Original Article

Breast cancer patients' postoperative outcomes in nipple-sparing mastectomy and reconstruction with subpectoral implant placement: a single center experience

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Background: The continuous increase in the rate of nipple sparing mastectomy (NSM), the development of several reconstructive techniques and the following introduction of acellular derma matrix (ADM) has revolutionized implant-based breast reconstruction. This study aimed to investigate postoperative complications, health-related quality of life (HRQoL) and patients' satisfaction in patients undergoing NSM and breast reconstruction with or without ADM.

Methods: Enrolled patients were divided into three groups: immediate breast reconstruction (IBR) with definitive implant and ADM (Group A), IBR only with definitive prosthesis (Group B), and two-stage breast reconstruction (Group C). The postoperative complications, BREAST-Q outcomes and reoperations were compared.

Results: A total of 105 BC patients were enrolled and a total of 139 post-mastectomy breast reconstructions were performed. Seroma was the most prevalent complication observed: 8.3% in Group A, 2.9% in Group B and 5.7% in Group C. Postoperative infection occurred in two patients of Group A (5.6%), one patient of Group B (2.9%) and one of Group C (2.9%). Group A reported larger drain volume (1,125±243.5 cc), longer drain period (13.2±2.8 days), and the lowest incidence of capsular contracture (5.6%). The BREAST-Q patient-reported outcome measures document that all patients aged ≥50 years presented a higher score in "Satisfaction with breast" ($P<0.001$) and "Satisfaction with outcome" domains ($P<0.05$). Performing a bilateral breast reconstruction was associated to higher scores in "Physical wellbeing chest domain" ($P<0.05$). In addition, patients in Group A and Group B reported higher score in "Satisfaction with the breast" domain ($P<0.001$) but only in Group B we reported a higher score in "Satisfaction with outcome" ($P<0.001$).

Conclusions: Subpectoral IBR results in manageable complications and greater personal satisfaction. The ADM could improve breast reconstruction reducing the rate of capsular contracture. The prepectoral placement of ADM could minimize complications and optimize aesthetic results.

Keywords: Acellular derma matrix (ADM); nipple sparing mastectomy (NSM); breast reconstruction; breast cancer (BC)

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Introduction

Breast cancer (BC) is the most frequent female cancer worldwide and the second cause of death for neoplasm (1,2). All types of cancer bring patients into contact with the idea of death, and, in addition, BC patients must fight also with severe psychological issues and, altered body image and the loss of their physical integrity (3). Losing the mammary gland after mastectomy means facing an alteration of the body image, sexuality, self-esteem, and social interactions (3). Fortunately, BC patients have the option to have breast reconstruction after mastectomy and, in particular, immediate breast reconstruction (IBR) may severely improve their health-related quality of life (HRQoL) (4). The IBR is proposed to women who observe specific criteria, and it has the advantage of a single hospital admission and improved psychological outcomes (5).

Several surgical techniques may be pursued for IBR after mastectomy and can be divided into 2 large groups: implant-based reconstruction and autologous reconstruction. Implant-based breast reconstruction is the reconstructive surgical technique most widely used and can be performed immediately after mastectomy or later [delayed breast reconstruction (DBR)]. Traditional breast implant reconstruction includes tissue expander followed by implant: the positioning of the tissue expander is necessary to create a sub-muscular pocket where the definitive prosthesis will subsequently be inserted (4).

This traditional surgical technique has two substantial limits: two accesses in the operating room and two second hospital admission with possible clinical complications and an increase in care costs (6). Subpectoral implant reconstruction has been considered the standard of care in the 20st century (7), and the following introduction of acellular derma matrix (ADM) has revolutionized implant-based breast reconstruction, allowing surgeons to prefer IBR over DBR (8). However, although subpectoral reconstruction with ADM facilitates reconstruction in one surgical step, it could be associated with complications such as seroma, infection and implant loss that can interfere with the HRQoL of BC patients (results of breast reconstruction) (9). The experience gained in the last years, the refinement of techniques and the knowledge of the ADM-related complications slowly led more surgeons to limit direct tissue implant retropectoral reconstruction in favor of prepectoral reconstruction (10-12).

We performed a monocentric observational study aimed at investigating postoperative complications, HRQoL and patient's satisfaction of aesthetic outcomes, assessed by BREAST-Q questionnaire, in a cohort of BC patients eligible to nipple-sparing mastectomy and subpectoral breast reconstruction with or without ADM placement. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-58/rc).

Highlight box

Key findings

- The use of acellular derma matrix (ADM) in post-mastectomy reconstruction with subpectoral implant could improve breast reconstruction results and patients' satisfaction reducing capsule contracture rate, while a pre-pectoral placement could reduce complications and optimize aesthetic results.

What is known and what is new?

- After a mastectomy for breast cancer (BC), breast reconstruction improves patients' quality of life, even if traditional two-times prosthetic reconstruction is doomed by specific complications.
- Immediate reconstruction with prosthesis and ADM increases patients' satisfaction and decreases capsule contracture rate compared to two-times reconstruction with tissue expander.

What is the implication, and what should change now?

- Although the design of the study did not fully support the results obtained given the nature of patient pathways to treatment, quality of life must be further investigated on BC patients, in order to further increase personal wellbeing and adjust surgical techniques to patients' satisfaction.

Methods

Study design

We conducted an observational longitudinal study on a population of patients with a diagnosis of BC or BRCA carrier who underwent nipple-sparing mastectomy (NSM) and subpectoral breast implant reconstruction with or without ADM, not eligible for neoadjuvant treatment,

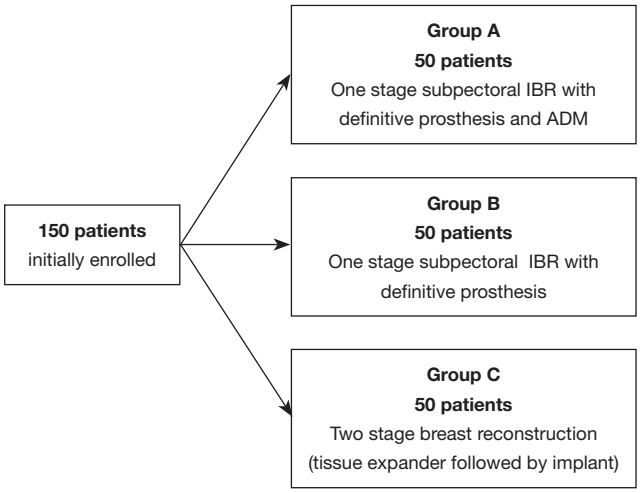

Figure 1 Study design. IBR, immediate breast reconstruction; ADM, acellular dermal matrix.

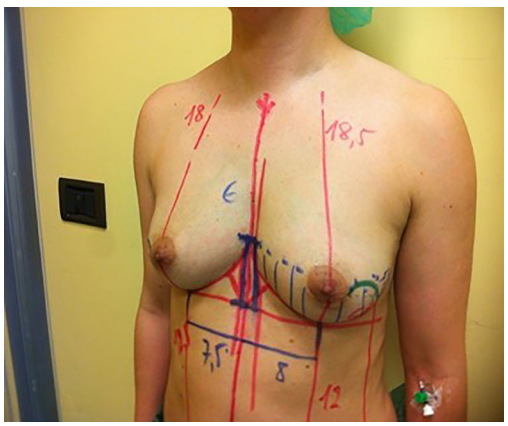

Figure 2 Preoperative drawings in standing position in a patient undergone bilateral NSM with "Lazy S" incision. NSM, nipple-sparing mastectomy.

consecutively enrolled from January 2014 to May 2017, at the Department of Surgical Sciences, Sapienza University of Rome. Before surgery, each patient was counseled and fully informed of all surgical treatment options.

The indication for surgical treatment was discussed during the periodical multidisciplinary breast board and the choice of the reconstructive technique was determined by preoperative and intraoperative anatomic evaluations.

Patient were selected according to inclusion criteria and grouped in 3 groups according to the type of surgery to be performed (*Figure 1*).

Data were collected and updated in a specific database during the hospital stay and the subsequent outpatient medical visits. Twelve months after surgery, a HRQoL questionnaire was administered to all patients.

Inclusion criteria were: age 18 years or older, pre-operative histological diagnosis of BC and/or BRCA mutation carriers, no cutaneous and/or muscle infiltration, small-medium-sized breasts with first or second grade ptosis according to the three-tier Regnault ptosis scale (13) eligibility for mastectomy intervention and subsequent reconstruction. All patients were cN0 at the pre-operative imaging and in the case of clinic-radiological lymphadenopathy, fine-needle aspiration for cytology was performed. All patients underwent sentinel lymph node biopsy (SLNB).

Exclusion criteria were: previous radiation therapy, connective tissue disease, alterations of cutaneous trophism, patients eligible for autologous reconstruction, body mass index ≥30 kg/m^2, active smoking patients (required not to smoke more than or equal to 3 months before surgery and for 4 months after surgery), patients undergone neoadjuvant chemotherapy. We excluded neoadjuvant treated patients to eliminate a possible bias of our results, who would interfere with ADM integration and eventual postoperative complications, such as seroma or wound infection.

We included all the consecutive patients who met inclusion criteria and that were treated at our Center in the time-period considered.

The study was performed according to the ethical standards of the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of Sapienza University of Rome (No. 5140). Written informed consent was obtained from all subjects and/or their legal guardian(s).

Surgical technique

Patients enrolled were marked preoperatively, in the standing position, with different colors and the fundamental measures for breast reconstruction were detected (*Figure 2*).

Breast volume was estimated preoperatively. Prophylactic antibiotic (cefazolin or clindamycin) was administered at appropriate dosage 30 minutes before the skin incision. All the patients continued antibiotic treatment therapy every 12/24 h until drain removal. Nipple-sparing mastectomy was performed with the patient in a supine position with the arm abducted at 90°. The preferred skin incisions used were in "lazy S" (horizontal S-shaped, localized in the outer quadrants) (*Figure 1*), allowing a single incision in BC patients undergoing SLNB. The single skin incision allows

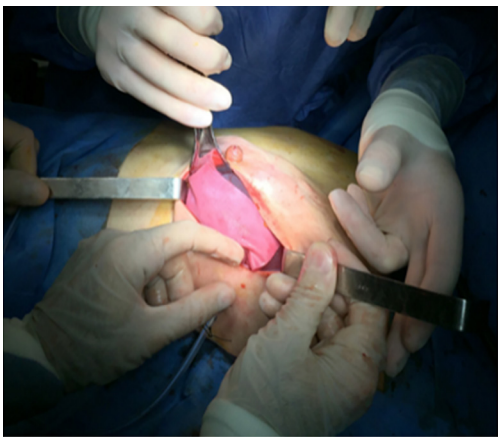

Figure 3 Intraoperative image of a patient undergone unilateral NSM and IBR with ADM, showing the ADM sutured at the inferior border of the muscle. NSM, nipple-sparing mastectomy; IBR, immediate breast reconstruction; ADM, acellular dermal matrix.

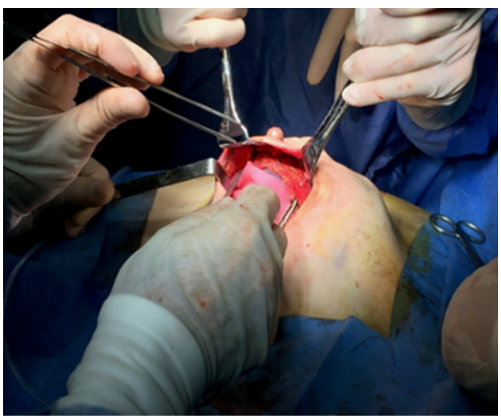

Figure 4 Intraoperative image of a patient undergone unilateral NSM and IBR with ADM, showing ADM positioning. NSM, nipple-sparing mastectomy; IBR, immediate breast reconstruction; ADM, acellular dermal matrix.

to perform mastectomy and remove the hypercaptant lymph node. In BRCA1/2 carrier we preferred submammary skin incision.

The choice of the type of surgery and breast reconstruction was related to the quality of the major pectoralis muscle (muscle tone and thickness) and the absence of breast gland ptosis. In women with good muscle tone and grade I–II ptosis we performed a subpectoral reconstruction that specifically was a partial submuscular reconstruction and the pocket was completed with the serratus muscle and/or by dissecting the rectus fascia. Determinants of the choice were: the dermal-epidermal flap, the muscle tone, the trophism of the muscle and the breast ptosis. The definitive implant choice was carefully made using intraoperative sizers and avoiding to exert an excessive tension on the muscle and skin flap to prevent blood supply reduction. Only in selected cases with grade I and II ptosis, good dermal-epidermal flap, tonic and trophic muscle and fascia, we performed a DTI with definitive breast implant.

We used the ADM when was necessary to offer support to the lower pole of the submuscular pocket, ensuring less tension and greater coverage of the breast implant.

Prior to ADM implant, it was removed from its sterile packaging, rehydrated in normal saline solution for 10 minutes and soaked in an antibiotic solution. To ensure better coverage and at the same time a better aesthetic result, the ADM was sutured at the inferior border of the muscle, from the 4 to 8 o'clock position (*Figures 3*,*4*), and fixed with detached resorbable stitches.

Before ending the surgery, 2 suction drains were positioned, the first one in subcutaneous space and the other one in the inframammary fold between the implant and the ADM (inframammary pocket). To reduce dead spaces, the breast was compressed using an elastic band.

Drains were removed when the drained volume was less than 20 mL/day for 2 consecutive days. All patients wore a postoperative bra for an average of 45 days after surgery.

Assessments

Post-operative data

Drained fluid volume was collected every day at the same hour, with reservoir opened (not in vacuum mode) by nursing staff during hospital stay and by the patients while they were at home. Hospital stay was counted in days, from the day of hospital admittance. Permanence of drainage tubes was calculated from the day of surgery.

Post-operative complications

We recorded participants' demographic and anthropometric characteristics (age, weight, height, body mass index), the presence/absence of comorbidities, histological diagnosis, tumor staging, and a detailed medical history. Particular attention was paid to registration of complications and relative frequencies. To facilitate the identification of complications, we defined before patients' enrollment, the following classification: seroma, when a fluid collection

that needs to be aspirated was clinically identified (14); hematoma, when a pool of mostly clotted blood that forms in a tissue or body space was documented; capsular contracture, when an alteration of the prosthetic profile was demonstrated by MRI scan (15,16); wound dehiscence was defined as a disruption of sutured tissue; infection, according to the definition of the Center for Disease Control and prevention criteria, was defined by: (I) presence of purulent drainage; (II) positive aseptically obtained culture; (III) peri-incisional erythema and incision opened by the surgeon; or (IV) physician diagnosis of infection (17) despite antibiotic prophylaxis (18) and management of risk factors (19). Major infections required the removal of the prosthetic device, while minor infections were resolved only with antibiotic therapy, as seen in literature (20).

Patients satisfaction

To investigate the satisfaction of aesthetic outcomes we used post-reconstruction BREAST-Q questionnaire, routinely used at our institution, and widely recognized and validated for research in breast reconstruction (21-24).

BREAST-Q questionnaire was submitted after 12 months from the placement of the definitive breast implant and all the patients answered the five domains of the questionnaire (Satisfaction with breasts, Satisfaction with outcome, Psychosocial wellbeing, Sexual wellbeing and Physical wellbeing chest).

All patients performed clinical, ultrasound and MRI exam at 18 months after implant placement to control the reconstruction outcomes and define presence/absence of capsule contracture and its severity according to Baker scores (25).

Statistical analysis

Statistical analysis was performed using the Vassarstats and MedCalc statistical software.

Pearson's χ^2 test, *t*-test, and Mann-Whitney test were used to assess statistical significance.

Patients with missing data were excluded from the study.

The "BREAST-Q" questionnaire scores for each patient were converted from the survey scores (1 to 5) to a continuous range from 0 to 100 using QScore Scoring Software kindly provided to us by Memorial Sloan-Kettering Cancer Center. A higher score indicated grater satisfaction or a better HRQoL.

Results

We initially considered a total of 150 potentially eligible patients (50 patients per group). Of these, 139 were enrolled in the study and 131 were then confirmed eligible (4 smoker patients, 2 patients underwent neoadjuvant chemotherapy in another hospital and 2 patients undergone to previous chest radiotherapy were excluded). After 12 months from surgery, only 105 patients, were contactable and successfully completed HRQoL questionnaire (18 patients were lost during follow-up period and were excluded from the study due to incomplete clinical data and 8 patients refused to answer to HRQoL questionnaire, *Figure 5*).

At 12-month from the enrollment, a total of 105 patients were considered and 37 of them received a bilateral mastectomy and bilateral breast reconstruction, therefore a total of 139 post-mastectomy breast reconstructions were considered, and divided into 3 groups: 45 subpectoral IBR with definitive prosthesis and ADM (Group A), 49 subpectoral IBR only with definitive prosthesis (Group B), and 45 two-stage subpectoral breast reconstruction (Group C) (*Table 1*, *Figure 6*).

Patients' clinical and surgical characteristics

The clinical characteristics of the study population are reported in *Table 2*. The mean age of patients in Group A was 55.6±5.1 years, 56±10.2 years in Group B, and 53.2±5.5 years in Group C.

In all the enrolled patients, BMI did not exceed 24.9 kg/m^2. The most represented histology subtype was invasive ductal carcinoma (Group A: 41.5%; Group B: 47.1%; Group C: 48.6%).

In the pre-operative assessment, in Group A, all patients had first-degree ptosis and 84.4% small size breast. In Groups B and C, we documented second-degree breast ptosis in 38.8% and 37.8%, respectively, of the patients, and medium size breasts in 44.9% and 44.4%, respectively.

The peri-implant drain was maintained for 13.2±2.8 days in Group A, 11.0±2.8 days in Group B and 10.2±2.8 days in Group C, and no differences in number of hospital stay days were observed between the 3 groups. The postoperative complications' rates are shown in *Table 3*.

Seroma was the most prevalent complication observed: 8.3% in Group A, 2.9% in Group B and 5.7% in Group C. We reported 2 cases (5.6%) of hematoma in

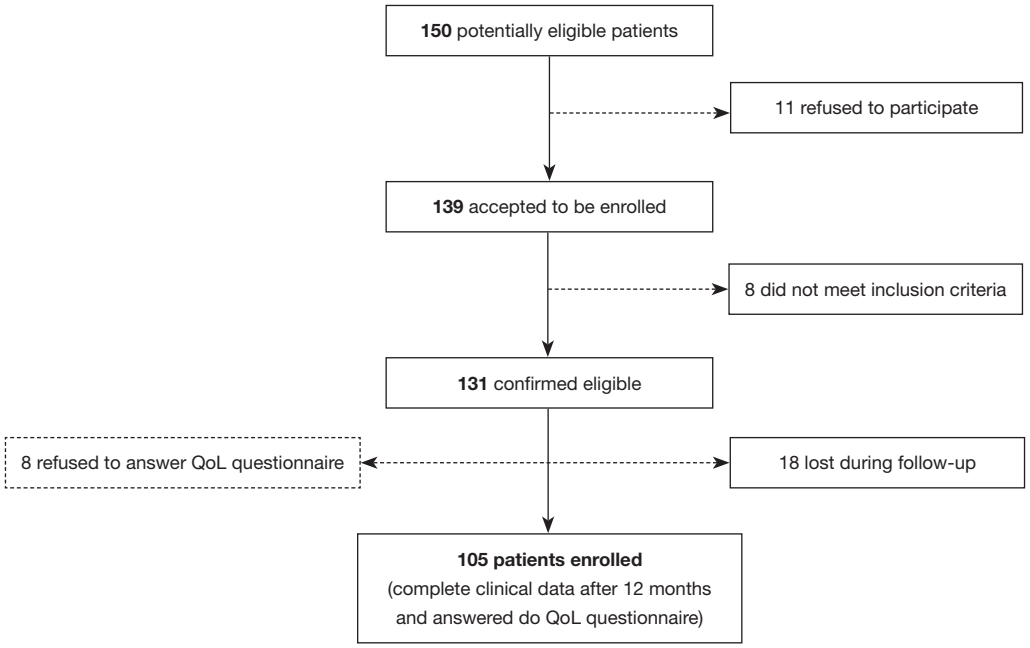

Figure 5 Enrolled patients and drop-outs. QoL, quality of life.

Table 1 Breast reconstruction procedures and patients enrolled

Patient characteristics	Group A	Group B	Group C
Number of patients (%)	36 (34.3)	34 (32.4)	35 (33.3)
Unilateral	27 (75.0)	19 (55.9)	25 (71.4)
Bilateral	9 (25.0)	16 (47.1)	12 (34.3)
Total number of breasts (%)	45 (32.4)	49 (35.3)	45 (32.4)
NSM for cancer, n (%)	34 (94.4)	29 (85.3)	35 (100.0)
Risk reducing mastectomy (NSM), n (%)	2 (5.6)	5 (14.7)	0

Group A: one stage subpectoral IBR with definitive prosthesis and ADM; Group B: one stage subpectoral IBR with definitive prosthesis; Group C: two stage breast reconstruction (tissue expander followed by implant). IBR, immediate breast reconstruction; ADM, acellular dermal matrix; NSM, nipple-sparing mastectomy.

Group A, 1 case (2.9%) in Group B and no cases in Group C. We reported 3 cases (8.3%) of wound dehiscence in Group A, 1 case (2.9%) in Group B and no cases in Group C.

Postoperative infection occurred in 2 patients of Group A (5.6%), one patient of Group B (2.9%) and one of Group C (2.9%). In Group A, one patient had an episode of major infection with consequent implant loss that required inpatient readmission and reoperation (*Figure* 7).

No episodes of red breast syndrome were reported as well as episodes of nipple or skin necrosis in our entire cohort. This was probably in part due to the pre-operative patient selection to be candidate to NSM and breast reconstruction and to the small number of patients enrolled.

In Groups B and C, we did not observe cases of implant loss.

Capsule contracture rate was 5.6% in Group A, 11.8% in Group B and 8.6% in Group C. Severe capsule contracture (grade three according to Baker classification) was observed only in one patient in Group B. We documented animation deformity in 25.0% of Group A, 14.7% of Group B and only 8.6% in Group C. The median follow-up time after the last reconstructive surgery was 36 months

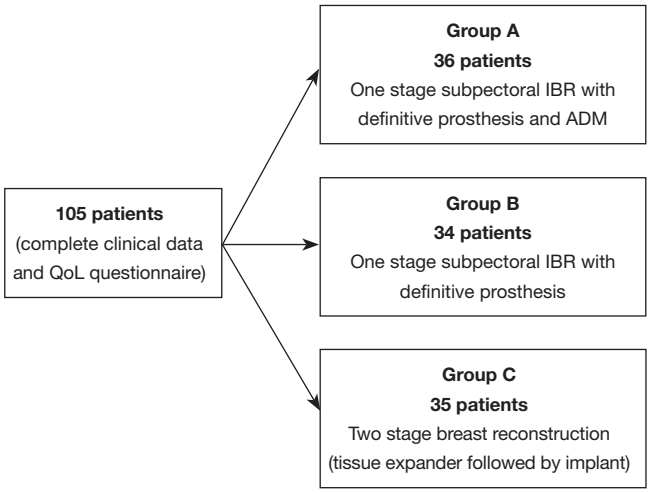

Figure 6 Study groups. IBR, immediate breast reconstruction; ADM, acellular dermal matrix; QoL, quality of life.

(from 13 months to 5.5 years).

Assessment of the HRQoL and aesthetic outcomes

We did not find any significant associations between patients age and the 5 "Breast-Q" questionnaire domains explored. The bilateral reconstruction showed a better patients' satisfaction with the appearance, although we did not find a significant association between the unilaterality/bilaterality of the breast reconstruction and the questionnaire's domains (*Table 4*).

Group A presented a significant higher score for the domain "Satisfaction with breasts" (58.4) (*Figures 8-10*) compared to Group B (55.4) and Group C (42.4) (P<0.01), while a lower score in Group A regarding "Satisfaction with outcome" domain (59.2) with respect to Group B (63.3) and Group C (63.8) even if not statistically significant.

No differences between the 3 groups were documented for the domains "Psychosocial wellbeing", "Sexual wellbeing", and "Physical wellbeing chest".

We conducted a multivariate analysis considering patients' age and unilaterality/bilaterality of the breast reconstruction (*Table 5*) and we documented that all patients aged ≥50 years presented a higher score in "Satisfaction with breast" (beta: 5.198; P<0.001) and "Satisfaction with outcome" domains (beta: 5.421; P=0.01) with respect to patients aged <50 years.

In addition, performing a bilateral breast reconstruction was associated to higher scores in "Physical wellbeing chest domain" with respect to performing monolateral breast surgery (beta: 3.278; P=0.01).

When considering the timing of breast reconstruction (one- versus two-stage reconstruction), we found that patients in Group A and Group B (who both underwent IBR) reported higher score in "Satisfaction with the breast" domain (P<0.001) and in "Physical wellbeing chest" (P<0.001) when compared to Group C (two-stage breast reconstruction), and only in Group B a higher score in "Satisfaction with outcome" domain when compared to Group C (beta: 13.916; P<0.001) (*Table 6*).

In addition, the immediate reconstruction with ADM (Group A) was negatively associated with the scores obtained in "Sexual wellbeing" domain (beta: −7.852; P=0.007) (*Table 6*).

Discussion

The introduction of wide screening programs and personalized medical care determined an increase in the incidence of the BC and decrease in mortality (26). These epidemiological changes have led to significant evolutions in the surgical approach of BC, attributing an important value to HRQoL and aesthetic outcomes (27,28). These aspects led us to record postoperative complications, HRQoL and patient's satisfaction of aesthetic outcomes patients eligible to nipple-sparing mastectomy and subpectoral breast reconstruction with or without ADM placement. In the last decade, breast reconstruction has involved a progressive improvement of older techniques with the introduction of new approaches and new devices to achieve the most natural appearing of the breast following NSM, including ADM (11,29).

With the use of ADM, we documented an increase of drain volume, but minor complications and lower risk of capsular contracture, as well as a higher patient satisfaction for immediate breast satisfaction, with respect to the other breast reconstruction groups.

In addition, our results revealed that the use of ADM in subpectoral technique seemed to determine a longer drain period and an increased risk of implant's infection with respect to breast reconstruction without ADM, as well as a higher incidence of seroma, hematoma, wound dehiscence and rate of implant loss and animation, in line with previous results (29,30). The ADM group included more BRCA cases and more wound dehiscence episode with respect to the other groups. Reflecting on this aspect, our results were probably in part due to the factors that,

Table 2 Population study, comorbidities, and risk factors

Characteristics	Group A	Group B	Group C
No. of patients	36 (34.3)	34 (32.4)	35 (33.3)
No. of breasts	45 (32.4)	49 (35.3)	45 (32.4)
Age, years	55.6±5.1	56±10.2	53.2±5.5
Weight, kg	67.3±7.6	68.3±6.7	66.9±6.5
Height, m	1.66±0.05	1.64±0.03	1.66±0.04
BMI, kg/m^2	24.5±2.7	25.4±3.1	24.4±2.5
Breast size			
Small size	38 (84.4)	27 (55.1)	25 (55.6)
Medium size	7 (15.6)	22 (44.9)	20 (44.4)
Ptosis grade sec Regnault			
First degree	45 (100.0)	30 (61.2)	28 (62.2)
Second degree	0	19 (38.8)	17 (37.8)
Comorbidities			
Diabetes	1 (2.8)	0	1 (2.9)
Hypertension	6 (16.7)	4 (11.8)	6 (17.1)
Ischemic heart disease	0	0	0
Smoking status			
Non-smoker	24 (66.7)	24 (70.6)	15 (42.9)
Former smoker	12 (33.3)	10 (29.4)	8 (22.9)
Smoker	0	0	2 (5.7)
Diagnosis			
IDC	15 (41.7)	16 (47.1)	17 (48.6)
ILC	8 (22.2)	7 (20.6)	12 (34.3)
DCIS	4 (11.1)	5 (14.7)	4 (11.4)
LCIS	1 (2.8)	1 (2.9)	2 (5.7)
BRCA 1–2	2 (5.6)	5 (14.7)	0
BRCA 1–2 + IDC/DCIS	6 (16.7)	0	0
BRCA 1–2 + ILC/LCIS	0	0	0
Neoadjuvant treatment	3 (8.3)	2 (5.9)	2 (5.7)
Radiation therapy	2 (5.6)	3 (8.8)	3 (8.6)

Data are presented as mean ± standard deviation or number (percentage). Group A: one stage subpectoral IBR with definitive prosthesis and ADM; Group B: one stage subpectoral IBR with definitive prosthesis; Group C: two stage breast reconstruction (tissue expander followed by implant). BMI, body mass index; IBR, immediate breast reconstruction; ADM, acellular dermal matrix; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

Table 3 Post-operative assessment and complications: drainage permanence, drained fluid, hospital stay, seroma, hematoma, wound dehiscence, infection, capsular contracture, implant loss and animation deformity rates

Characteristics	Group A	Group B	Group C
Number of patients	36 (34.3)	34 (32.4)	35 (33.3)
Permanence of drainage (days)	13.2±2.8	11.0±2.8	10.2±2.8
Drained fluid (cc)	1,125±243.5	875±222.2	720.3±187.0
Hospital stay (days)	6.0±0.6	7.0±0.92	6.1±0.7
Seroma	3 (8.3)	1 (2.9)	2 (5.7)
Hematoma	2 (5.6)	1 (2.9)	0
Wound dehiscence	3 (8.3)	1 (2.9)	0
Infection	2 (5.6)	1 (2.9)	1 (2.9)
Minor	1 (2.8)	1 (2.9)	1 (2.9)
Major	1 (2.8)	0	0
Capsular contracture	2 (5.6)	4 (11.8)	3 (8.6)
Grade I	1 (2.8)	1 (2.9)	2 (5.7)
Grade II	1 (2.8)	2 (5.9)	1 (2.9)
Grade III	0	1 (2.9)	0
Grade IV	0	0	0
Implant loss	1 (2.8)	0	0
Animation deformity	9 (25.0)	5 (14.7)	3 (8.6)

Data are reported as mean ± standard deviation or number (percentage). Group A: one stage subpectoral IBR with definitive prosthesis and ADM; Group B: one stage subpectoral IBR with definitive prosthesis; Group C: two stage breast reconstruction (tissue expander followed by implant). IBR, immediate breast reconstruction; ADM, acellular dermal matrix.

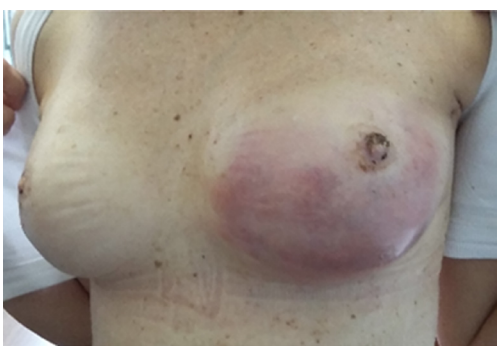

Figure 7 Patient undergone NSM and IBR with ADM affected by major infection requiring reoperation. NSM, nipple-sparing mastectomy; IBR, immediate breast reconstruction; ADM, acellular dermal matrix.

performing the procedure bilaterally, the implant size was selected larger than preoperatively decided and determining the need of using ADM and a higher seroma rate was documented. Nevertheless, interestingly, peri-implant capsular contracture was lower in breast reconstruction with ADM with respect to the reconstruction without ADM. Lee *et al.* analyzed 23 studies including more than 6,000 patients, comparing the outcome of ADM use with traditional submuscular breast reconstruction technique, and demonstrated that the ADM use and the subsequent reduction in pocket stiffness limited significantly the risk of capsular contracture (31). In addition, from the histopathological point of view, ADM induces a reduction of chronic inflammation and fibroblasts' proliferation

Table 4 Univariate analysis, "BREAST-Q" questionnaire results

BREAST-Q questionnaire items	Age (years)		Unilaterality/bilaterality (breast reconstruction)		Study groups		
	<50	≥50	Monolateral	Bilateral	Group A	Group B	Group C
Satisfaction with breasts	51.2 (8.1)	53.6 (12.1)	51.2 (8.0)	53.8 (12.4)	58.4* (9.3)	55.4 (5.3)	42.4 (5.1)
Satisfaction with outcome	65.9 (9.8)	72.2 (13.6)	68.0 (12.1)	68.6 (12.5)	59.2 (18.1)	63.3 (9.7)	63.8 (10.2)
Psychosocial wellbeing	57.4 (9.3)	58.2 (15.2)	57.8 (12.1)	57.6 (12.1)	59.2 (18.1)	56.4 (5.2)	57.4 (7.3)
Sexual wellbeing	42.3 (10.3)	46.2 (11.6)	44.0 (12.0)	43.1 (8.4)	50.0 (8.6)	36.3 (7.7)	44.4 (11.5)
Physical wellbeing chest	60.3 (5.9)	58.3 (10.8)	58.9 (8.6)	61.0 (6.7)	65.3 (5.4)	60.1 (4.5)	53.4 (8.6)

Data are reported as mean (standard deviation). Variables considered: age (≥50 *vs.* <50 years) and unilaterality/bilaterality (breast reconstruction). Group A: one stage subpectoral IBR with definitive prosthesis and ADM; Group B: one stage subpectoral IBR with definitive prosthesis; Group C: two stage breast reconstruction (tissue expander followed by implant). *, P<0.001. IBR, immediate breast reconstruction; ADM, acellular dermal matrix.

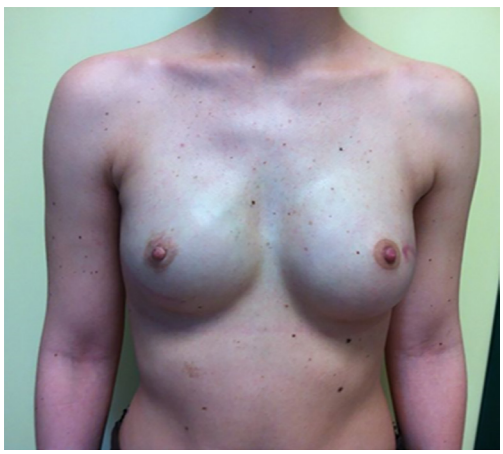

Figure 8 Three months result of a patient undergone bilateral NSM and immediate reconstruction with ADM, front view with arms lowered. NSM, nipple-sparing mastectomy; ADM, acellular dermal matrix.

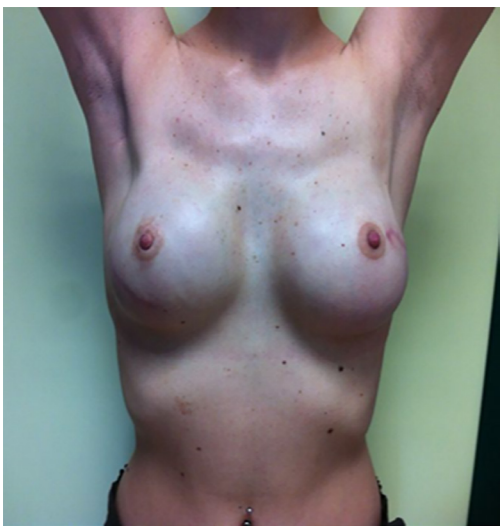

Figure 9 Three months result of a patient undergone bilateral NSM and immediate reconstruction with ADM, front view with arms raised. NSM, nipple-sparing mastectomy; ADM, acellular dermal matrix.

preventing or minimizing capsule formation (32). Our study documented that two-stage reconstruction was characterized by a shorter hospital stay, less drained liquid with respect to IBR, and no cases of reoperation, confirming it is potentially the safest surgical breast reconstruction choice, determining a general prevalence of implant loss around 1% when compared to the 5–10% in IBR (33-35).

Several studies highlighted that seroma is the most common complication found in women undergoing IBR with ADM (36,37) and this may be associated with the membrane's behavior which, acting as a scaffold, determines a rapid neoangiogenesis (7 days) and a late formation of the lymphatic system (14 days) (38). Moreover, ADM, anchored to the pectoralis major muscle in the dual plane technique, may lead to a further delay in the integration of the membrane caused by the continuous mechanical stimuli, with an increased incidence of seroma, fluid production and longer drain permanence (39). In this light, utilizing at least two drains, prolonged drain maintenance and adequate antibiotic coverage allow to reduce the incidence of seroma and, most importantly, limits the transformation of seroma into minor or major infection (40). Timely diagnosis of complications and proper management of patients allow the safe use of the ADM without increasing the risk of

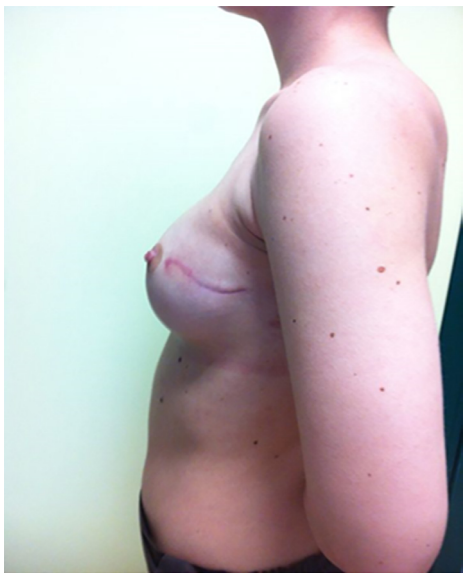

Figure 10 Three months result of a patient undergone bilateral NSM and immediate reconstruction with ADM and breast implant, side view. NSM, nipple-sparing mastectomy; ADM, acellular dermal matrix.

readmission, reoperation, and implant loss (11).

When considering breast surgery and reconstruction surgery results, it is essential to investigate patients' quality of life and satisfaction. We documented that all patients undergoing IBR compared to delayed two-stage breast reconstruction reported more satisfactory outcomes both in terms of "satisfaction with breast" and "physical well-being with the chest". The IBR technique offers benefits to women undergoing NSM by improving their psychological well-being and ensuring a high HRQoL (41,42). The new techniques in breast surgery allow to counteract the mutilating surgery of the last century not only sparing organs and tissues but also improving the physical and psychological discomfort of BC patients (41,42).

Although the placement of ADM facilitating one-stage breast reconstruction permitted to recreate a natural appearing breast improving lower pole projection, natural-looking ptosis and satisfaction with operated breast (43,44), our ADM group reconstruction showed a lower score in terms of "satisfaction with outcome" with respect to the

Table 5 Multivariate analysis, "BREAST-Q" questionnaire results

Dependent variables	Independent variables				R^2 of the model
	Age ≥50 *vs.* <50 years		Bilaterality *vs.* unilaterality (breast reconstruction)		
	Beta	P	Beta	P	
Satisfaction with breasts	5.198	<0.001	2.209	0.10	0.59
Satisfaction with outcome	5.421	0.01	1.707	0.40	0.357
Psychosocial wellbeing	0.297	0.90	0.128	0.96	0.010
Sexual wellbeing	1.020	0.62	0.934	0.64	0.272
Physical wellbeing chest	–1.684	0.22	3.278	0.01	0.414

Table 6 Multivariate analysis, one- versus two-stage reconstruction, "BREAST-Q" questionnaire results

Dependent variables (BREAST-Q questionnaire items)	Independent variables				R^2 of the model
	Subpectoral IBR with definitive prosthesis and ADM		Subpectoral IBR with definitive prosthesis		
	Beta	P value	Beta	P value	
Satisfaction with breasts	14.704	<0.001	16.645	<0.001	0.59
Satisfaction with outcome	1.346	0.58	13.916	<0.001	0.357
Psychosocial wellbeing	–0.949	0.75	1.834	0.52	0.010
Sexual wellbeing	–7.852	0.007	5.758	0.004	0.272
Physical wellbeing chest	5.777	<0.001	12.018	<0.001	0.414

IBR, immediate breast reconstruction; ADM, acellular dermal matrix.

other reconstruction modalities. Probably, the unilateral ADM placement for breast reconstruction determines an asymmetry with respect to the healthy contralateral breast and this may explain the lower score documented in terms of satisfaction with the outcome. When considering the bilaterality/unilaterality, we documented a significant association between doing a bilateral breast reconstruction and higher scores in "Physical Wellbeing Chest" domain, as confirmed by the literature (45,46). The results of our study show lower post-operative satisfaction with breast ant with outcome in women <50 years. Young women probably have a greater attention to the aesthetic result and consequently higher expectations from breast reconstruction (47,48). Investigating the "Sexual Wellbeing" domain, a negative association with the ADM breast reconstruction was documented. This type of IBR, determining a higher incidence of seroma, hematoma, longer permanence of the breast drain, consequent longer antibiotic therapy duration, and slower recovery of daily and work activities, may negatively impacts on quality of life and the preservation of sexuality (49).

Conclusions

This study was completed in a prospective manner from a single institution with relatively small number of patients in each group, due to very narrow selection inclusion criteria to limit possible bias, representing a limitation of our study.

We described our advantages and limits in breast reconstruction to share our experience and our choices in the literature and to guide patients' selection for the type of reconstruction based on our experience.

Our results confirm that IBR remains, whenever possible, the best choice for psychological and physical well-being in women undergoing NSM. The use of ADM in the subpectoral technique has allowed to obtain the good results, in terms of post-operative complications, only in women with small breasts, without ptosis, strongly reducing the incidence of capsule contracture, and in terms of patients' satisfaction. Despite sub-pectoral breast reconstruction has been the mainstay of implant-based reconstruction for the last half century, the higher complications detected in the subpectoral ADM technique and the impossibility of extending the reconstructive surgery to women with ptotic and large breasts lead us to support the advantages of the ADM in the prepectoral technique. Changing the position of ADM from the sub-pectoral to the pre-pectoral plane would offer the opportunity to minimize ADM-related complication and eliminate distortion seen with sub-pectoral implant positioning with lower capsule contracture rate.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-58/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was performed according to the ethical standards of the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of Sapienza University of Rome (No. 5140). Written informed consent was obtained from all subjects and/or their legal guardian(s).

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