European Journal of Surgical Oncology 45 (2019) 1357–1363

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

# A retrospective comparative analysis of risk factors and outcomes in direct-to-implant and two-stages prepectoral breast reconstruction: BMI and radiotherapy as new selection criteria of patients

D. Casella, MD, PhD [a], G. Di Taranto, MD [b, *], M.G. Onesti, MD [b], M. Greco, MD [c], D. Ribuffo, MD [b]

[a] Department of Oncologic and Reconstructive Breast Surgery, "Breast Unit Integrata di Livorno, Cecina, Piombino, Elba, Azienda USL Toscana Nord Ovest", Italy
[b] Plastic Surgery Unit, Department of Surgery "P. Valdoni", Sapienza University, Rome, Italy
[c] Department of Plastic Surgery, University of Catanzaro Hospital, Catanzaro, Italy

ARTICLE INFO

*Article history:*
Received 25 October 2018
Received in revised form
24 January 2019
Accepted 6 February 2019
Available online 10 February 2019

*Keywords:*
Sparing mastectomy
Tiloop
Subcutaneous breast reconstruction
Muscle sparing reconstruction
BREAST-Q
Prepectoral reconstruction

ABSTRACT

Recently prepectoral breast reconstruction (PBR) has showed acceptable outcomes in the short-term. There are few evidence on long-term results and variables which could influence surgical safety. So far, no specific guidelines or indications have been developed for prepectoral technique and heterogeneous inclusion criteria had been used in previous reports.

This study revises a series of 397 patients. We conducted a retrospective comparative analysis of risk factors and outcomes between patients undergoing direct to-implant (DTI) and patients undergoing two-stages expander-assisted (TSE) PBR. Univariate binary logistic regression was performed to investigate the association between the incidence of postoperative and aesthetic complications and several variables.

521 breasts were included in the analysis, with an average follow-up of 38 months. 210 patients underwent DTI and 187 TSE PBR. No statistical differences were found between the two populations in term of the characteristics of patients, surgeries and outcomes. Binary logistic regression found no significant association in the TSE group. In the DTI group, a significant association was found between surgical complications and BMI and adjuvant radiotherapy. The association remained significant only for BMI, when investigated with the onset of aesthetic complications.

Lower BMI and adjuvant radiotherapy are significantly associated to a higher risk of developing a surgical complication in DTI PBR. Patients at lowest BMI with DTI are prone to develop an aesthetic complication. According to this analysis, we suggest to carefully choose candidates for PBR and propose new selection criteria for subcutaneous techniques.



## Introduction

The effectiveness of prosthetic prepectoral breast reconstruction (PBR) either using acellular dermal matrix (ADM) or synthetic mesh to cover the implant has been demonstrated in several study [1–7]. These multiple studies have evaluated the outcomes of PBR techniques, with marked variability in their study design, sample size and observed incidence of complications.

PBR spares the muscles, minimizing morbidity of patients and preserving the natural anatomy, while providing complete coverage and avoiding direct implant contact with the mastectomy flaps [7]. Albeit the purported advantages of PBR over the traditional submuscular approach include drop of postoperative pain, improved aesthetic outcome and decreased operative time, there are some concerns regarding the placement of the implant in the subcutaneous plane [8].

Complications rate and reported outcomes broadly vary between studies. Indeed, owing to the small sample size and heterogeneity of these reports, the results should be interpreted

* Corresponding author. Via dei Latini, 33, 00185, Rome, Italy.
*E-mail address:* giuseppeditaranto89@gmail.com (G. Di Taranto).

https://doi.org/10.1016/j.ejso.2019.02.009

cautiously and further researches looking at the long-term follow-up are required to assess the aesthetic outcomes and patients' morbidity.

So far, no specific guidelines or indications have been developed for PBR and heterogeneous inclusion criteria had been used in previous reports. Almost all the authors refer to the Joint Guidelines of the Association of Breast Surgeons and the British Association of Plastic, Reconstruction, and Aesthetic surgeons for ADM assisted submuscular breast reconstruction procedures. Following these criteria good candidates are those patients with a body mass index (BMI) under 30 kg/m$^2$, no history of radiotherapy and smoking, an estimated mastectomy weight not exciding 600 g, undergoing sparing mastectomies leaving well-vascularized subcutaneous layer >1 cm[9]. These guidelines have been produced to assist physicians willing to undertake ADM assisted breast reconstruction and to identify clinical standards and quality indicators for techniques, which exploit ADM to supplement the pectoralis major muscle in submuscular breast reconstruction.

Two recent studies by our group evaluated the long-term outcomes of PBR assisted by a synthetic mesh in a large series of patients, undergoing either direct-to-implant (DTI) or two stages expander-assisted (TSE) reconstruction [2,10]. We conducted a retrospective comparative analysis of risk factors and outcomes between DTI and expander-assisted PBR. To our knowledge, no previous reports have compared the complication rates of these two methods, accounting for the influence of selected factors on the safety of the techniques. In this study, we present and discuss the results of this retrospective analysis on a series of 397 patients. According to this analysis, we suggest to carefully choose candidates for PBR and propose new selection criteria for subcutaneous techniques.

## *Patients and methods*

A retrospective chart review was conducted to identify PBR performed between January 2012 and December 2016 September at our Institutions, Azienda Ospedaliero-Universitaria Careggi, Florence and Breast Unit Integrata, Livorno, Cecina, Piombino, Elba, Azienda USL Toscana Nord Ovest. We recently described our experience with mesh-assisted PBR, either DTI or TSE, in three studies, accounting for long-term and patients reported outcomes [2,11,12]. In this retrospective analysis, we compare the results of PBR between these two approaches [11,12]. The prepectoral reconstruction is currently exploited in plastic surgery applications at our Institutions, as approved by our institutional Ethics Committee and our study was performed with respect to the ethical standards of the Declaration of Helsinki.

As previously described, prior to surgery, all patients were thoroughly informed about the different modalities of reconstruction and were evaluated for both autologous or alloplastic BR [2]. All women had confirmed breast cancer diagnosis or harbored a genetic predisposition to it (*BRCA1/2* mutations), were aged 18 years or older, and willing and eligible to undergo skin-sparing mastectomy (SSM) or nipple sparing mastectomy (NSM) followed by PBR, assisted by a synthetic mesh, with grade I-II ptosis. Only patients with a minimum follow-up of 1 year from reconstruction were included. Exclusion criteria were body-mass index greater than 35 kg/m2, pregnancy, and breast size larger than C cup. Delayed breast reconstructions were excluded from this analysis [2]. Patients were divided into two groups according to the PBR technique: DTI or TSE approach.

Patients demographics, medical history, family history, surgical complications, aesthetic outcomes were collected from our prospectively designed databases. Data regarding health-related quality of life (HRQOL) were retrospectively analyzed, along with the changes between the preoperative and 1-year postoperative BREAST-Q scores. In our previous studies, surgical complications were classified as those occurring in the first postoperative month, requiring a reoperation, including skin-nipple necrosis, seroma, wound dehiscence, wound infection and hematoma. Other surgical interventions performed purely for aesthetic purposes were considered separately in the statistical analysis. According to BRAVO group core outcomes, surgical complications and aesthetic complications were also defined as "major complications" and "unplanned surgery for any reason" respectively [13]. Baker Scale scores were examined to assess capsular contracture grade.

### *Surgical technique*

Our PBR technique has already been described elsewhere [1,2,14]. Briefly, for DTI group after NSM or SSM, patients underwent immediate breast reconstruction using definitive implant placement wrapped in a titanium-coated polypropylene mesh (TCPM), specifically TiLoop® Bra (TiLOOP® Bra, pfm medical, Cologne, Germany). When the post resection skin flaps were considered clinically adequate and healthy, with a well-vascularized subcutaneous layer, a TiLoop® Bra mesh bag was created around the implant. The TCPM bag was then placed in a totally subcutaneous prepectoral position, anchored to the pectoral fascia with interrupted absorbable sutures. One vacuum drain was inserted in the inframammary fold and patients received oral antibiotics until these surgical drains were removed.

The procedure was similar for TSE reconstruction. In this case the bag was tailored around the expander at its final expansion volume, which was than deflated to one third before the implantation. The first postoperative expansion was scheduled 3 weeks following discharge, unless a delay of wound healing occurred. Two other expansions were scheduled and one third of the final volume was injected at each time. The expander was replaced with definitive implant six months after the last expansion. All the procedures were performed by the same surgeons (DC).

### *HRQOL outcomes and BREAST-Q*

As already described, HRQOL evaluation was conducted using the preoperative and the postoperative BREAST-Q modules for reconstructive surgery [15,16]. Briefly patients received the preoperative questionnaire one month before surgery. The BREAST-Q postoperative module was administered 1 years after the completion of the reconstruction during a clinic visit. Using the QScore Scoring Software, BREAST-Q scores for each matrix were converted from survey raw scores Absolute scores and their changes over time (Δ, Delta) were studied [2].

### *Aesthetic outcome*

All the patients were evaluated for subjective assessment of the aesthetic outcome [17]. The aesthetic outcome was assessed by an expert panel of five plastic surgeons who were not directly involved in the surgical procedures [2,18,19]. The breast appearance was evaluated basing on standardized photographs taken postoperatively 1 year after the last surgery. Evaluated parameters were symmetry, shape, volume, position of the IMF. Outcomes were measured using 5-point Likert Scales, gradually escalating from '1' (i.e. very poor result) to '5' (i.e. excellent result). In addition, they were asked to give an overall evaluation score on a 10-point scale.

### *Statistical analysis*

SPSS software (IBM Corp., Armonk, NY) was used for statistical

analysis. The Shapiro-Wilk test was used to verify for normal distribution of continuous variables. Then, paired or unpaired T-Test or Mann-Whitney test were conducted accordingly. The chi-square test was used to compare categorical variables. For each group a univariate binary logistic regression was performed to investigate the association between the incidence of postoperative and aesthetic complications and several variables including age, BMI, history of smoking and breast irradiation. In case of significant association of two or more variables a multiple regression was performed. Statistical significance was defined as $p < 0.05$. DR and GDT revised the databases and were in charge of the data analysis and interpretation.

## Results

Retrospective cohort review identified 397 consecutive patients undergoing NSM or SSM and PBR. A total of 521 breasts were included in the analysis.

Two hundred and ten patients underwent DTI PBR, accounting for 284 breast surgeries. TSE PBR was performed in 187 patients (237 breasts). Mean age was $46.5 \pm 13.6$ (range 23–80) years and the mean BMI was $24.5 \pm 3.9$ kg/m$^2$ (range 19–35).

All demographic and clinical characteristics of the population (and the two cohorts) are presented in Table 1. No statistical difference were found between DTI and TSE for age, BMI, comorbidities, follow-up, smoking, previous breast surgery, and radiotherapy.

The groups were not statistically different as well for surgery outcomes: rate of postoperative complications and aesthetic complications (Table 3), HRQOL (Table 4), and aesthetic results (Table 5).

The rate of surgical complication requiring a second operation was as low as 5.8%. The most reported complication was infection, with 12 cases (2.3%). Seroma occurred in 5 cases and in 16 cases the implant was removed. Intravenous antibiotics injection was required only in the cases who underwent then a reoperation.

Eighty-eight aesthetic complications were recorded (16.9%): 39 (16.4%) with TSE and 49 (17.2%) with DTI. The most frequent complication was rippling (12.5%). 19 cases of severe capsular contracture (Baker Scale grade III and IV) occurred and required surgical revision. The groups were comparable for the number of aesthetic complications.

HQOL was assessed through BREAST-Q questionnaire and scores were comparable and balanced. The comparison between pre- and postoperative self-reported scores is summarized in Table 4. Overall satisfaction with breasts, psychosocial well-being and sexual well-being were all significantly increased after surgery ($p < 0.05$) in both groups. Patient scored high level of overall satisfaction with outcome index, measured post-operatively. No statistical differences were found comparing the deltas of the two populations.

The panel's mean satisfaction scores for each aesthetic parameter are presented in Table 5. According to the panel, breast volume, shape, position of IMF and scars reported high postoperative scores. Mean satisfaction with the overall aesthetic result was also high after breast reconstruction. The groups were comparable also for this scoring.

The binary logistic regression found no significant association between the rate of surgical and aesthetic complications with any other variables considered, in the TSE group.

In the DTI group, a significant association was found between surgical complications and BMI and adjuvant radiotherapy. In the multiple regression model, BMI had a regression coefficient of $-1.15$ (standard error (SE): 0.33; $p = 0.001$) while adjuvant radiotherapy had a regression coefficient of 1.39 (SE:0.68; $p = 0.04$).

The association remained significant only for BMI, when investigated with the onset of aesthetic complications, with a regression coefficient of $-0.41$ (SE: 0.084 $p < 0.001$).

Following the significant association between BMI and complications after DTI, we decided to set a BMI threshold and test the odds ratio for each group. We found that applying a threshold of BMI<22, values of BMI under this point were associated with significant increased risk of developing both aesthetic and surgical complication in the DTI group (odds ratio 11.41 and 25.03

**Table 1**
Demographic and clinical characteristics of patients.

| | Total (n = 397) | TSE (n = 187) | DTI (n = 210) | p-value TSE vs DTI |
|---|---|---|---|---|
| Age [years, mean (range)] | 55.8 (23–80) | 55.5 (29–80) | 56.1 (23–79) | 0.64[a] |
| BMI [kg/m$^2$, mean (range)] | 24.5 (19–35) | 24.9 (19–35) | 24.1 (19.7–35) | 0.16[a] |
| Comorbidities [n, (%)] | 33 (8.3) | 15 (8) | 18 (8.6) | 0.84[b] |
| Smokers [n, (%)] | 60 (15.1) | 24 (12.8) | 36 (17.1) | 0.23[b] |
| *BRCA* Mutation carriers [n, (%)] | 95 (23.9) | 37 (17.6) | 58 (27.6) | 0.07[b] |
| Previous breast surgery [n, (%)] | 113 (28.5) | 53 (28.3) | 60 (28.6) | 0.8[b] |
| Previous radiotherapy [n, (%)] | 71 (17.9) | 29 (15.5) | 42 (20) | 0.26[b] |
| Adjuvant radiotherapy [n, (%)] | 60 (15.1) | 24 (12.8) | 36 (17.1) | 0.27[b] |

Similarly, no significant differences were found for the characteristics of surgeries (as reported in Table 2).
[a] Mann-Whitney test.
[b] Chi square test; BMI: Body mass index.

**Table 2**
Baseline characteristics of the surgeries.

| | Total (n = 521) | TSE (n = 237) | DTI (n = 284) | p-value TSE vs DTI |
|---|---|---|---|---|
| Mastectomy [n (%)] | | | | 0.17 |
| Bilateral | 248 (47.6) | 100 (42.2) | 118 (52.1) | |
| Unilateral | 273 (52.4) | 137 (57.8) | 136 (47.9) | |
| Type of mastectomy [n (%)] | | | | 0.07 |
| NSM | 302 (58) | 145 (61.2) | 157 (55.3) | |
| SSM | 219 (41) | 92 (38.8) | 127 (44.7) | |
| Axillary surgery [n (%)] | | | | 0.98 |
| Axillary resection | 54 (10.4) | 23 (10.5) | 31 (10.9) | |
| Sentinel lymphnode biopsy | 195 (37.4) | 89 (40.6) | 106 (37.3) | |

All p-values were calculated using the Chi-squared test. NSM: nipple sparing mastectomy; SSM: skin-sparing mastectomy.

**Table 3**
Rate of surgical and aesthetic complications.

| | Total (n = 521) | TSE (n = 237) | DTI (n = 284) | p-value TSE vs DTI |
|---|---|---|---|---|
| Surgical complications [n, (%)] | 30 (5.8) | 16 (6.7) | 14 (4.9) | 0.37 |
| skin-nipple necrosis | 5 (1) | 2 (0.8) | 3 (1.1) | |
| infection | 12 (2.3) | 7 (3.0) | 5 (1.8) | |
| wound dehiscence | 7 (1.3) | 4 (1.7) | 3 (1.1) | |
| seroma | 5 (1) | 3 (1.2) | 2 (0.7) | |
| hematoma | 1 (0,2) | 0 (0) | 1 (0.3) | |
| Implant removal [n, (%)] | 16 (3.1) | 9 (3.8) | 7 (2.5) | 0.38 |
| Aesthetic complications [n, (%)] | 88 (16.9) | 39 (16.4) | 49 (17.2) | 0.81 |
| Severe capsular contracture | 19 (3.6) | 9 (3.8) | 10 (3.5) | |
| Implant dystopia | 4 (0.8) | 2 (0.8) | 2 (0.7) | |
| Rippling | 65 (12.5) | 28 (11.8) | 37 (13) | |

All p-values were calculated using the Chi-squared test.

**Table 4**
BREAST-Q scores recorded preoperatively and one year postoperatively, expressed as mean ± standard deviation. Changes in scores are expressed as Delta (postoperative score minus preoperative score). *P < 0.05.

| | TSE | | | | DTI | | | | TSE vs DTI (p-value) |
|---|---|---|---|---|---|---|---|---|---|
| | Preoperative | Postoperative | Pre vs post (p-value) | Delta | Preoperative | Postoperative | Pre vs post (p-value) | Delta | |
| Satisfaction-breasts | 59.2 ± 11.8 | 72.2 ± 9.9 | <0.01* | 13.1 ± 15.5 | 59.4 ± 11.9 | 72.1 ± 19.8 | <0.01* | 12.7 ± 5.4 | 0.82 |
| Psychosocial wellness | 64 ± 14 | 77.5 ± 11.9 | <0.01* | 13.3 ± 18.5 | 64.3 ± 13.9 | 77.2 ± 11.7 | <0.01* | 13 ± 18.3 | 0.86 |
| Sexual well-being | 57,3 ± 14.5 | 61.6 ± 12.8 | <0.01* | 4.2 ± 17 | 56.9 ± 14.6 | 59.8 ± 13.2 | 0.03* | 2.8 ± 19.5 | 0.45 |
| Physical impact (chest) | 77.1 ± 11.7 | 75.4 ± 13 | 0.18 | −1.7 ± 17.4 | 77 ± 11.4 | 75.2 ± 12.8 | 0.13 | −1.8 ± 17 | 0.96 |
| Overall satisfaction with outcome | – | 74 ± 12 | – | – | – | 74.2 ± 12.1 | – | – | 0.87 |

All data are presented as mean ± standard deviation. P values for pre-vs postoperative comparison were calculated using paired T-test. P-values for TSE and DTI comparison were calculated with unpaired T-test: deltas were compared for breasts satisfaction, psychosocial wellness, sexual well-being, and physical impact; the postoperative scores were compared for overall satisfaction with outcome.

**Table 5**
Panel evaluation of postoperative results. Scores were rated on a five-point Likert scale ranging from 1 (very dissatisfied) to 5 (very satisfied). Overall aesthetic result scored on a 10-point scale ranging from 1 (very poor result) to 10 (excellent result).

| Scores | TSE Postoperative mean ± SD | DTI Postoperative mean ± SD | TSE vs DTI (p-value) |
|---|---|---|---|
| Breast symmetry | 3,8 ± 0,6 | 3.8 ± 0.4 | 0.19 |
| Breast shape | 3,9 ± 0,6 | 4 ± 0.5 | 0.06 |
| Breast scars | 3,9 ± 0,5 | 4.1 ± 0.5 | 0.16 |
| Breast volume | 4 ± 0,5 | 4.1 ± 0.5 | 0.11 |
| Position of IMF | 3,7 ± 0,5 | 3.6 ± 0.5 | 0.12 |
| Overall aesthetic result | 8,6 ± 0,6 | 8.5 ± 1 | 0.32 |

P-values for TSE and DTI comparison were calculated with Mann-Whitney test.

**Table 6**
Complication rate for DTI and TSE by BMI risk category. The risk categories are BMI<22 and BMI≥22. CI: confidence interval; N/A: not applicable; *: odds ratio were calculated using risk BMI≥22 as the reference in both surgical groups.

| Surgery | | DTI | | TSE | |
|---|---|---|---|---|---|
| Groups | | BMI≥22 | BMI<22 | BMI≥22 | BMI<22 |
| Surgical Complications | Actual complication rate | 0.77% (1/130) | 16.25% (13/80) | 7.5% (10/133) | 11.1% (6/54) |
| | Odds ratio* (95% CI) | Reference | 25.03 (3.2–195.46) | Reference | 1.53 (0.53–4.46) |
| | p value | N/A | 0.002 | N/A | 0.429 |
| Aesthetic complications | Actual complication rate | 7.69% (10/130) | 48.75% (39/80) | 22.56% (30/133) | 16.67% (9/54) |
| | Odds ratio* (95% CI) | Reference | 11.41 (5.23–24.9) | Reference | 0.68 (0.3–1.56) |
| | p value | N/A | <0.001 | N/A | 0.37 |

respectively) but not in the TSE group (Table 6).

## Discussion

Despite preliminary reports suggested that PBR, at least in the short-term, could lead to predictable and aesthetically stable outcomes, no studies have investigated the long-term results and reported evidence concerning the variables which could influence surgical safety [3,4,6,7,20,21].

In this retrospective analysis, we reported the outcomes of a population of 397 patients undergoing NSM or SSM and immediate PBR. The number of surgeries performed was 521, with an average follow-up of 38 months. We proved that PBR is a reliable procedure, reporting a complication rate as low as 5.8% and successful aesthetic and HRQOL outcomes.

This study is original in that it evaluates clinical endpoints to

determine which factors can influence and predict the surgical outcome. The analysis comparing DTI and TSE prepectoral reconstruction found that, although there were no significant difference between the two populations, a lower BMI and adjuvant radiotherapy were significantly associated to a higher risk of developing a surgical complication only in DTI group. The design of a multiple regression model confirmed these findings, and BMI showed a strong association with surgical outcome. Patients at lowest BMI were found also more prone to develop an aesthetic complication, if they had a DTI reconstruction.

Following these evidence, BMI and adjuvant radiotherapy could be examined as potential parameters for the selection of candidates to PBR. Indeed, although a flood of early studies on PBR has been reported, they exploited a marked variety of criteria for the enrollment of the patients. No guideline has already been produced and there is no consensus about the proper indications for this technique. So far, PBR has been generally performed after NSM or SSM in non-smokers patients, under 30 kg/m2 of BMI, with no history of radiation therapy and with a breast excision volume not exciding 600 g, following the criteria from British Association of Plastic Reconstructive and Aesthetic Surgeons and Association of Breast Surgery associations for prepectoral reconstruction with ADM [9]. Nevertheless, these criteria were designed for implant-based partially submuscular techniques, which uses biological matrices as an extension of the pectoralis major. Although valid and suitable for ADM assisted submuscular breast reconstruction, these criteria exclude a big number of patients with heterogeneous characteristic, who would otherwise benefit from PBR. Indeed recent studies investigated the use of PBR in challenging patients, with large and ptotic breast and a BMI>30 kg/m$^2$, with promising results in term of surgical safety and aesthetic outcome.

In our clinical practise, we found convenient using the BMI to evaluate patients candidate to PBR. We feel that every patient could be a good candidate, unless an adequate skin coverage is provided and adequate thickness and vascularisation of the mastectomy flaps assessed. What surgeons should carefully consider most is the pattern of the mastectomy along with the PBR modality. We usually apply a skin-reducing patter and DTI for patients over 35 kg/m$^2$ of BMI, with big breast and redundant skin. Our analysis suggest that, for patients with BMI$\leq$35 kg/m$^2$, physicians should weight the characteristics of the patients. At lower levels of BMI and whenever postoperative radiotherapy is planned, STE reconstruction would be considered a more reliable approach, even at the cost of a surgical procedure involving two stages. On the other hand, average BMI patients, not undergoing radiation therapy would benefit from either DTI or STE. In these cases, we prefer to apply a single-stage technique, in order to reduce patients' morbidity, while improving cost-effectiveness. Anyway, we believe that the proper indication should be tailored on and discussed with the patient, taking into account his preferences, physical and clinical characteristic.

In our study, every unit of drop in BMI increases the odds of complication by 1.15 times in patients undergoing DTI. We found that applying a threshold of BMI<22, values of BMI under this point were associated with significant increased risk of developing both aesthetic and surgical complication in the DTI group. These data fit well with our clinical experience and currently we carefully evaluate patients at lower BMI. While this cut-off point in BMI can notably support physician in the management of patients undergoing breast reconstruction with prepectoral approach, we recommend to cautiously weigh all the different characteristics relating to the patient in the decision making process.

Furthermore, we recommend that careful attention should be given to the evaluation of mastectomy skin flap perfusion prior to reconstruction. Especially patients at lowest BMI can have delicate appearance of postmastectomy skin flaps because they lack or have a thin subcutaneous fat layer. The concerns with these flaps are the risks of ischemia and dehiscence in the immediate post-reconstructive period and implant visibility at long term [22]. Although these are important concerns, they should not preclude the prepectoral approach in thin patients. In recent reports, prepectoral reconstruction has been performed in case of mastectomy flap layer more than 1 cm in thickness [6,7,9]. Indeed eligibility of thin patients for immediate prepectoral reconstruction should be determined intraoperatively, following mastectomy. We believe that flap thickness is not a criterion for the prepectoral approach; rather, skin perfusion determines eligibility. Clinical assessment of skin viability should be performed before proceeding with the prepectoral approach. Clinical evaluation is critical for assessing mastectomy skin flap perfusion and can be combined with adjunct measures, like objective assessment of skin perfusion using a tissue perfusion system. Indocyanine green (ICG) angiography, preoperative imaging or devascularization and surgical delayed procedure have been proposed as reliable methods for assessing perfusion of mastectomy flaps, in the attempt to reduce the likelihhod of skin necrosis and complications [7,23–27]. Despite of the encouraging results of preliminary studies, strong evidence are required to support the application of imaging methods for evaluation of thickness and perfusion of the flaps in the routinely clinical practice. In the current practice, the viability of the skin flaps is broadly determined by clinical intraoperative assessment.

The role of the prepectoral emerging techniques in the context of postmastectomy radiation or prior radiotherapy has been also evaluated by several reports. A retrospective analysis evaluating subcutaneous versus submuscular placed expanders, confirmed a higher intraoperative and first postoperative expansion ratio without increased complication rates in the prepectoral group [7]. Another study reported the early data of TSE in patients with post-mastectomy radiation therapy, arguing that no risk factors, including radiation was associated with any complication [28]. We confirmed these evidences and agree that postoperative radiation should not be an absolute contraindication to PBR. So far, no study has compared DTI and TSE in the setting of postoperative radiotherapy and we support the idea that in this case TSE should be preferred.

The use of the PBR assisted by biological or synthetic devices have been associated with an increased risk of seroma [2,4,6,8]. Interestingly, in our series, we reported 5 cases of seroma requiring a second operation. A possible explanation to this issue could rely on the knitting of the mesh used to wrap the implant, which, conversely to other devices, allows an easy fluid drainage. Unlike acellular dermal matrix, meshes do not require any rehydration or long treatment before use, and we estimated a time of exposure as low as 3–5 min, resulting in a shorter surgical time and decreased likelihood of infection and implant contamination. Furthermore, the web-knitted design of the mesh can promote the drainage of fluid and a faster colonization and formation of connective tissue surrounding the implant.

In our analysis, the association between radiotherapy and complications in DTI group lost significance for the onset of aesthetic complications. Although we evaluated patients over a long-term period, certain complications, like capsular contracture can take years to develop. Therefore, we believe that a longer follow-up is required to confirm this data regarding long-term aesthetic complications. Furthermore, albeit concerns about capsular contracture have firmly established the submuscular approach as the gold standard for prosthetic breast reconstruction over the past decades, the use of ADMs or meshes to create a 'protective' pre-pectoral pocket has been recently associate to a decreased risk of capsular contracture, attributed to a diminished

inflammatory response [4,6,7]. In our study, we confirmed these findings. Moreover, some studies reported also histological data of the tissue surrounding the implant and the ADM/mesh after the surgery. They found that these devices show fast integration, promote cell proliferation, colonization by miofibroblasts and angiogenesis spots, with decreased fibroblast cellularity [3,29–31]. The mesh seemed to act like a sieve layer between the prosthesis and the subcutaneous tissue, reducing inflammatory response along with the likelihood of capsular contracture.

Owing to the short follow-up, few studies have examined the impact of subcutaneous reconstruction on HRQOL [2,20]. In our analysis, we reported high patient satisfaction following mastectomy and PBR and an increase of scores in the main domains of BREAST-Q questionnaire from the preoperative to the postoperative period. No significant difference was found between the scores of the groups. Another remarkable aspect of our study is that we examined BREAST-Q scores and their changes over time. Indeed, in our series all the postoperative data were evaluated both in absolute term and in relation to preoperative results, as changes in scores are considered a more reliable and comparable measurement. Without a baseline measurement it would impossible to genuinely compare the scores between the groups and estimate if and how a good level of HRQOL was actually an improvement [15].

Although the study found interesting and original evidence, there are some limitations. First, the study has a retrospective design and a larger multicentre prospective trial would provide better evidence to support our conclusions. We evaluated patients over a long-term period, but certain complications, like capsular contracture can take years to develop. Therefore, longer follow-up is required to confirm robust data regarding long-term outcomes and capsular contracture.

## Conclusion

Lower BMI and adjuvant radiotherapy are significantly associated to a higher risk of developing a surgical complication in DTI PBR. Patients at lowest BMI with DTI are prone to develop an aesthetic complication. According to this analysis, we suggest to carefully choose candidates for PBR; BMI and adjuvant radiotherapy could be examined as potential parameters for the selection of candidates to PBR.

## Acknowledgments

We report to that the author Donato Casella has been recently contracted (March 2018) for attending events and workshop as guest speaker, on an “ad hoc” basis contractor or freelance consultant agreement with Pfm Medical, TiLOOP Bra manufacturing company. The rest of the authors have nothing to disclose. No funding was received for this article. None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

## References

[1] Casella D, Bernini M, Bencini L, Roselli J, Lacaria MT, Martellucci J, et al. TiLoop® Bra mesh used for immediate breast reconstruction: comparison of retropectoral and subcutaneous implant placement in a prospective single-institution series. Eur. J. Plast. Surg. 2014;37:599–604. https://doi.org/10.1007/s00238-014-1001-1.

[2] Casella D, Di Taranto G, Marcasciano M, Sordi S, Kothari A, Kovacs T, et al. Nipple-sparing bilateral prophylactic mastectomy and immediate reconstruction with TiLoop® Bra mesh in BRCA1/2 mutation carriers: A prospective study of long-term and patient reported outcomes using the BREAST-Q. Breast Edinb. Scotl. 2018;39:8–13. https://doi.org/10.1016/j.breast.2018.02.001.

[3] Maruccia M, Di Taranto G, Onesti MG. One-stage muscle-sparing breast reconstruction in elderly patients: a new tool for retaining excellent quality of life. Breast J 2018;24(2):180–3. https://doi.org/10.1111/tbj.12860.

[4] Onesti MG, Maruccia M, Di Taranto G, Albano A, Soda G, Ballesio L, et al. Clinical, histological, and ultrasound follow-up of breast reconstruction with one-stage muscle-sparing "wrap" technique: A single-center experience. J. Plast. Reconstr. Aesthetic Surg. JPRAS 2017;70:1527–36. https://doi.org/10.1016/j.bjps.2017.06.023.

[5] Berna G, Cawthorn SJ, Papaccio G, Balestrieri N. Evaluation of a novel breast reconstruction technique using the Braxon® acellular dermal matrix: a new muscle-sparing breast reconstruction. ANZ J Surg 2017;87(6):493–8. https://doi.org/10.1111/ans.12849.

[6] Vidya R, Masià J, Cawthorn S, Berna G, Bozza F, Gardetto A, et al. Evaluation of the effectiveness of the prepectoral breast reconstruction with Braxon dermal matrix: First multicenter European report on 100 cases. Breast J. 2017;23:670–6. https://doi.org/10.1111/tbj.12810.

[7] Zhu L, Mohan AT, Abdelsattar JM, Wang Z, Vijayasekaran A, Hwang SM, et al. Comparison of subcutaneous versus submuscular expander placement in the first stage of immediate breast reconstruction. J. Plast Reconstr. Aesthetic. Surg. JPRAS 2016;69:e77–86. https://doi.org/10.1016/j.bjps.2016.01.006.

[8] Sigalove S, Maxwell GP, Sigalove NM, Storm-Dickerson TL, Pope N, Rice J, et al. Prepectoral implant-based breast reconstruction: rationale, indications, and preliminary results. Plast. Reconstr. Surg. 2017;139:287–94. https://doi.org/10.1097/PRS.0000000000002950.

[9] Martin L, O'Donoghue JM, Horgan K, Thrush S, Johnson R, Gandhi A, et al. Acellular dermal matrix (ADM) assisted breast reconstruction procedures: joint guidelines from the Association of Breast Surgery and the British Association of Plastic, Reconstructive and Aesthetic Surgeons. Eur. J. Surg. Oncol. J. Eur. Soc. Surg. Oncol.Br. Assoc. Surg. Oncol. 2013;39:425–9. https://doi.org/10.1016/j.ejso.2012.12.012.

[10] Casella D, Di Taranto G, Marcasciano M, Lo Torto F, Barellini L, Sordi S, et al. Subcutaneous expanders and synthetic mesh for breast reconstruction: long-term and patient-reported BREAST-Q outcomes of a single-center prospective study. J. Plast. Reconstr. Aesthetic. Surg. JPRAS 2018. https://doi.org/10.1016/j.bjps.2018.12.018.

[11] Casella D, Di Taranto G, Marcasciano M, Sordi S, Kothari A, Kovacs T, et al. Evaluation of prepectoral implant placement and complete coverage with TiLoop Bra Mesh for Breast Reconstruction: a prospective study on long-term and patient-reported BREAST-Q Outcomes. Plast. Reconstr. Surg. 2019;143:1e–9e. https://doi.org/10.1097/PRS.0000000000005078.

[12] Casella D, Di Taranto G, Marcasciano M, Lo Torto F, Barellini L, Sordi S, et al. Subcutaneous expanders and synthetic mesh for breast reconstruction: Long-term and patient-reported BREAST-Q outcomes of a single-center prospective study. J. Plast. Reconstr. Aesthetic. Surg. JPRAS 2018. https://doi.org/10.1016/j.bjps.2018.12.018.

[13] Potter S, Holcombe C, Ward JA, Blazeby JM, BRAVO Steering Group. Development of a core outcome set for research and audit studies in reconstructive breast surgery. Br J Surg 2015;102(11):1360–71. https://doi.org/10.1002/bjs.9883.

[14] Casella D, Calabrese C, Bianchi S, Meattini I, Bernini M. Subcutaneous tissue expander placement with synthetic titanium-coated mesh in breast reconstruction: long-term results. Plast Reconstr Surg Glob Open 2015;3(12):e577. https://doi.org/10.1097/GOX.0000000000000549.

[15] Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: the BREAST-Q. Plast Reconstr Surg 2009;124(2):345–53. https://doi.org/10.1097/PRS.0b013e3181aee807.

[16] Wei CH, Scott AM, Price AN, Miller HC, Klassen AF, Jhanwar SM, et al. Psychosocial and sexual well-being following nipple-sparing mastectomy and reconstruction. Breast J. 2016;22:10–7. https://doi.org/10.1111/tbj.12542.

[17] Cardoso JS, Pinto da Costa JF, Cardoso MJ. Modelling ordinal relations with SVMs: an application to objective aesthetic evaluation of breast cancer conservative treatment. Neural Netw Off J Int Neural Netw Soc 2005;18(5–6):808–17. https://doi.org/10.1016/j.neunet.2005.06.023.

[18] Fino P, Di Taranto G, Toscani M, Scuderi N. Surgical therapy of breast hypertrophy: a comparison of complications and satisfaction rate in large and small superior pedicle custom-made reduction mammaplasty. Eur Rev Med Pharmacol Sci 2016;20(21):4411–5.

[19] Fino P, Di Taranto G, Toscani M, Scuderi N. Breast reduction: personal technique. Clin Ter 2016;167(6):e167–70.

[20] Onesti MG, Fanelli B, Di Taranto G. Subcutaneous implant breast reconstruction: the importance of objectively assessing the outcomes. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol 2018;44(2):271–2. https://doi.org/10.1016/j.ejso.2017.11.025.

[21] Reitsamer R, Peintinger F. Prepectoral implant placement and complete coverage with porcine acellular dermal matrix: a new technique for direct-to-implant breast reconstruction after nipple-sparing mastectomy. J Plast Reconstr Aesthetic Surg JPRAS 2015;68(2):162–7. https://doi.org/10.1016/j.bjps.2014.10.012.

[22] Gabriel A, Maxwell GP. Prepectoral breast reconstruction in challenging patients. Plast Reconstr Surg 2017;140:14S–21S. https://doi.org/10.1097/PRS.0000000000004046. 6S Prepectoral Breast Reconstruction.

[23] Bahl M, Pien IJ, Buretta KJ, Hwang ES, Greenup RA, Ghate SV, et al. Can vascular patterns on preoperative magnetic resonance imaging help predict skin necrosis after nipple-sparing mastectomy? J. Am. Coll. Surg. 2016;223:279–85. https://doi.org/10.1016/j.jamcollsurg.2016.04.045.

[24] Bertoni DM, Nguyen D, Rochlin D, Hernandez-Boussard T, Meyer S, Choy N, et al. Protecting nipple perfusion by devascularization and surgical delay in

patients at risk for ischemic complications during nipple-sparing mastectomies. Ann. Surg. Oncol. 2016;23:2665–72. https://doi.org/10.1245/s10434-016-5201-8.

[25] Frey JD, Salibian AA, Choi M, Karp NS. Mastectomy flap thickness and complications in nipple-sparing mastectomy: objective evaluation using magnetic resonance imaging. Plast Reconstr Surg Glob Open 2017;5(8):e1439. https://doi.org/10.1097/GOX.0000000000001439.

[26] Rancati AO, Angrigiani CH, Hammond DC, Nava MB, Gonzalez EG, Dorr JC, et al. Direct to implant reconstruction in nipple sparing mastectomy: patient selection by preoperative digital mammogram. Plast. Reconstr. Surg. Glob. Open 2017;5:e1369. https://doi.org/10.1097/GOX.0000000000001369.

[27] Negenborn VL, Young-Afat DA, Dikmans REG, Smit JM, Winters HAH, Don Griot JPW, et al. Quality of life and patient satisfaction after one-stage implant-based breast reconstruction with an acellular dermal matrix versus two-stage breast reconstruction (BRIOS): primary outcome of a randomised, controlled trial. Lancet Oncol. 2018;19:1205–14. https://doi.org/10.1016/S1470-2045(18)30378-4.

[28] Elswick SM, Harless CA, Bishop SN, Schleck CD, Mandrekar J, Reusche RD, et al. Prepectoral implant-based breast reconstruction with postmastectomy radiation therapy. Plast. Reconstr. Surg. 2018;142:1–12. https://doi.org/10.1097/PRS.0000000000004453.

[29] Stump A, Holton LH, Connor J, Harper JR, Slezak S, Silverman RP. The use of acellular dermal matrix to prevent capsule formation around implants in a primate model. Plast Reconstr Surg 2009;124(1):82–91. https://doi.org/10.1097/PRS.0b013e3181ab112d.

[30] Dieterich M, Stubert J, Gerber B, Reimer T, Richter D-U. Biocompatibility, cell growth and clinical relevance of synthetic meshes and biological matrixes for internal support in implant-based breast reconstruction. Arch Gynecol Obstet 2015;291(6):1371–9. https://doi.org/10.1007/s00404-014-3578-9.

[31] Schmitz M, Bertram M, Kneser U, Keller AK, Horch RE. Experimental total wrapping of breast implants with acellular dermal matrix: a preventive tool against capsular contracture in breast surgery? J Plast Reconstr Aesthetic Surg JPRAS 2013;66(10):1382–9. https://doi.org/10.1016/j.bjps.2013.05.020.