Pre-pectoral implant-based breast reconstruction after mastectomy: a narrative review

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Background and Objective: Over two million women are diagnosed with breast cancer (BC) worldwide each year and up to 40% of these require mastectomy and immediate reconstruction. Pre-pectoral breast reconstruction (PBR) is an innovative reconstructive modality capable of restoring the volume of the breast in a simple natural-looking way, by placing the implant directly above the pectoralis major muscle. The aim of this paper is to provide a narrative review of the current literature regarding PBR following mastectomy for BC with a focus on published papers in the last five years.

Methods: A narrative review of the literature was carried out. The electronic database PubMed was searched for studies on PBR using the terms "breast reconstruction" and "mastectomy" and "prepectoral" or "pre-pectoral" or "subcutaneous". The search was carried out in March 2021 including papers from January 2016 to December 2020. Studies not written in English were excluded.

Key Content and Findings: (I) PBR is safe and feasible with or without meshes; (II) as compared to subpectoral reconstruction, PBR is absolutely better in terms of pain and animation deformity; (III) post-mastectomy radiotherapy after PBR is well tolerated; (IV) PBR is an alternative to standard subpectoral reconstruction in case of suboptimal aesthetic result or complications or patient unsatisfaction; (V) the application of the skin reducing mastectomy pattern to PBR allows to extend the indication to patients having large and ptotic breasts; (VI) hybrid PBR combines the natural effect of autologous reconstruction with the comfort of a PBR.

Conclusions: To date, PBR should absolutely be included in the breast surgeon's armamentarium of reconstructive procedures as it offers a relatively simple and quick one-step solution to restore the breast immediately after mastectomy.

Keywords: Pre-pectoral breast reconstruction (PBR); breast cancer; immediate breast reconstruction; direct-toimplant breast reconstruction

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Introduction

Breast cancer (BC) is the most frequently diagnosed tumor in women and the leading cause of death from cancer in females (1). More than two million women worldwide are diagnosed with BC every year and up to 40% of these require mastectomy. Furthermore, discovering hereditary factors involved in BC genesis, the benefit of mastectomy in high-risk patients has increased the demand for riskreducing mastectomy and immediate reconstruction. In fact, about 33.3% of patients between 22 and 44 years old, with unilateral cancer, undergo contralateral risk reduction mastectomy and about 40% of patients with genetic mutations in the BRCA1 and BRCA2 genes decide to undergo bilateral mastectomy (2-5).

The breast is the aesthetic element at the basis of the female image, fundamental to a woman's psychological and sexual identity and a universal symbol of seduction. The loss of one or both breasts can represent a serious trauma for a woman's identity with strong impact on the woman's psychology and relationships (6).

Breast reconstruction after mastectomy is therefore of crucial importance in the view of the physical impairment caused by a demolitive surgery (7). Historically, in the 1970s when the implants were placed directly under the mastectomy flap, there were reported high rates of implant loss (28%), flap necrosis (13.5%) and capsular contracture (56%), which led to the quick abandonment of this technique (8,9). In 1982, Radovan introduced the so-called "two-stage" technique (10) with a tissue expander placed in an "artificially"-made pocket under pectoralis major muscle and serratus anterior fascia in order to have complete muscle coverage at the time of mastectomy. Following an expansion phase, once desired volume had been reached and approximately 4-6 weeks after completion of adjuvant therapy, the second reconstructive time could be carried out, replacing the expander with a definitive implant. The "two-stage" breast reconstruction technique, which has been increasingly perfected over time, has dramatically reduced implant loss, flap necrosis and capsular contracture rates (11-13).

However, even the "two-stage" technique has its disadvantages, including chronic chest pain, physical impairment due to the limited use of the pectoralis major muscle, Breast Animation Deformity (BAD), and discomfort for patients as the subpectoral expander often gives the image of an "unnatural" breast (14,15). In addition, this technique always requires at least two surgeries and two hospitalizations, which is more expensive for the healthcare system.

The history of breast reconstructive surgery has evolved towards becoming increasingly less invasive and the use of direct-to-implant procedures which allow the patient to complete the reconstructive procedure as soon as possible with a rapid return to normal activities. For this purpose, devices called mesh or matrices, have been introduced in order to allow the one-stage immediate breast reconstruction. The term matrix usually refers to products of biological origin, while mesh refers to products in synthetic materials. There is a wide variety of meshes and matrices, which differ in physical properties and composition. The use of acellular dermal matrix (ADM) in breast reconstruction with implants began with Breuing (16) in 2005 and Salzberg (17) in 2006. The authors described the use of the biological matrix in breast implant reconstruction in order to close the inferolateral portion of the subpectoral pocket, thus creating the necessary space for the immediate implantation of the definitive implant, without the need for a tissue expander. Since then, the popularity of meshes and matrices has continued to grow, increasing immediate breast reconstruction with implants from 30% to 50% between 2007 and 2014 (18). Mylvaganam and colleagues (19) showed that, in the UK, 75% of immediate breast reconstructions (IBR) are performed using biological matrices and 24% using synthetic mesh.

Then, surgeons re-introduced the concept of implanting the prosthesis in the pre-pectoral position to reconstruct the breast. With this reconstructive technique, the pectoralis major muscle is left intact on the chest wall and the implant is only covered by the mesh or the matrix and the mastectomy skin flap (20,21). The implant is enveloped in mesh or matrix before being placed under the skin flap or, alternatively, the device is sutured to the fascia of the pectoralis major muscle and then the prosthesis is inserted underneath thus providing only an anterior cover for the implant (22,23).

The technique of breast reconstruction with prepectoral implants has been rapidly adopted as an innovative approach in breast reconstruction (24). Avoiding dissection of the pectoralis major muscle means reduced rates of BAD, chronic pain and no loss of muscle function, resulting in improved patient comfort and postoperative functional recovery (25,26). However, results from randomized trials are still not available and literature data mainly derives from large case series.

The aim of this paper is to provide a narrative review

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Items	Specification
Date of search	March 1, 2021
Databases and other sources searched	PubMed
Search terms used	"breast reconstruction" and "mastectomy" and "prepectoral" or "pre-pectoral" or "subcutaneous"
Timeframe	from January 2016 to December 2020
Exclusion criteria	(I) Letters, case reports, reviews, commentary, conference paper and author's views
	(II) Studies not written in English
	(III) Non-human studies
Selection process	Independently

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of current literature on pre-pectoral breast reconstruction (PBR) after BC over the last five years with a focus on the safety of this procedure in terms of complication rate and the advantages of PBR when compared to submuscular reconstruction Additionally, we reported the results of PBR in the special settings of postmastectomy radiotherapy, revision surgery, skin-sparing mastectomy and hybrid reconstruction. We present the following article in accordance with the Narrative Review reporting checklist (available at https://abs.amegroups.com/article/view/10.21037/abs-21-147/rc).

Methods

A narrative review of the literature was carried out according to the criteria of Green *et al.* (27) (*Table 1*). The electronic database PubMed was searched for studies on pre-pectoral implant-based breast reconstruction using the terms "breast reconstruction" and "mastectomy" and "prepectoral" or "pre-pectoral" or "subcutaneous". The search was carried out in March 2021 including papers from January 2016 to December 2020. Exclusion criteria were as follows: (I) letters, case reports, reviews, commentary, conference paper and author's views; (II) studies not written in English; (III) non-human studies.

Results

Figure 1 shows the search strategy and literature retrieval workflow. Eighty-four papers were included in this review. Characteristics of the included papers are reported in *Table 2*.

The included studies were divided according to the primary outcome of papers into six groups:

- (I) PBR complication profile (34 papers): in this group, there are studies that focused on the feasibility and complication rates of pre-pectoral reconstruction (22,25,26,28-43), including studies with different implants forms and surfaces (44,46,47,49-51,53,55-58); in the end, in this subgroup are present studies without any coverage of implants (neither mesh nor ADM) (45,48,52,54);
- (II) Comparison between PBR and submuscular reconstruction (27 papers): studies comparing prepectoral with submuscular reconstruction, both in direct-to-implant (11,59-72) and "two stage" reconstruction (73-84);
- (III) Radiotherapy after PBR (7 papers): studies evaluating the effects of adjuvant radiotherapy on pre-pectoral reconstruction (85-91);
- (IV) Secondary PBR (5 papers): studies reporting the conversion to pre-pectoral reconstruction in revision surgeries of previous reconstructed breast (92-96);
- (V) PBR following skin-reducing mastectomy (8 papers): studies reporting patients who underwent skin-reducing mastectomy and PBR (97-104);
- (VI) Hybrid PBR (3 papers): studies that focused on breast reconstruction combining autologous tissue transfer with pre-pectoral implant placement (105-107).

PBR complication profile

The most common complications of pre-pectoral reconstruction are (108):

 Seroma: it is usually the most common minor complication and may form after removal of the drain. Some experts say it should always be

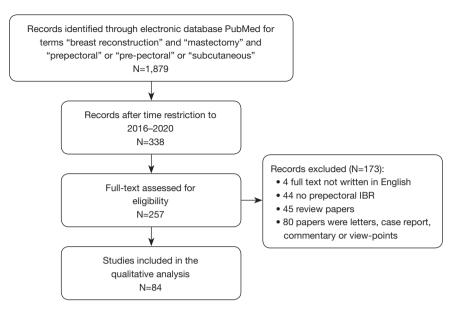


Figure 1 Decisional flow-chart of papers included in review.

aspirated, even under ultrasound guidance, while others are more conservative and only aspirate if the seroma is expanding or persistent, as it puts the surgical wound at risk of dehiscence (28,29,44).

- Red breast syndrome (109): a very rare complication whose occurrence can be reduced by washing implants, matrices and meshes before insertion. It should be differentially diagnosed with infection and can be treated conservatively, although it takes several weeks for complete resolution (29,32,47).
- Wound dehiscence/flap necrosis/infection: superficial dehiscence can be managed on an outpatient basis eventually with advanced dressing. Major dehiscence, flap ischaemia and infection require reoperation (30,45,46,110).
- Rippling: an unaesthetic adverse effect of the discussed technique. It is likely to be influenced by the thickness of the mastectomy flap, the type of implant used and the eventual presence of implant coverage (111). It is frequently associated to the visibility of the implant upper pole, which is more evident in underweight patients. In these cases, adipose tissue grafting is the most common corrective procedure for this type of complication (35,37,50).
- Capsular contracture: is one of the most common complications in breast implant surgery, both cosmetic and reconstructive. It has been reported that the risk of experiencing this complication after reconstructive

surgery is 12% at one year after surgery, rising to 30% at 5 years after surgery (39,48,112).

In this subgroup, all studies focused on the feasibility of PBR and its complication rate. Although PBR was historically associated to a high complication rate, more recent studies showed that current anatomical and technical knowledge together with modern biocompatible prosthetic materials increasingly allow an acceptable complication rate. In fact, in the largest study population within this subgroup (406 reconstructions performed across 18 centres) (29) the overall complication rate was 28.6%, of which 62 major (15.3%) and 54 minor (13.3%) complications. As regards the management of complications, 51 women (15.7%) needed unplanned readmission and 54 (16.7%) had a surgical exploration within 90 days from the primary operation. Of these, 44 women (13.6%) had a surgical exploration for implant-related complications and the overall implant loss rate was 6.4%. Of these, 4.9% of implants were removed within 90 days from the primary surgery. Six women had a delayed implant loss, more than 3 months after the reconstruction.

In 2017, Sigalove and colleagues (46) published their preliminary results on 353 pre-pectoral, implant-based, primary reconstructions in 207 patients, of whom 146 were bilateral, following skin- or nipple-sparing mastectomies. In this case series, complications after reconstructive surgery included infection, seroma, and flap necrosis, each occurring at an incidence of less than 5%, additionally there

Table 2 Characteristics of the included papers

Study authors	Patients undergoing PBR, No. [%]	Breasts No. [%]	Follow-up [months]	Overall complication rate	Capsular contracture rate (Becker III– IV)	Implant	Implant surface	Post- mastectomy RT [%]	DTI or expander [%]
PBR complication profile	Э								
Lo Torto F 2020 (22)	18	22	12 [11–15]	16.7	0	TCPM pocket	NR	NR	TE: 81.8; DTI: 18.2
Kobraei EM 2016 (25)	13	23	10 [6–18]	46	NR	ADM/Vic mesh	NR	13	DTI
Jafferbhoy S 2017 (26)	64	78	9.98	48.4	NR	ADM	NR	NR	DTI
Urquia LN 2020 (28)	118	183	9.26 [1–30]	17.5	5.4	ADM	NR	29.6	DTI: 73.1; TE: 26.9
Chandarana M 2020 (29)	324	406	9.7 [3–35]	28.6	0.2	ADM	NR	15.3	DTI
Downs RK 2016 (30)	45	79	23.1±10.4	35.0	10.1	ADM	NR	NR	DTI
Vidya R 2017 (31)	51	60	16.4 [8–25]	11.6	NR	ADM	NR	2.0	DTI
Highton L 2017 (32)	106	166	15.3±9.3	11.4	0	ADM	NR	11.8	DTI: 92.8; TE: 7.2
Woo A 2017 (33)	79	135	10 [2–36]	10.6	NR	ADM	NR	0	DTI: 10; TE: 85
Vidya R 2017 (34)	79	100	17.9±3.6	13	NR	ADM	NR	3.8	DTI
Jones G 2017 (35)	50	73	12 [3.2–25.7]	3	1.3	ADM	NR	10	DTI
Paydar KZ 2018 (36)	10	18	14.1	22.2	0	ADM	NR	10	DTI: 88.8; TE: 11.2
Jones G 2019 (37)	234	357	15.1	0.9–44	0.9	ADM	NR	NR	DTI: 68
Chopra K 2019 (38)	115	185	Least 6	32–46	NR	ADM	-	NR	TE
Gabriel A 2019 (39)	197	366	21.7±12	12	1.1	ADM	NR	NR	DTI: 84.7; TE: 15.3
Momeni A 2019 (40)	58	99	Nr	23–42	NR	ADM	-	20.6	TE
Kraenzlin FS 2020 (41)	169	267	At least 12	43–60	NR	ADM	-	16.0	TE
Safran T 2020 (42)	201	313	Nr	17.9	NR	ADM [77.6]	NR	18.5	DTI
Casella D 2019 (43)	187	237	36.5 [12–72]	6.7	3.8	TCPM	-	11	TE
Lee JS 2019 (44)	23	NR	12	21.7	4.3	ADM	Textured	8.7	DTI
Salibian AH 2017 (45)	155	250	55.5 [23.6–138]	0.4–4	4	None	-	22.0	TE
Sigalove S 2017 (46)	207	353	26	<5	0	ADM	Textured	8.2	DTI: 11.1; TE: 85.5
Onesti MG 2017 (47)	52	64	24	9.6	0	ADM	Smooth	3.8	DTI
Becker H 2019 (48)	25	37	Nr	40	4	Nothing	Smooth	12	Spectrum

Table 2 (continued)

Table 2 (continued)

Study authors	Patients undergoing PBR, No. [%]	Breasts No. [%]	Follow-up [months]	Overall complication rate	Capsular contracture rate (Becker III– IV)	Implant	Implant surface	Post- mastectomy RT [%]	DTI or expande [%]
Reitsamer R 2019 (49)	134	200	36 [3–68]	14.5	0	ADM [56.5] versus TIGR mesh [43.5]		16	DTI
Nahabedian MY 2020 (50)	90	139	21.6 [12–51.6]	NR	10.1	ADM	Smooth	31.1	TE: 78.9 DTI: 21.1
Woo J 2020 (51)	21	23	11.4	17	NR	ADM	Textured	4.3	DTI
Franck P 2020 (52)	30	66	8.3	13–20	NR	Nothing	-	NR	TE
Gunnarsson GL 2018 (53)	27	47	12 [8.1–17.7]	14.8	NR	ADM/Vic mesh	Smooth: 13; Textured: 87	NR	DTI
Manrique OJ 2020 (54)	40	75	15 [13.5–17]	12.5	0	ADM [47.5]	-	10	TE
Casella D 2019 (55)	179	250	38.5 [24–60]	2.4	2	TCPM	Textured	10	DTI
Fredman R 2019 (56)	94	153	8.5 ±3.9	27	0	ADM	Textured: 11; Smooth: 89	6	DTI
de Vita R 2019 (57)	21	34	4 [2–6]	4.7	0	Nothing	Polyurethane	NR	DTI
Neamonitou F 2020 (58)	41	52	14.3 [6–36]	16	2	ADM	Polyurethane	29	DTI
Comparison between PE	3R and subm	nuscular rec	construction						
Potter S 2019 (11)	42 [2]	63 [2]	3	26	NR	ADM: 54; Synthetic mesh: 12	NR	NR	DTI: 86 TE: 14
Nealon KP 2020 (59)	114 [44.5]	183 [43.5]	19.8±9.9	14	1.8	ADM/vic/vic + ADM	NR	24.6	DTI
Yang JY 2019 (60)	NR	32 [40.5]	11.9	NR	0	ADM	NR	6.3	DTI: 50 TE: 50
Chandarana MN 2018 (61)	61 [46.9]	71 [46]	9.8	5.4	1.6	ADM	NR	31.1	DTI
Antony AK 2019 (62)	31 [48.4]	47 [45.2]	16.5	2	0	ADM	NR	2	DTI
Thangarajah F 2019 (63)	34 [54]	NR	18	35.3	3	NR	NR	8.8	DTI
Sobti N 2020 (64)	20 [42.5]	32 [39.5]	22.9±10	10	30	Vic or Vic + ADM	NR	80	DTI
Mirhaidari SJ 2020 (65)	62 [48]	112 [50]	24	19.6	NR	ADM	NR	9.6	DTI
Viezel-Mathieu A 2020 (66)	39 [50.6]	60 [50.4]	13.6 [±9.7]	25	NR	ADM	Smooth	NR	DTI
Manrique OJ 2020 (67)	33 [44]	55 [36.6]	20.3 [12–27]	7.2	0	ADM	Smooth 33%; Text 67%	5.5	DTI

Table 2 (continued)

Table 2 (continued)

Study authors	Patients undergoing PBR, No. [%]	Breasts No. [%]	Follow-up [months]	Overall complication rate	Capsular contracture rate (Becker III– IV)	Implant	Implant surface	Post- mastectomy RT [%]	DTI or expande [%]
Scheflan M 2020 (68)	49 [38.9]	71 [40.3]	18.6 [±13]	26.8	8.5	ADM	NR	14.5	DTI: 77.5 TE: 22.5
Kim JH 2020 (69)	53 [31.7]	53 [31.7]	Nr	37.7	3.8	ADM	NR	11.3	DTI
Avila A 2020 (70)	116 [50]	203 [50.1]	Least 1	5.9	NR	ADM	NR	NR	DTI: 73.9
Baker BG 2018 (71)	28 [70]	43 [69.3]	Least 3	13.9	NR	ADM	NR	0	DTI: 88.7 TE: 11.3
Cattelani L 2018 (72)	39 [46.4]	46 [46.4]	12 [4–22]	7.7	NR	ADM	NR	13	DTI
Schnarrs RH 2016 (73)	NR	188 [89]	At least 3	19.7	NR	ADM	-	NR	TE: 98
Bettinger LN 2017 (74)	110 [51.6]	165 [56.1]	Minimum 6	13.3	NR	ADM	-	14	TE
Sbitany H 2017 (75)	51 [30.7]	84 [31.1]	11.1±5.8	17.9	NR	ADM	-	8.30	TE
Nahabedian MY 2017 (76)	39 [43.8]	62 [42.7]	8.7 [3–21]	20.5	0	ADM	NR	30.8	TE: 90; DTI: 10
Manrique OJ 2019 (77)	100 [59.1]	187 [60.1]	17.9 [12–24]	10.7	NR	ADM [99.5]	-	17.1	TE
Wormer BA 2019 (78)	32 [31.7]	60 [32.6]	6±3.3	30	NR	ADM	-	21.9	TE
Momeni A 2019 (79)	40 [50]	69 [50]	Nr	32.5	NR	ADM	-	20	TE: 43.6
Gabriel A 2020 (80)	68 [51.1]	129 [50.2]	22.7± 3.5	14.7	0.8	ADM	-	NR	TE
Braun SE 2020 (81)	116 [72.5]	209 [72.5]	16±8.3	24	NR	ADM [98]	NR	6.7	TE: 88; DTI: 12
Walia GS 2018 (82)	26 [19.2]	NR	Least 2	31	NR	ADM	-	12	TE
Copeland- Halperin LR 2019 (83)	94 [61.8]	160 [62]	12	5.3	NR	ADM	NR	NR	TE: 60.2 DTI: 39.8
Schaeffer CV 2019 (84)	24 [33.3]	45 [33.3]	Least 6	21	NR	ADM	-	NR	TE
Radiotherapy after PBR									
Sigalove S 2019 (85)	33	52	25.1±6.4	5.9	0	ADM	NR	65.4	DTI: 36.5 TE: 63.5
Elswick SM 2018 (86)	54	93	19 [1–36]	24.7	1.9	ADM	-	96.4	TE
Sbitany H 2019 (87)	NR	175 [42.6]	9	NR	NR	ADM	-	14.9	TE
Sigalove S 2017 (88)	33	52	25.1±6.4	3.8	0	ADM	NR	65.4	DTI: 36.5 TE: 63.5
Sinnott CJ 2018 (89)	274 [73.2]	426 [72.3]	19±16.9	12	22	ADM	NR	56	DTI
Casella D 2019 (90)	397	521	38	5.8	3.6	TCPM	NR	15.1	TE: 47.1 DTI: 52.8
Polotto S 2020 (91)	160	206	Nr	25.7	1.9	ADM	Textured	84.9	DTI
Secondary PBR									
Gabriel A 2018 (92)	57	102	16.7 [4–65.8]	3.9	0	ADM	-	8.8	TE

Table 2 (continued)

Table 2 (continued)

Study authors	Nr. patients undergoing PBR, No. [%]	Nr. breasts No. [%]	Follow-up [months]	Overall complication rate	Capsular contracture rate (Becker III– IV)	Implant	Implant surface	Post- mastectomy RT [%]	DTI or expander [%]
Lentz R 2019 (93)	31	55	8.3 [1.1–26.9]	14.5	7.3	ADM	Smooth	NR	DTI
Jones GE 2019 (94)	90	142	19.2	9.1	0	ADM	NR	NR	DTI
Sigalove S 2019 (95)	64	124	18.9±11	3.2	0	ADM + mesh P4HB	Smooth	4.8	DTI
Holland MC 2020 (96)	45	80	15.2 [± 7.14]	42.5	6.3	ADM	NR	12.5	DTI
PBR following skin-redu	cing mastect	omy							
Manrique OJ 2020 (97)	9	17	23.5 [17–55]	12	0	ADM	-	NR	TE
Caputo GG 2016 (98)	27	33	14.7 [6–24]	11.2	NR	ADM	Textured	0	DTI
Becker H 2018 (99)	20	36	Nr	45	NR	Nothing	-	NR	TE
Komorowska-Timek E 2019 (100)	24 [44.4]	42 [48.2]	9.6 [0.7–26.4]	40.5	2.7	Nothing	-	62.5	TE
Thuman J 2019 (101)	21	37	7.76 [3–17]	30	NR	ADM [32.4]	Smooth	33.3	TE
Khalil HH 2019 (102)	8	16	12 [3–24]	0	NR	ADM	NR	NR	DTI
Onesti MG 2020 (103)	10	13	31 [24–39]	10	0	ADM	NR	0.3	DTI
Maruccia M 2020 (104)	19	23	23.2 [±3.4]	21	0	ADM	Smooth	13	DTI
Hybrid PBR									
Momeni A 2018 (105)	23	46	8.4 [2–17]	38	NR	ADM	Smooth	30.4	DTI
Stillaert FBJL 2020 (106)	33	56	24.1 [6–54]	12	0	None	-	27	TE
Momeni A 2019 (107)	31	62	7.3 [2–12]	32	NR	ADM	-	NR	TE

Spectrum: it is an inflatable breast implant having a detachable filling reservoir, that can be filled under controlled conditions postoperatively. This implant functions either as a tissue expander or as a delayed-filling implant. Once the desired breast size is achieved, the reservoir is removed, leaving the filled implant in position. PBR, pectoral breast reconstruction; RT, radiotherapy; DTI, direct to implant; NR, not reported; ADM, acellular dermal matrix; TCPM, titanium covered polyurethane mesh; TE, tissue expander (or 2 stage reconstruction); vic, vicryl mesh.

was no capsular contracture. Even when only one surgeon's experience was described, the complication rate was still acceptable. Similarly, Safran *et al.* (42) reported a minor complication rate of 9.3% and the major complication rate was 8.6%.

Studies included in this subgroup included different types of implants (anatomical or round) and implant surfaces (smooth or textured), whilst De Vita (57) and Neamonitou (58) used implants with a polyurethane-foam coated surface. The polyurethane-foam coated implants are breast implants coated with micro-polyurethane foam, which minimizes the capsular contracture rate to 0-3% (113-115). The low capsular contracture rate is attributed to the internal growth and microencapsulation of fibroblasts in the polyurethane foam matrix. Unlike implants with both smooth and textured surfaces where a single large capsule is created around, implants covered with micro-polyurethane foam favor the growth of numerous microcapsules around the foam, which is why the contractile forces are neutralised. De Vita *et al.* (57) reported their preliminary experience with micropolyurethane-foam coated breast implants placed in the pre-pectoral position without any type of covering.

The results of 21 patients were encouraging: no major complications, good aesthetic results and excellent patient satisfaction.

Despite the fact that most authors in this subgroup used a coverage device, Manrique *et al.* (54) reported the Mayo Clinic's experience on a series of pre-pectoral implant-based breast reconstruction with and without ADM and compared their outcomes. Twenty-one patients reconstructed without the use of meshes had equally good results compared to prepectoral reconstruction with mesh, additional to reduced cost and operating time.

Comparison between PBR and submuscular reconstruction

Several cohort studies reported positive outcomes of breast reconstruction with a pre-pectoral implant, with complication rates comparable to that of reconstruction with a subpectoral implant. Braun *et al.* (81) reported a retrospective series of patients undergoing nipple sparing mastectomy and immediate breast reconstruction in either the pre-pectoral or submuscular plane from January 2015 to June 2019. A total of 288 breasts (160 patients) were included. Overall, the rate of nipple-areola complex necrosis was 15.1%, with no differences between the two cohorts (P=0.79). Similarly, there were no significant differences in overall postoperative complications (P=0.46), including hematoma, seroma, infection, and device exposure.

In 2020, Nealon et al. (59) concluded that pre-pectoral direct-to-implant reconstruction is a safe alternative to subpectoral direct-to-implant reconstruction and that, given the low morbidity and elimination of BAD, it should be considered when the mastectomy skin flap is robust. In fact, their cohort of 114 pre-pectoral versus 142 subpectoral direct-to-implant patients, the results of the penalized regression model demonstrated equivalence in safety metrics including seroma, cancer recurrence, explantation, capsular contracture, mastectomy skin flap necrosis, infection, hematoma, and revision (P>0.05). Similarly, Bettinger et al. (74) demonstrated that pre-pectoral and subpectoral (with or without ADM) breast reconstructions had comparable grade IIIb Clavien score complications. Furthermore, this study showed that BMI >40 kg/m², stage IV cancer, and contralateral prophylactic mastectomy were associated with adverse expander outcomes and a prior history of radiation therapy adversely impacted implant outcomes.

Overall, PBR can be performed safely and with significantly less pain and earlier return to routine activities

compared to submuscular implant placement. In fact, Schaeffer et al. (84) showed that comparing postoperative pain and early functional outcomes between pre-pectoral and partial submuscular breast reconstruction, the first group had significantly lower inpatient pain scores, required significantly fewer intravenous opioids, fewer oral opioids as outpatients, and returned to full active range of shoulder motion in half time. Also, Copeland-Halperin et al. (83) reported a reduced demand for opioids: the pre-pectoral reconstruction group remained for 33% fewer days on opioid analgesic medication (P=0.016) and were 66% less likely to require opioid prescription refills (P=0.027). Therefore, immediate pre-pectoral reconstruction resulted in lower pain intensity and significant upper limb functional advantages in addition to considering a series of ascertained benefits, economically advantageous (72).

To date, further evidence supporting pre-pectoral reconstruction over subpectoral are awaited from ongoing randomized controlled trials (ClinicalTrials. gov Identifier: NCT04293146; ClinicalTrials. gov Identifier: NCT05125991; ClinicalTrials. gov Identifier: NCT04688697; ClinicalTrials. gov Identifier: NCT03959709; ClinicalTrials.gov Identifier: NCT04391296; ClinicalTrials.gov Identifier: NCT04716959). They are going to investigate improvements in arm mobility, quality of life, aesthetic outcomes, complication rate and recurrence risk. Additionally, good quality data will also come from the prospective multicenter cohort study Pre-BRA, setting the basis for a future pragmatic randomized trial (116).

Radiotherapy after PBR

Studies included in this subgroup showed that postmastectomy radiotherapy appears to be well tolerated in immediate PBR with no great adverse effects. Sbitany *et al.* (87) reported on 57 breasts receiving postmastectomy radiotherapy and found no difference in complication rates between pre-pectoral and subpectoral implant-based breast reconstruction. In general, the capsular contracture rate after submuscular reconstruction is three times greater and with more severe contractures (Baker grade 3 or 4) than after PBR and adjuvant radiotherapy (89).

In 2019, Casella *et al.* (90) conducted a retrospective comparative analysis of risk factors and outcomes between patients undergoing direct to-implant and patients undergoing two stages expander-assisted pre-pectoral reconstruction. The binary logistic regression found no

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significant association between the rate of surgical and aesthetic complications with any other variables considered, in the tissue expander group. Furthermore, in the direct-toimplant group, a significant association was found between surgical complications and BMI and adjuvant radiotherapy. However, the association remained significant only for BMI, when correlated with the aesthetic outcome.

Secondary PBR

PBR is often proposed as a secondary procedure in order to correct BAD and capsular contracture, by changing the implant pocket from underneath to over the muscle. The dramatic improvement in aesthetic outcome with PBR, in particular as regards the reduced animation deformity, improved inframammary fold definition and the postoperative comfort with enhanced shoulder range of motion, triggered an interest in the concept of prepectoral conversion as a means of dealing definitively with the problem of animation deformity in the subpectoral patient population. BAD is an almost universal problem that causes patients embarrassment and often discomfort on a daily basis. Previous attempts of ameliorating BAD with fat grafting had mixed results and have never eliminated the deformity at all. Additionally, fat grafting had no impact whatsoever on patient comfort and physical function whilst PBR did. Jones et al. (94) reported their experience with 142 breasts in 90 patients who had undergone elective subpectoral to pre-pectoral implant site conversion. Postoperative resolution of BAD was 100%, the overall complications rates were 4.2% for infection, 2.1% for seroma, and 0.7% for hematoma, dehiscence, partial thickness necrosis, and explantation; therefore, Baker grades II-IV capsular contractures were 0% at 43 months.

A retrospective study including patients who previously had undergone subpectoral (dual plane), implantbased, breast reconstruction and presented for revision reconstruction was published by Sigalove *et al.* (95). Reasons for revision included animation deformity, pain, asymmetry, implant malposition, size change, capsular contracture, and rippling. A total of 64 patients (124 breasts) met the inclusion criteria and complications occurred in 4 breasts (3.2%), included implant loss (1.6%), seroma (1.6%), hematoma (0.8%), surgical site infection (0.8%), and skin necrosis (0.8%). There was no incidence of capsular contracture, and the presenting complaints were resolved in all cases.

Also, Gabriel et al. (92) solved successfully 102 cases

of BAD post-subpectoral implant placement. In this case series, complications occurred in 4 breasts (3.9%) and included seroma (2 breasts), skin necrosis (3 breasts), and wound dehiscence (1 breast). All 4 breasts with complications had their implants removed and replaced. There was no infection or clinically significant capsular contracture, on the contrary, the patient selection was deemed again to be critical for the success of this technique.

PBR following skin-reducing mastectomy

In PBR, a breast prosthesis is placed in the subcutaneous plane, practically replacing the removed breast tissue. Although such an approach represents an attractive strategy in small/moderate breasts, it is not applicable in large and/or severely ptotic breasts, where a skin reduction is required. A Wise mammoplasty pattern with a deepithelialized dermal sling and submuscular direct-toimplant has been described by Nava et al. (117) to optimize implant-based reconstruction in this patient population. The original technique of immediate breast reconstruction following skin reduction mastectomy was associated with a substantial risk of implant exposure at the inframammary fold. The reason for this complication stemmed from the fact that the inferior portion of the implant was located directly under the inverted "T" incision line, which frequently experiences malperfusion and breaks down (118). The technique was further modified by Bostwick who utilized the deepithelialized inferior breast skin to enhance the coverage of the implant under the troublesome skin juncture (119). In this approach, the superior edge of the deepithelialized skin flap was sutured to the inferior edge of the raised pectoralis major muscle, creating thus a separate well-vascularized implant pocket (119,120). Although the risk of implant exposure decreased with the use of the inferior mastectomy skin flap, the drawbacks associated with subpectoral implant placement persisted. Moreover, although enhanced tissue padding over an implant is frequently desired, additional soft-tissue boost consisting of superiorly located pectoralis muscle does not protect against ischemic complications occurring mostly in the inferior portions of the reconstructed breast.

Therefore, some authors hypothesized that immediate PBR following skin reduction mastectomy could have similar outcomes to the subpectoral counterpart. In fact, Komorowska-Timek *et al.* (100), compared the complications of pre-pectoral and subpectoral immediate prosthetic breast reconstructions following skin reduction mastectomy in large and ptotic breasts. A total of 54 patients underwent 87 immediate breast reconstructions including 45 subpectoral and 42 pre-pectoral tissue expander placements. The subpectoral patients had more skin flap necrosis (40.0% versus 16.7%, P=0.044) and infections (37.8% versus 11.9%, P=0.01) than their pre-pectoral counterparts, whereas seromas were more common in the pre-pectoral group (4.4% versus 26.2%, P=0.015). The overall complication rate, although higher in the subpectoral group, was not significantly different (62.2% versus 40.5%, P=0.072).

A further advance in the skin-reducing PBR approach was proposed by Caputo *et al.* (98), who suggested creating a complete pre-pectoral pocket with a dermal flap along with ADM for lower- and upper-pole coverage, respectively, achieving promising results: in only 3 cases (out of a total of 33 breasts), there was skin ischemia, one healed spontaneously, while two patients underwent a minor surgical revision. No implant loss occurred.

Finally, Thuman *et al.* (101) demonstrated that a prepectoral, two-stage breast reconstruction with Wise pattern skin reduction can be a suitable option in patients who have a high BMI.

Hybrid PBR

The hybrid PBR promises to be the next frontier of PBR as it aims at combining the natural effect of autologous reconstruction (i.e., free flaps or fat grafting) with the comfort of a PBR as the transfer of soft tissue allows to reconstruct a natural breast ptosis and the addition of an implant provides the desired projection (105). In particular, this solution could ameliorate the breast profile when the mastectomy flap is too thin and the implant upper pole is visible or the rippling occurs. Stillaert et al. (106) performed 56 hybrid breast reconstructions with good aesthetic outcomes and patient satisfaction showing pleasant breast projection, natural breast motion, and optimal coverage of the pre-pectoral implants. The complication rate was 12.1% and no patients reported capsular contraction, rippling, or major discomfort at a median follow-up of approximately 24 months. Their hybrid approach was based on placing a tissue expander in the first procedure followed by serial sessions of fat grafting to augment the residual autologous (subcutaneous) compartment and the second step foresaw the insertion of a pre-pectoral, ergonomic implant to obtain central core projection and additional volume.

Momeni et al. (105), instead, preferred to combine

autologous reconstruction with free flaps and PBR planning a two-step procedure in one or two stages. In detail, they reported results from a retrospective analysis of 23 patients (46 free flaps) who underwent immediate microsurgical breast reconstruction with an autologous free flap and the simultaneous pre-pectoral implant placement. Postoperative complications were acceptable, including hematoma (4.3%), mastectomy skin flap necrosis (21.7%), fat necrosis (13%), and delayed wound healing at the flap donor site (17.4%). Furthermore, in another study (107) they showed that a delayed-immediate hybrid breast reconstruction improves the ability to match patient expectations related to breast size and that it is associated with a reduction in the rate of mastectomy skin necrosis. This technique consists of a stage 1, in which it is placed bilateral pre-pectoral tissue expander with ADM, and of a stage 2, in which bilateral pre-pectoral expander was replaced with a free abdominal flap with simultaneous silicone gel implant placement, thus obtaining a better patient satisfaction and reduced skin flap necrosis (0%).

Discussion

Breast reconstruction is an essential component in the surgical treatment of women with BC and the main step in ensuring a good quality of life. Good breast reconstruction after mastectomy has a positive impact on the patient's psychological recovery (121). So far, pre-pectoral breast reconstruction is the easiest way to reconstruct the breast with an implant, as it replaces the missing volume exactly where it was removed. This type of breast reconstruction presents several advantages: the surgical technique is simple and minimally invasive (45), the duration is relatively short (26), blood loss is limited, the muscle function is preserved (32) and the BAD is absent (21). Consequently, the pain is milder, easily controlled (75), in addition to a more rapid recovery time after surgery (30).

Ideal indications for pre-pectoral breast reconstruction are: immediate breast reconstruction, immediate-delayed breast reconstruction following neoadjuvant therapy, delayed breast reconstruction, risk-reducing surgery, breast revision surgery for animation, capsular contracture, breast deformity, muscular problems associated with submuscular implant reconstruction (108).

The surgical procedure requires particular attention to specific surgical steps in order to minimise the risk of complications. In fact, patient selection (*Figure 2*) is crucial for the success of the operation, and the presence of risk factors is associated with an increased risk of adverse

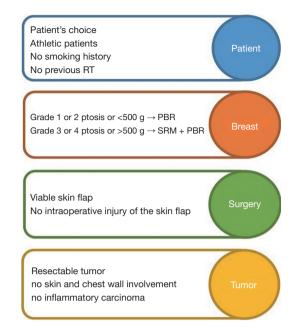


Figure 2 Ideal selection criteria for PBR-RT, SRM. RT, radiotherapy; PBR, prepectoral breast reconstruction; SRM, skin reducing mastectomy.

events (34). Theoretically, the ideal conditions to choose a PBR have been reported by Vidya et al. (108). The authors reported that this procedure should be offered to patients who are fit and well, with no major or well-controlled comorbidities, body mass BMI index <35 kg/m², no previous radiotherapy damage, no current smoking, mild ptosis, medium-sized breast (<500 g for one-stage, >500 g for twostage procedures) and with a resectable tumour not invading skin/chest wall. However, elevated BMI (>40 kg/m²), poorly controlled diabetes mellitus, immunosuppression and previous radiation damage should be considered as relative contraindications (23,46,110). In practice, reviewed studies showed that PBR can be considered for all patients who are candidates for breast reconstruction with implants after mastectomy for cancer or risk reduction, even though risks and benefits must be always well balanced and discussed with the patient (32,59,122). On a technical level, the preservation of the subcutaneous layer of the mastectomy flap and perforator vessels is the key to success. In particular, the vascularity can be assessed intra-operatively by clinical observation (capillary refill time, skin color, texture and temperature, dermal bleeding), or by using special devices such as the SPY Elite System (37,97,104) or other perfusion imaging technology (42). If the flap perfusion is compromised, another type of breast reconstruction

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should be chosen (30,35). As a result, PBR could be always considered as a reconstructive option in breast surgeon's armamentarium when a simple natural-looking and fast-recovery procedure is required, but both the surgeon and the patient should be well aware that in patients who do not fulfill the ideal selection criteria the risk of complications is much higher.

Patients can receive antibiotic prophylaxis at the time of induction of anaesthesia (26,35) or postoperatively, antibiotics administered after stratification of infectious risk or according to hospital policy (47,103). Drains should be placed in all patients and removed when the daily output is less than 10–30 mL/day or at the surgeon's discretion (34). The type of postoperative dressing is determined by the surgeon's preference (108).

In almost all revised papers, a wide variety of biological matrices and synthetic meshes have been used. The use of meshes and matrices has allowed better control of the implant position, a better definition of the inframammary fold, a reduction in the capsular contracture rate due to a reduced inflammatory response (30,123), and in general, an improvement in aesthetic results (113,114,124). Matrices have also been used in the 'two-stage' reconstructions with tissue expander (115,125), allowing a greater initial expander filling and faster expansion. However, a systematic review has shown that breast reconstruction with mesh and matrices significantly increases the rates of seroma, infection and reconstruction failure, compared to procedures without these devices (126). In a further study of 415 reconstructions with implants, the risk of infection was shown to increase 5-fold with the use of ADM (127). Furthermore, the use of no ADM reduces costs and operative time (54,57). As a result, some authors do not use any device to cover the implant or expander in PBR (45,48,52,54,57,99,100). In particular, De Vita et al. (57) used implants with micropolyurethane surface, which represent an integrated ready-to-use device without need further coverage, obtaining the benefits of a coverage (greater biocompatibility, increase in the thickness of the flap), but using only one device (reduced cost and operative time). Other authors, instead, positioned implant or expander without any coverage directly under the skin flap. Their data demonstrated no significant differences in aesthetic scores and in postoperative complications. Therefore, this alternative technique has shown promising results, although data available, follow-up duration and sample size are still limited to derive strong recommendations. However, waiting for stronger evidence, we are not able to define

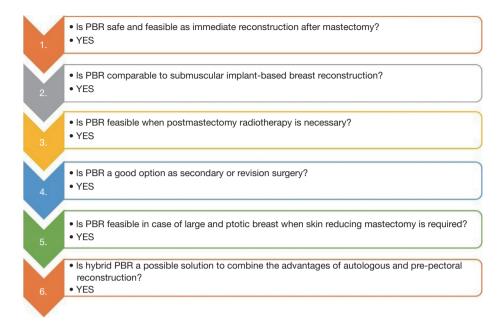


Figure 3 Concepts of pre-pectoral breast reconstruction: take-home messages. PBR, prepectoral breast reconstruction.

whether the ADM will fall into disuse.

The strength of this study is evident by the supporting fonts of comprehensive data regarding a relatively new technique that has emerged and spread in the last five years, focusing on special issues related to this procedure. The complication profile, the comparison with the standard twostage breast reconstruction, radiotherapy issues, the option for revision surgery and the possibility of PBR after skinsparing mastectomy or like a hybrid operation represent fields of great interest for the breast surgeon who applies or is going to start applying this technique. However, the main limitation of this review is that it is not systematic and includes only studies from 2016 to 2020, therefore the available follow-up is often relatively short.

To summarize, reviewed studies showed that (*Figure 3*):

- (I) PBR, despite being a relatively new technique, has rapidly become widespread and numerous case series have been published. The evidence available demonstrates that PBR is safe and feasible with the use of meshes but they could eventually be abandoned in the future if preliminary data will be confirmed.
- (II) The complication profile is not inferior to subpectoral reconstruction and is absolutely better in terms of pain and animation deformity, ongoing randomized controlled trials will give further evidence about this.

- (III) Regarding the special setting of post-mastectomy radiotherapy after PBR, it is well tolerated in immediate PBR with no great adverse effects, in fact, the capsular contracture rate is three less great than after submuscular reconstruction and radiotherapy.
- (IV) PBR could be a useful and good alternative to standard subpectoral reconstruction in case of suboptimal aesthetic results or complications or patient unsatisfaction instead of recurring of opting for autologous reconstruction.
- (V) The application of the skin reducing mastectomy pattern to PBR allows extending the indication to PBR to patients having large and ptotic breasts with results comparable to subpectoral reconstruction also providing a dermal sling to cover the inferior pole in place of meshes.
- (VI) Hybrid PBR looks at the future combining the natural effect of autologous reconstruction with the comfort of a PBR. It could allow correcting common complications after PBR like rippling or the visibility of implant upper pole by improving the breast profile. However, data is still too limited to derive meaningful conclusions.

Conclusions

Until a few years ago, subpectoral implant placement

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was undoubtedly the gold standard for implant-based breast reconstruction. Recently, considerable attention has been paid to performing immediate and delayed reconstruction with the implant in the pre-pectoral position thus overcoming many of the complications associated with subpectoral implant positioning. Although minor complications are quite frequent after PBR, they could be managed conservatively and this remains a promising technique, which gives women natural-looking breasts immediately after mastectomy. The procedure is technically simple minimally invasive, has an acceptable complication rate, and is becoming more and more popular. Although there are ideal candidates, indications can be extended also in cases of relative contraindications while still obtaining a safe complication profile even in special settings such as: when postmastectomy radiotherapy is needed, as a secondary procedure after a previously failed or complicated implant reconstruction, in large or ptotic breast requiring ski-reducing mastectomy or in combination with autologous reconstruction in order to ameliorate the breast profile.

To date, PBR should definitely be included in the breast surgeon's armamentarium of reconstructive procedures as it offers a relatively simple and quick one-step solution to restore the breast immediately after mastectomy.

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