Review Article

Immediate direct-to-implant breast reconstruction with prepectoral *vs.* subpectoral approach: a narrative review

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Background and Objective: We are still far from define a gold standard for reconstruction procedures after mastectomy for breast cancer and this review aim to investigate current literature to offer a wide point of view on the most performed approaches and their evolution. The use of skin sparing (SSM) and nipple sparing (NSM) mastectomies has risen significantly during the last few years and this is strictly lead to the possibility of immediate breast reconstruction (IBR). Direct-to-implant (DTI) breast reconstruction could be performed both with a sub pectoral and a pre pectoral approach: in the past the most commonly used approach was a subpectoral dual plane technique which gained popularity for the low incidence of complications and good cosmetic results.

Methods: Current literature was reviewed to analyze outcomes from both sub and prepectoral approach: the research was performed all electronic databases (PubMed, Web of Science, Scopus, EMBASE) until December 2021 and only studies written in English language were selected.

Key Content and Findings: Prepectoral IBR (PBR) was widely used as reconstruction approach after radical mastectomy until evidences underlined a high incidence of complications; to avoid this setting, submuscular reconstruction started to be carried out, recruiting the pectoralis major and serratus anterior muscle for a total implant coverage. The transition from radical to NSM has upset the reconstructive point of view, allowing surgeons to perform IBR with skin flap viability; moreover, the utilization of new surgical materials have converged to optimize prepectoral reconstructive outcomes.

Conclusions: Although it is evident that there is still no gold standard, current literature seems to veer towards the choice of a prepectoral strategy for IBR; this technique appears to be safe, reliable, with equivalent results to other reconstructive possibilities. Accurate evaluation of patients' characteristics and patient wish will ultimately drive the reconstructive choice.

Keywords: Breast reconstruction; subpectoral breast reconstruction; prepectoral breast reconstruction

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Introduction

The growing adoption of skin sparing mastectomy (SSM) and nipple sparing mastectomy (NSM) during the last few years is strictly related to the possibility of direct-to-implant (DTI) reconstruction which has become more feasible with modern mastectomy techniques (1). Nowadays, considering its oncological safety, immediate breast reconstruction (IBR) is considered indispensable in the surgical management of breast cancer patients (2).

The psychological impact of mastectomy, which is lead to body image disruptions and negative impact on sexual well-being, took advantage by the opportunity of one-stage procedures, with breast demolition and reconstruction in the same operative episode (3).

Immediate reconstruction is considered technically and economically more advantageous than a delayed procedure; moreover, from a psychological point of view, patients can benefit from immediate reconstruction both for a greater sense of self-esteem and for a better body posture (4).

DTI breast reconstruction could be performed with both a sub pectoral and a pre pectoral approach: in the past the most commonly used approach was a sub pectoral dual plane technique which gained popularity for the low incidence of complications and good cosmetic results (5); recently, pre pectoral approach has gained popularity in the field of implant-based breast reconstruction, with successful progresses represented by the evolution in the use of acellular dermal matrix (ADM) (6,7).

We are still far from define a gold standard for reconstruction procedures after mastectomy for breast cancer and this review aim to investigate current literature to offer a wide point of view on the most performed approaches and their evolution. We present the following article in accordance with the Narrative Review reporting checklist (available at https://abs.amegroups.com/article/view/10.21037/abs-21-150/rc).

Methods

To identify the "state of art" about DTI IBR, research was performed in all electronic databases (PubMed, Web of Science, Scopus, EMBASE). We used medical subject headings (MeSH) and free-text words using the following search terms in all possible combinations: "breast cancer", "prepectoral implant", "subpectoral implant", and "breast reconstruction". The last search was performed in December 2021.

Inclusion criteria regarded all studies reporting on DTI IBR for breast cancer. The search strategy was limited to articles written in English language; moreover, papers regarding animal studies, editorials and case series with less than 10 patients were excluded (*Table 1*).

Oncological safety of SSM and NSM

Oncological safety of SSM has been widely discussed: some authors analyzed skin flap specimens after SSM studying the residual breast tissue and they found 9.5% of skin flaps with residual disease, concluding that skin flaps thicker than 5 mm were associated with the presence of residual disease (8,9). On the other hand, Rocco *et al.* (10), in their review on 58 studies, found the rate of local recurrence (LR) following SSM range from 0% to 7%; considering the LR rates after non-SSM in tumors up to 4 cm was shown to be 10% after 20 years of follow-up (11), authors concluded SSM do not compromise the oncological safety of mastectomy. Similarly, Slavin and colleagues found no recurrences at a follow-up of 45 months after SSM in 26 cases with ductal carcinoma *in situ* (12).

About NSM, many studies reported data on the pathological involvement of the nipple, with the incidence ranging from 5.6% to 31% (13,14). Benediktsson *et al.* (15) reported a LR rate of 20.8% at a mean follow-up time of 13 years in patients treated with NSM but no patients had recurrences at the Nipple-Areolar Complex (NAC). Moreover, authors found a statistically significant reduction in the LR when adding post-mastectomy radiotherapy to NSM. Similarly, Gerber *et al.* provided data at a follow-up of 10 years, finding only one NAC recurrence out of 112 NSMs performed, without statistical significance in overall LR between NSM and radical mastectomy (16). Even if no high-level evidence is available in literature, NSM has been considered safe for the treatment of breast cancer, without absolute contraindications, except for the direct invasion of retroareolar ducts and inflammatory breast cancer, as recently confirmed in an International consensus conference (17).

DTI breast reconstruction: indications, major contraindications and possible complications

In the last 40 years, breast reconstruction was based on the utilization of tissue expanders in a two-stage reconstructive program which included the recovery of the skin lost after mastectomy; the introduction of new mastectomy techniques, oriented to preserve larger amounts of skin as

Table 1 The search strategy summary

Items	Specification
Date of search	15 December 2021
Databases and other sources searched	PubMed, Web of Science, Scopus, EMBASE
Search terms used	"breast cancer", "prepectoral implant", "subpectoral implant", "breast reconstruction"
Timeframe	Until December 2021
Inclusion and exclusion criteria	Inclusion criteria: all studies reporting on Direct-to-implant immediate breast reconstruction for breast cancer were included. The search strategy was limited to articles written in English language
	Exclusion criteria: papers regarding animal studies, editorials and case series with less than 10 patients were excluded

in the case of NSM, DTI reconstruction has become more practicable (18).

DTI IBR aims to create a more naturally breast appearing with a single-stage surgery: this became necessary following advances in screening tests and molecular genetics which lead to an increase in breast cancer diagnosis, also in young women, and to an easier assess of inherited predisposition for breast cancer. These conditions enhanced the request for therapeutic or prophylactic mastectomy.

Implant-based reconstructions have become the most performed approach since 2008 and constitute about 65% of reconstructions with the advantages of preserving the skin envelope and allowing the patients to undergo chemotherapy without delay (19,20).

Bilateral or unilateral breast reconstruction have their best indication in small and medium-sized breasts; for large breasted patients, although an implant-based reconstruction may be offered, they are candidate for skin/breast reduction and contralateral surgery which may lead to mastopexy, reduction, or augmentation to achieve bilateral symmetry (21).

High body mass index, history of smoking, scleroderma and pre-operative radiation are risk conditions for implant loss (22,23); by this point of view, previous radiotherapy can lead to implant infection and extrusion and for these patients an autologous tissue reconstruction should be proposed (24). Actual evidences indicate that skin-flap necrosis is the most common major complication (10.9%), followed by seroma (6.9%), infection (5.7%), cellulitis (2%), and hematoma (1.3%); implant removal is generally necessary in 5.1% of cases (25-27).

DTI IBR have demonstrated a similar rate of postoperative complications when compared to two-stage tissue expander/implant-based breast reconstructions: a recent meta-analysis underlined that rates of infection (7.8% *vs.* 7.4%), seroma (6.8% *vs.* 7.1%), hematoma (4.3% *vs.* 5.2%), and capsule contracture (13.5% *vs.* 13.8%) did not significantly differ between DTI and two-stage tissue expander/implant-based reconstructions (28). Similarly, Jagsi and colleagues demonstrated, on a series of 14,894 women who received DTI IBR *vs.* autologous reconstruction, that patients with autologous reconstruction had higher wound complication rates (9.5% *vs.* 4.4%) and higher infection rates (20.7% *vs.* 20.5%) (29).

Per-operative imaging in implant-based breast reconstruction

The pre-operative assessment of a women who will undergo implant-based breast reconstruction should include the evaluation of the thickness of subcutaneous tissues at digital mammography and MRI and the pattern of vascularity at MRI (30-32).

Frey and colleagues reported that ischemic complications after NSM are significantly associated with thinner postoperative NSM flap thickness. In particular NSM flap thickness less than 8 mm is a positive independent predictor of ischemic complications (30). The ratio of post-operative to preoperative NSM flap thickness was significantly lower in reconstructions with ischemic complications. Rancati and colleagues proposed the breast tissue coverage classification (BTCC) at digital mammography (31). They consider three types of breasts on the basis of the thickness of subcutaneous tissues: type 1 (less than 1 cm); type 2 (1–2 cm) and type 3 (more than 2 cm). The authors conclude that patients with a type 3 breast will have reduced risk of

immediate ischemic complications following NSM and DTI immediate reconstruction.

The best reconstructive approach for each type of breast according to the BTCC in order to improve outcomes has been described by Nava and colleagues (33), with a standard two stage approach being preferable for type 1 breasts, one stage sub-pectoral ADM-assisted for type 2 breasts and one-stage pre pectoral ADM-assisted for type 3 breasts. Bahl and colleagues have described three patterns of vascularity at MRI: (I) dual blood supply with co-dominance of the medial and lateral vessels; (II) dual blood supply with dominance of the medial vessel; (III) single blood supply (32). The authors reported that ischemia or necrosis after NSM was less likely to occur in breasts with dual compared with single blood supply (20.8% *vs.* 38.2%; P<0.03).

Intraoperatively the assessment of mastectomy flap perfusion with indocyanine green angiography (ICGA) could be a useful tool to predict the rate of flap ischemia or necrosis. ICGA can reduce postoperative tissue loss and aid in intraoperative flap design and inset. Anyway, despite the benefits of ICGA, its technical use and interpretation have yet to be standardized, limiting its widespread acceptance (34).

Reconstruction in the setting of post-mastectomy radiation

Post mastectomy radiation therapy (PMRT) is known to enhance the oncological outcome of patients with T3/T4 breast cancer or more than three positive axillary lymph nodes (35,36).

Although there is a general agreement on the possibility to delay breast reconstruction in patients who require post mastectomy radiation therapy, the increasing experience with implants and improved implant technology, such as the use of acellular dermal matrices, changed this point of view, opening to option for implant-based reconstruction also in patients planned for post mastectomy radiotherapy (37-40).

Recent reviews underlined that pre-pectoral breast reconstruction with acellular dermal matrices in case of PMRT is a safe surgical option: Graziano *et al.*, pooling data from 175 breasts with a mean follow-up of 18 months, found a total of 3 (1.7%) hematomas, 4 (2%) seromas, 32 breasts with infections (18%), 9 (5.1%) cases of wound dehiscence and a total of 22 (12.6%) implants loss (41).

Apte *et al.*, in their trial on 91 consecutive patients who underwent DTI breast reconstruction with ADMs using sub-pectoral or pre-pectoral approach, found that the RT group had 3–7% of early complications like seroma, wound infections and delayed healing, with 20.7% of capsular contractures; in the non-RT group, 7–9% cases had seroma or wound infections, 3.06% had delayed wound healing and 7.25% had capsular contracture (42).

Prepectoral *vs.* subpectoral approach

Prepectoral IBR (PBR) was first reported in 1971 and widely used as reconstruction approach after radical mastectomy until evidences underlined a high incidence of complications, varying from capsular contracture to skin necrosis and implant extrusion, particularly related to the lack of tissue coverage (43). To avoid this issues, submuscular reconstruction started to be carried out, recruiting the pectoralis major and serratus anterior muscle for a total implant coverage. However, this approach, with the manipulation of the pectoralis muscle, is not without consequence: major recurrent problems were pain and animation deformity (44,45).

The transition from radical to NSM in the last 20 years transformed the reconstructive point of view, allowing surgeons to perform IBR with good skin flap viability (46); moreover, recent tissue vascularization imaging techniques and the utilization of new surgical materials have converged to optimize pre pectoral reconstructive outcomes (47,48). By this point of view, the need for total sub muscular coverage was widely substituted by the introduction of acellular dermal matrices and biological or synthetic meshes (49-53). The widespread application of ADM has contributed to significantly reduce the rate of capsular contracture also in PBR technique and this is probably due to the reduction in granulation tissue formation in a setting which allow to avoid skeletal muscle fibrosis (54). ADMs varies from human to bovine or porcine-derived tissues underwent a biotechnology processing which removes cellular antigens to avoid antibody response accountable for rejection but, at same time, it allows to maintain a structural matrix that promotes tissue regeneration (55). Verdanian and Kim firstly reported on ADM outcomes in reducing complications related to PBR (capsular contracture ADM *vs.* non-ADM, OR: 0.18) and found that the levels of myofibroblasts were significantly lower in ADM capsules than in submuscular capsules (56,57). Since pre-pectoral breast reconstruction has gained new popularity, several techniques have been introduced to cover the implant with ADM: (I) covering the anterior profile of the device; or (II)

complete coverage of both the anterior and the posterior surfaces of the implant with ADM before its insertion (58).

According with Li *et al.* recent review (59), pre pectoral reconstruction shows the advantage of placing the implant in the anatomical position of breast tissue; authors reported no differences in overall complication rate between PBR and SBR approach (OR: 0.93), particularly in terms of implant loss (OR: 0.99), seroma/hematoma (OR: 2.41/1.77), re-operation (OR: 0.99), wound dehiscence (OR: 1.73) or infection (OR: 0.67). They also found PBR determines fewer nipple and skin flap necrosis when compared with tissue expander (OR: 0.48) and fewer capsular contracture rates in case of implant (OR: 0.16). Finally, they underlined PBR has less postoperative pain with a good oncological outcome which is not burdened by a higher rate of LR. Similar results were found by Sbitany *et al.* (60), who compared complications rates between immediate pre pectoral tissue expander placement and immediate partial submuscular expander placement (17.9% *vs.* 18.8%), concluding that no differences were recorded between the two groups. Data from 654 breast underwent PBR were recently pooled by Chatterjee and colleagues (61), concluding that complication rates are comparable following pre pectoral and dual-plane reconstruction (infection, OR: 0.46; explantation, OR: 0.83; necrosis, OR: 1.61; seroma, OR:1.88; dehiscence, OR: 1.84; capsular contracture, OR: 0.14), indicating the pre-pectoral technique is a safe and feasible option.

The Italian multicentric experience from Ribuffo *et al.* on 716 DTI reconstructions, showed seroma, hematoma and surgical site infection were the most common postoperative complications observed and were more frequent after a dual-plane retropectoral reconstruction when compared with a pre pectoral implant (seroma: 4.34% *vs.* 11.2%; hematoma: 1.45% *vs.* 4.71%; surgical site infection: 1.93% *vs.* 3.93%; capsular contracture: 8.7% *vs.* 13.87%); moreover, pre pectoral approach had a lower rate of animation deformity with better aesthetic, clinical and functional outcomes (62).

Also King (63) in a recent retrospective review of 405 cases of NSM with IBR demonstrated that prepectoral reconstruction have a significantly reduced prosthetic failure rate compared with subpectoral reconstruction (OR: 0.30) and prepectoral patients experienced decreased animation deformity (19.7% *vs.* 0%).

Interestingly, Walker *et al.* (64) compared the two reconstructive approaches in high-body mass index patients (BMI >35 kg/m^2) recording no significant differences in complications rate between the two techniques. Among patients with BMI greater than 35 kg/m^2, authors found pre pectoral group had a higher rate of implant exposure with the odds of reoperation increased by 7% per point increase in BMI; the authors concluded that here is a trend toward higher complication rates in prepectoral *vs.* subpectoral breast reconstruction with increasing BMI.

Considering initial reports comparing PBR and SBR and recent published data (47,65), it appears to be fundamental to fit the best approach for the single patient; considering that, good IBR outcomes are strictly related to patient selection. By this point of view, Yang *et al.* proposed a well-defined algorithm (66): if the tumor is close to the chest wall in continuity with the pectoralis major muscle, subpectoral approach is preferable while when it is located more than 1 cm from the pectoralis major muscle on MRI, prepectoral reconstruction can be the treatment of choice; if the vascularity of the skin flap after mastectomy appears to be poor at clinical examination or at fluorescence angiography with indocyanine green, subpectoral IBR with a tissue expander should be preferred; finally, if the thickness of skin flap is near to 1 cm or the subcutaneous fat tissue is well-preserved, the flap is considered to be well-vascularized and a prepectoral reconstruction could be considered.

Authors summarized with the conclusion that favorable indications for prepectoral IBR include moderately-sized breasts with a thick well-vascularized mastectomy flap and concomitant bilateral breast reconstruction including prophylactic mastectomy.

Conclusions

Our review demonstrates that, although it is evident that there is still no gold standard regarding the best approach in case of IBR, current literature seems to veer towards the choice of a pre pectoral strategy; this technique, according with Yang's algorithm, appears to be safe, reliable, and a promising reconstructive option for selected patients, with equivalent results to other reconstructive possibilities. Accurate evaluation of patients' characteristics and patient wish will ultimately drive the reconstructive choice.

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