast reconstruction, whether performed at the time of delayed CPM or at a later date. This may be attributable to achievement of improved breast symmetry when a similar type of procedure is undertaken concomitantly for the therapeutic and prophylactic sides. Of note, Skin-Sparing Mastectomy (SSM) cannot be employed in the context of delayed breast reconstruction but can be used for delayed CPM with immediate reconstruction. A DIEP

flap may be suitable for simultaneous bilateral breast reconstruction (if sufficient volume) but is not an option for reconstruction after delayed CPM when previously used after therapeutic mastectomy. Table 5 shows that scores for satisfaction with the breasts were higher for both groups undergoing simultaneous bilateral reconstruction (either at the time of delayed CPM or subsequently) compared with immediate reconstruction for each side (approximate scores of 60 vs. 40 respectively). This may relate to the opportunity for autologous reconstruction with a DIEP flap in the former group. Amongst the group with simultaneous bilateral breast reconstruction, scores were lower for DIEP than with implant as the patients with DIEP flaps had complications. Interestingly, there were very high breast satisfaction scores (70-80) for patients without reconstruction and this most likely

Table 3: Table showing potential reasons for seeking delayed CPM along with the mean Likert scores and standard deviations.

QUESTIONS	# 1's	#2's	#3's	#4's	#5's	MEAN	SD
1. I wanted a delayed CPM as this would not have affected my life expectancy compared to an immediate CPM	5	3	12	2	0	2.5	4.1
2. My decision to undergo CPM was dependent on results of genetic testing and these were not available at the time of my therapeutic mastectomy for breast cancer	7	4	4	4	3	2.64	1.4
3. I made a decision to have CPM after my original therapeutic mastectomy due to a recent change in my family history of breast cancer	5	6	8	0	3	2.55	2.7
4. I needed a delayed CPM because I changed my mind about wanting CPM after my initial therapeutic mastectomy for breast cancer	9	6	6	1	0	1.95	3.4
5. I preferred to undergo delayed CPM due to concerns about an excessively long operating time with a simultaneous procedure	3	8	9	1	1	2.5	3.4
6. I preferred to undergo CPM as a delayed procedure to allow a shorter recovery time from my initial surgery for breast cancer (time in hospital and recuperation at home)	4	6	6	6	0	2.64	2.3
7. I preferred to undergo CPM as a delayed procedure in order to get back to work as soon as possible after my initial surgery for breast cancer	9	7	6	0	0	1.86	3.7
8. I requested a delayed CPM (with reconstruction) in order to maximize the chances of achieving symmetrical/matching breasts following my initial therapeutic mastectomy (with immediate reconstruction) for breast cancer	7	5	6	4	0	2.32	2.4
9. I wanted to have CPM as a delayed procedure as I was concerned that any complications from more extensive surgery might delay the start of non-surgical treatments such as chemotherapy or radiotherapy	4	8	7	1	2	2.5	2.7
10. I wanted to have CPM as a delayed procedure in order to complete all treatments for my breast cancer (including post-mastectomy radiotherapy) before having surgery on the opposite non-affected breast	4	5	6	3	4	2.91	1.0

Table 4: Examples of post-operative complications according to C-D score.

CD Score 1 (n=6)	<ul style="list-style-type: none"> Seroma in donor site, blood-stained fluid Scar not healing Wound breakdown
CD Score 2 (n=5)	<ul style="list-style-type: none"> Cellulitis treated with oral antibiotics Infection of wound site Erythema and pain over port site and anterior breast
CD Score 3 (n=5)	<ul style="list-style-type: none"> Wound dehiscence leading to hospital admission and treatment with IV antibiotics, fat necrosis Haematoma evacuation post LD flap Breast dehiscence and abdominal wound dehiscence, implant loss Venous congestion of flap, taken to theatre within 24 hours post-operatively for re-anastomosis that was successfully salvaged Serious infection of skin flap, IV antibiotics (in hospital)

Table 5: Scores for Breast-Q.

	Q1: Satisfaction with breast score – patient reported outcomes	Q2: Satisfaction with breast score – physical appearance	Q3: Physical wellbeing score
General Average	56.1	54.5	23.8
IBR on each unilateral breast	44.8	39.4	33.6
Bilateral BR at the time of CPM	61.5	58.8	23.5
Delayed bilateral BR	61	58	8
No reconstruction	71	82	8

relates to lower levels of expectation and a clear decision not to opt for breast reconstruction. Scores for physical well-being were also higher for these patients having simultaneous bilateral reconstruction, with significantly better scores for those having delayed bilateral reconstruction rather than at the time of delayed CPM (8 vs. 23.5). It is unclear why delayed breast reconstruction should be associated with superior scores for physical well-being than reconstruction performed at the time of delayed CPM but could relate to the type of reconstruction. The majority of these patients had autologous tissue reconstruction without implants and symptoms of pain and tightness in the region of the chest may be less for this group. This difference is reflected in the complications and data collected above. Furthermore, scores for this domain were similar for patients having delayed bilateral breast reconstruction and no reconstruction.

Discussion

There is a dearth of published information on reasons why women seek a delayed CPM rather than undergoing contralateral risk-reducing surgery at the time of therapeutic mastectomy. The current analysis from a single tertiary referral center is one of the first studies

to specifically address this question and highlights some important issues relating to this group of patients. Reasons for choosing CPM are complex but key factors involve ‘fear of recurrence’ and ‘avoidance of decisional regret’; few women regret their decision for pursuing CPM but might regret not having undergone prophylactic surgery in the event of contralateral malignancy following diagnosis of a unilateral breast cancer [13-15]. The advent of rapid techniques for genetic testing (massive parallel sequencing) has permitted more accurate assessment of contralateral breast cancer risk and increased rates of simultaneous therapeutic and prophylactic mastectomy in conjunction with bilateral breast reconstruction [16]. The recent surge in CPM has coincided with widespread availability of genetic testing and more frequent identification of a pathogenic mutation predisposing to contralateral breast cancer.

This study reveals a broad range of reasons for women choosing to undergo CPM as a delayed procedure. The strongest indication was to allow completion of adjuvant non-surgical cancer treatments prior to any contralateral surgery. Women expressed concerns about delays in commencement of chemotherapy or radiotherapy



Image 4: This 51-year-old lady had a bilateral DIEP flap breast reconstruction - immediate on the right breast at time of risk-reducing mastectomy and delayed on the left. She did not seek nipple reconstruction.



Image 5: This 36-year-old lady had a right risk-reducing (LeJour skin-reducing pattern) mastectomy and an immediate reconstruction with a hemi-DIEP flap. She had a simultaneous delayed reconstruction of left breast with a hemi-DIEP flap. She declined nipple reconstruction offered to her at the same time as dog-ear excision.

if contralateral surgery increased the risk of complications. Another common reason for deferring CPM was due to unavailability of genetic test results at the time of therapeutic mastectomy with a related issue of change in family cancer history that raised the chance of a genetic predisposition and led to some women requesting CPM sometime after their initial breast cancer diagnosis. Just fewer than half the patients (17/39) in this cohort of delayed CPM patients had a pathogenic mutation in high or intermediate risk genes. Patients managed with primary chemotherapy have an interval of time between diagnosis and definitive surgery during which genetic test results may be forthcoming and determine appropriateness of CPM.

A new finding from this study was the influence of recovery times on decision-making for timing of CPM; many women wanted a short recovery period after surgery and believed that contralateral surgery would potentially increase duration of hospital stay and the period of recuperation once discharged from hospital. Similarly, there were concerns about more prolonged operating time with concomitant contralateral surgery, especially when immediate breast reconstruction was undertaken and the procedure done sequentially with the therapeutic side.

An interesting theme that has emerged recently is attainment of better symmetry with bilateral breast reconstruction compared with attempts to match the natural breast with reconstruction after therapeutic mastectomy alone. Repeat operation and complications are greater for bilateral therapeutic mastectomy and immediate BR in terms of flap failure, necrosis, infection and systemic recurrence. Interestingly, for bilateral procedures involving a CPM, there are more complications overall in the cancerous (therapeutic mastectomy) compared with the non-cancerous group (prophylactic mastectomy) (24.4% vs. 10.0%). Patients should be informed of the lower incidence of complications when mastectomy with immediate BR is carried out on a non-cancerous breast.

Delayed CPM with or without reconstruction is usually undertaken no earlier than 12 months after completion of initial cancer treatments. The average time interval between initial and contralateral surgery in this study was 2.67 years but is likely to vary widely depending on local resources and whether a managed or insurance-based healthcare system.

A particular challenge for patients undergoing delayed CPM with reconstruction is whether the same type of technique can be employed for both sides. Within this study cohort, 34 delayed CPM cases had the same reconstruction for the therapeutic and prophylactic sides whilst only 3 patients had different procedures on each side. Of note, abdominal flap-based reconstruction cannot be used for any subsequent contralateral reconstruction when employed for reconstruction after initial therapeutic mastectomy. Alternative sites for autologous tissue harvest include the LD flap and gluteal artery perforator flaps but these can be associated with significant donor site morbidity and poorer breast symmetry. Our group has documented a trend for replacement of implant-assisted LD flap reconstruction with implant-ADM based reconstruction in the cohort of patients.

The incidence of capsular contracture following irradiation of an implant-based reconstruction after therapeutic mastectomy is 20% in the current study and accords with published data [17-19]. More severe forms of capsular contracture (grades 3/4 adversely affect cosmetic outcomes and can hinder symmetrization of the breasts at the time of delayed CPM with implant-based reconstruction. Hence implant exchange (\pm capsulotomy) may be carried out at the time of contralateral breast surgery. Post-mastectomy radiotherapy can also impair the quality of tissues on the anterior chest wall and this has relevance to delayed reconstruction on the therapeutic side (if bilateral reconstructive procedures performed at the time of delayed CPM). This would apply especially to sub-pectoral approaches that involve dissection of tissues of the chest wall to create a pocket for the implant. It is likely to also render dissection more challenging for any pre-pectoral implant reconstruction. Ironically, there was a higher rate of complications amongst non-irradiated cases (4/6) but this was likely a chance observation due to small numbers of patients.

Levels of patient satisfaction for both cosmetic and physical



Image 6: This 46-year-old lady had a left skin-sparing mastectomy and immediate epieptoral reconstruction with a fixed volume implant (400cc) and total Braxon ADM coverage, alongside a right capsulotomy and expander-to-implant exchange via an inframammary incision. This is 7 months following a right therapeutic mastectomy for DCIS at which she was reconstructed with an epieptoral expandable implant covered with Braxon ADM. Despite her initial large breast size and shape, she has acceptable cosmetic results and retained the size. She has declined nipple reconstruction despite repeated offers.

domains in the BREAST-Q questionnaire were highest for bilateral simultaneous reconstruction, suggesting a better match between the two breasts when reconstructed at the same time- and using the same technique [20]. An emerging theme in the literature is greater attainment of symmetry with bilateral breast reconstruction compared with matching a natural breast when performing reconstruction after therapeutic mastectomy alone. Interestingly, levels of satisfaction with breast were higher when bilateral breast reconstruction was done subsequently and not concomitantly with CPM. The majority of these patients had bilateral DIEP flap reconstruction but SSM was precluded amongst this group of patients having delayed breast reconstruction (no cases of 'delayed-immediate' reconstruction). Moreover, this particular group of patients also scored more favorably for physical wellbeing with scores that were similar to patients without reconstruction (the latter group have no donor site morbidity and probably lower aesthetic expectations). It should be noted that some patients deliberately avoid reconstructive breast surgery in order to maintain optimum function and levels of physical activity (these patients are often content with being completely flat chested). The two non-reconstruction cases in the current study cited functional issues and lingering worries from complications of therapeutic surgery as reasons for declining reconstruction after delayed CPM.

Limitations of this study include the relatively small number of patients and moderate response rate to the questionnaires which makes any formal subgroup analysis impossible.

Conclusion

There is limited data available addressing factors that influence decision-making processes for women undergoing CPM. Recent increases in rates of CPM are well documented along with factors

underlying this upward trend. However, there is sparse information on reasons for choosing delayed rather than immediate CPM. The current study provides insight into why some women opt for a delayed approach and reveals a broad range of reasons relating to adjuvant treatments, genetic testing, changes in family history, recovery times and duration of surgery. Simultaneous bilateral breast reconstruction may be associated with improved PROMs scores compared with unilateral immediate breast reconstruction following delayed CPM with no clear differences in rates of complications depending on laterality, type or timing of breast reconstruction. This study provides reassurance that reconstruction can be successfully performed either at the same time as delayed CPM (with or without reconstruction of the therapeutic side) or as a delayed procedure. Patients appear to choose delayed CPM with confident knowledge that an immediate CPM does not prolong overall survival and delayed CPM does not compromise life expectancy.

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