INTRODUCTION

Breast reconstruction constantly advances, increasing the expectations of patients seeking natural aesthetic results, ideal breast size and shape, with a fast recovery time and low rate of complication.1 Implant-based breast reconstruction (IBR) is currently the most frequently performed reconstructive technique post mastectomy. Even though submuscular IBR continues to be the most commonly used technique, mastectomy technique optimization, the possibility to check skin viability with indocyanine green angiography, the enhanced propensity of patients undergoing prophylactic mastectomies, and the introduction of acellular dermal matrices (ADMs) have paved the way to the rediscovery of the subcutaneous reconstruction technique. The aim of this article is to update the complication rate of immediate and delayed prepectoral IBR using human ADMs (hADMs).

Methods: A literature search, using PubMed, Medline, Cochrane, and Google Scholar database according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, was conducted to evaluate complication rates of prepectoral implant–based reconstructions using hADMs. The following MeSH terms were used: “prepectoral breast reconstruction acellular dermal matrix,” “prepectoral breast reconstruction ADM,” “human ADM breast reconstruction,” and “human acellular dermal matrix breast reconstruction” (period: 2005–2020; the last search took place on April 2, 2020).

Results: This meta-analysis includes 1425 patients (2270 breasts) who had undergone immediate or delayed prepectoral IBR using different types of hADMs. The overall complication rate amounted to 19%. The most frequent complication was represented by infection (7.9%), followed by seroma (4.8%), mastectomy flap necrosis (3.4%), and implant loss (2.8%).

Conclusions: The overall complication rate was 19%. The most frequent complications were infection, seroma, and mastectomy flap necrosis, while capsular contracture was rare. (Plast Reconstr Surg Glob Open 2020;8:e3235; doi: 10.1097/GOX.0000000000003235; Published online 3 December 2020.)
the disappearance of functional deficits and pain caused by the pectoral muscle elevation. Similar to the submuscular IBR, the prepectoral IBR can be performed in 1 (direct to implant: DTI) or 2 stages following skin-sparing or nipple-sparing mastectomies. Moreover, patients affected by animation deformity or dysfunctional chronic chest pain can be selected for delayed IBR by way of a pocket conversion from a submuscular to a prepectoral plane.

The introduction of ADMs has certainly represented a key point in the modern prepectoral IBR. In fact, the ADM brings an additional interface between the implant and the mastectomy flap as well as additional support to keep the implant in the desired position, leading to the improvement of functional and aesthetic outcomes. ADMs consist of biodegradable soft connective tissue grafts created from a decellularization process that presents a regenerative capacity. Upon implantation, this structure serves as a scaffold for donor-side cells to facilitate subsequent incorporation and revascularization. ADMs are derived from human (AlloDerm, LifeCell, Branchburg, N.J.), porcine (Strattice—LifeCell Corporation; Branchburg, N.J. and Permacol—Covidien, Mansfield, Mass., USA), or bovine (SurgiMend—Integra Life Sciences, Plainsboro, N.J. and Braxon—Decomed S.r.l., Venezia, Italy) tissues.

In 2005, Breuing and Warren described the first submuscular IBR using a human-derived ADM (AlloDerm, LifeCell, Branchburg, N.J.) positioned between the inferior border of the pectoralis major muscle and the chest wall, with the aim to expand the lower pole of the breast. Since then, several series of IBR that adopted ADMs have been brought forth. Indeed, a recent study reports that more than 50% of IBRs are performed using an ADM in the United States. Nonetheless, the universal approval of ADMs for IBR has been restrained by worries concerning surgical complications such as seroma, infection, and mastectomy flap necrosis. In the last 10 years, many reports concerning the incidence of complications related to ADMs have been published. The aim of this article is to provide an update of the complication rates of immediate and delayed prepectoral IBR using human ADMs (hADMs).

MATERIALS AND METHODS
A literature search via PubMed, Cochrane, and Google Scholar databases according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines was conducted to evaluate the complication rates of prepectoral implant–based reconstructions using hADMs. The following MeSH terms were used: “prepectoral breast reconstruction acellular dermal matrix,” “prepectoral breast reconstruction ADM,” “human ADM breast reconstruction,” and “human acellular dermal matrix breast reconstruction” (period: 2005–2020; the last search was performed on April 2, 2020). Two independent reviewers performed two-stage screening and data extractions. Abstracts were screened to identify eligible papers. Reference lists of selected studies were screened for additional articles. The search strategy is shown in the flow chart below.

Inclusion and Exclusion Criteria
Studies were selected based on the following inclusion criteria: (i) studies selectively investigating prepectoral implant–based reconstructions using human acellular dermal matrix; (ii) registration of complication after surgical treatment; (iii) minimal sample of 10 breasts; (iv) full text available in English. Studies were excluded due to any of the following criteria: (i) review articles; (ii) case reports; (iii) articles only reporting surgical techniques and not outcomes or complication rates; (iv) articles describing studies that included fewer than 10 breasts; (vi) non-referenced articles; (vii) expert opinion (Level V).

Data Collection
Extracted data included:
1) Preoperative data: number of patients included, number of breasts included, age (mean and range), body mass index (BMI, mean and range), inclusion and number of patients who had undergone previous or adjuvant radiation therapy, inclusion and number of patients with BMI > 30 kg/m², eligibility criteria of prepectoral IBR (inclusion and exclusion criteria).
2) Intraoperative data: type of mastectomies (skin-sparing mastectomy SSM; nipple-sparing mastectomy NSM), implant or expander characteristics, type of HADM, size of HADM, ADM placement, presence of contemporary dermal flap.
3) Postoperative complications: follow-up (mean and range), overall incidence of complication, incidence of seroma, infection, implant loss, mastectomy flap necrosis, capsular contracture.
4) Outcomes: patient satisfaction, aesthetic outcomes, ripping, revision surgery (fat graft, implant exchange).

Moreover, patients who had undergone preoperative or postoperative radiation therapy (RT) and patients affected by obesity (presenting a BMI > 30 kg/m²) were analyzed separately to calculate the odds ratio relative to the overall complication rate.

Bias Assessment
The Q and the I² of each study were assessed using fixed-effect models.

Statistical Analysis
Statistical analysis was performed using SPSS statistical software (version 24.0; IBM Corporation, Somers, N.Y.). Pooled random effect estimates for each postoperative surgical complication and 95% confidence interval (95% CI) were calculated using Microsoft Excel (Microsoft Corp, Redmond, Wash.). Univariate logistic regression models were performed to identify two risk factors (radiation therapy and obesity) associated with overall complication rate, including seroma, infection, flap necrosis, implant loss, and capsular contracture.
RESULTS

After exclusion of duplicates, 359 articles were identified. Two different reviewers analyzed all the records by titles and abstracts. Sixty-five full-text articles were examined for eligibility. Eighteen studies published between 2015 and 2020 were considered eligible based on appropriateness, relevance, and recency (Fig. 1). A total of 1425 patients and 2270 breasts were included in the meta-analysis, and the sample size of each study ranged from 23 to 353 breasts. Figure 2 shows the Q and the I2 of each study assessed using fixed-effect models.

Patient age ranged from 19 to 83 years, bringing the average age to 42.2 years. Patient BMI ranged from 17.8 to 54 kg/m². Twelve studies included obese patients and 4 studies reported the exact number of obese patients included (104). Nine studies included patients who had undergone prior radiation therapy (133 patients). Sixteen studies reported the number of patients who had undergone postoperative radiation therapy (171 patients).

Exclusion criteria resulted to be heterogeneous. All the authors performed an intraoperative mastectomy skin flap evaluation using perfusion assessment devices. Active smokers and previous radiation therapy represented exclusion criteria respectively in 3 and 5 articles. Patients with a BMI greater than 30 or 40 kg/m² were excluded in 4 studies. Eleven studies included patients with a BMI greater than 30 kg/m² and 5 studies openly mentioned the number of obese women included in the sample, for a total of 126 patients. Fourteen articles included patients who had undergone previous radiotherapy or adjuvant radiotherapy (235 cases).

Table 1 shows each study’s patient preoperative characteristics in detail. Ten studies described cases of immediate IBR, 4 studies described cases of delayed IBR, and 4 studies reported both. In summary, 1015 patients underwent immediate breast reconstruction (DTI or two-stage), while 410 underwent delayed breast reconstruction. Among them, 274 patients (426 breast) underwent pocket conversion from a subpectoral to a prepectoral plane. Implant size ranged from 125 to 770 ml.

AlloDerm (LifeCell, Branchburg, N.J.) was the most common hADM (12 studies, 1062 patients), and size 16 × 20 cm was chosen in all cases. Four studies (201 patients) described prepectoral IBR using

Fig. 1. Flowchart according to PRISMA guidelines.
AlloDerm®RTU (LifeCell, Branchburg, N.J.) 16 × 16 cm or 16 × 20 cm. Three studies (58 patients) reported the adoption of FlexHD (Ethicon, Inc., Somerville, N.J.) and Musculoskeletal Transplant Foundation, Edison, N.J.), with a size of 16 × 16 cm or 16 × 20 cm. Dermacell (LifeNet Health, Virginia Beach, Va.) and Cryoderm (CGBio Corp., Seongnam, Korea) were used in 3 articles. Figure 3 shows the characteristics of hADM included in the review. Twelve of 18 studies reported author disclosures (affiliation with the company providing the breast implant or the ADM); no funding was received for any of the included studies.

Table 2 shows the intraoperative data of each study in detail. Mean follow-up was 17.6 months (range, 1–103). Pooled random effect estimates of overall complication rates (95% CI) resulted in 4.8% (CI 2.25%–7.49%; 59 patients) for seroma, 7.9% (CI 2.74%–7.9%; 107 patients) for infection, 2.8% (CI 0.34%–5.26%; 40 patients) for implant loss, 3.4% (CI 0.24%–7.03%; 51 patients) for mastectomy flap necrosis, and 1.2% (0%–2.4%; 8 patients) for capsular contracture (Table 3). With regard to infections (the most common complication found), only 1 study68 stated the grade of infection when reporting 10 cases of superficial cellulitis and 7 cases of pocket infection. Moreover, in 69 of 107 cases, the type of treatment put in place was specified: 27 patients had undergone oral antibiotic therapy, 18 patients had undergone intravenous antibiotic therapy, and 24 patients had undergone revision surgery. Among patients undergoing revision surgery, 11 had undergone an “explantation-washout-debridement-reimplantation” procedure. Lastly, 13 cases of implant loss due to infection were reported. One study26 reported 9 cases of implant loss without stating how many of them were due to infection.

Table 4 reports in detail the complication rate by study. A forest plot is provided to better visualize the pooled data on complications in Figure 4. Aesthetic outcomes were mentioned in 5 studies, and 2 studies used the “Aesthetic Items scale” and the “Likert scale.” Only 5 studies reported the number of patients showing postoperative rippling, the incidence of which ranged from 0.8% to 35%. Patient satisfaction was reported in 3 studies: 1 study adopted the “KNUH Breast Reconstruction Satisfaction Questionnaire” and another the “Breast Q” reporting satisfactory scores. Nine of 16 studies mentioned cosmetic revision procedures. The most common intervention consisted of one or more session of fat grafting. Implant exchange (cohesive implant or different size) was also performed in some cases.

Tables 3, and 5 report the postoperative outcomes in detail. Among the group of patients who had undergone prior (133) or postoperative (171) RT (total: 304), 22 showed postoperative complications (6 prior RT and 16 postoperative RT). In detail, 11 patients showed infection, 5 showed mastectomy flap necrosis, 3 showed seroma, and 1 showed a grade III capsular contracture. Overall, 3 patients who had undergone prior or postoperative radiation therapy underwent implant removal. With respect to obesity, neither of the studies reported complications in the obese patient subgroup. Univariate logistic regression models considered radiation therapy (RT) and obesity separately. Neither of the 2 subgroups showed an increased risk of complications compared with the control group (Table 6). Pooled complications stratified by RT exposure analyzing rate of implant loss and capsular contracture did not show an increased risk of complication when comparing the RT group with the control group (Table 7). Table 8 provides a descriptive overview on complications in patients who had undergone radiation therapy in the analyzed studies.

### DISCUSSION

One of the most meaningful advancements in prepectoral IBR was the introduction of ADMs. In 2015, Reitsamer41 described the first series of 13 patients who had undergone a prepectoral IBR using complete anterior implant coverage with a porcine ADM. Since then, several authors have published their series of 2-stage or DTI prepectoral IBRs using bovine, porcine, or human ADMs.15,20,42 In truth, prepectoral IBR can be performed with or without ADMs but different authors have assessed that complication rate and, in particular, the capsular contracture rates are significantly lower when prepectoral IBR is performed with an ADM support.12,43,44

However, there is a lack of long-term results regarding prepectoral IBR because the technique is relatively new. Our study has the aim to provide an update regarding complication rates related to prepectoral breast reconstruction using the subgroup of ADMS derived from human tissue. The present meta-analysis includes 1425 patients (2270 breasts) who have undergone immediate or delayed IBR employing different types of hADMs summarized in Figure 2. No comparative analysis between the different products has been performed in this study. Previous meta-analysis reported similar risks of complication using different types of hADMs.26 The most frequently described hADM was AlloDerm (LifeCell, Branchburg, N.J.), followed by AlloDerm®RTU (LifeCell, Branchburg, N.J.), FlexHD (Ethicon, Inc., Somerville, N.J.) and Musculoskeletal Transplant...
Table 1. Sample Characteristics

| Study       | Sample | Age (Mean-range in Years) | BMI | Radiation Therapy* | BMI > 30 | Inclusion Criteria | Exclusion Criteria |
|-------------|--------|----------------------------|-----|--------------------|---------|--------------------|-------------------|
| Becker      | 26 pts 56 b | 51                         | —   | —                  | —       | DTI prepectoral BR | None              |
| Woo         | 26 pts 135 b | 50.2 (26–76)              | 26.9 (17–44.6) | —                  | —       | Vertical mastectomy incision | Poor mastectomy flap perfusion (SPY Elite System) |
| Downs       | 43 pts 79 b | 46.8 ± 9.6                | 24.3 ± 5.4 | Included 34 pts    | Included | DTI prepectoral BR in NSM | Active smokers |
| Zhu         | 29 pts 50 p | 50.48 ± 8.8               | 27.8 ± 5.3 | Included 21 pts    | Included | Two-stage prepectoral BR | Poor mastectomy flap perfusion (SPY Elite System) |
| Schnarrs    | 188 b     | 54 (29–76)                | 27.3 (range 17, 8–51) | —                  | Included 32 pts | Prepectoral hADM primary or revision BR | Active smokers |
| Bodac       | 22 pts 26 b | 46 (30–69)                | 22–39 | Included 6 pts     | —       | Two-stage prepectoral BR | Cosmetic procedures |
| Sigalove    | 207 pts 353 b | 2570                     | —   | Included 27 pts    | Included | Prepectoral ADM BR | Xenogenic or synthetic ADM |
| Jones       | 50 pts/73 b | 47 (26–67)                | 27 (18–44) | Included 11 pts    | Included | Prepectoral ADM BR | Poor mastectomy flap perfusion (SPY Elite System) |
| Jones       | 90 pts 142 b | 55 (29–77)              | 28 (19–42) | Included 21 pts    | Included | Animation deformity after subpectoral BR | No exclusion criteria in terms of skin flap thickness, RT, BMI, smoke, or diabetes |
| Gabriel     | 57 pts 102 b | 53.2 (34–77)            | 27.3 (19–47) | Included 9 pts     | Included | Animation deformity or chronic pain ± implant malposition after subpectoral BR | Poor mastectomy flap perfusion (PDE, Hamamatsu) |
| Lentz       | 31 pts 55 b | 49.8 (34–72)             | 26.06 (20–39) | Included 7 pts     | Included | Animation deformity or chronic pain ± implant malposition after subpectoral BR | Active smokers |
| Jones       | 140 pts 194 b | 49.55 ADM               | —   | —                  | —       | Immediate implant-based BR | Poor mastectomy flap perfusion (SPY Elite System) |
| Sigalove    | 33 pts 52 b | 50.6 (23–75)             | 27.7 (16–42) | Included 33 pts    | Included | Immediate prepectoral BR following SSM or NSM + postoperative RT | Previous RT |
| Lee         | 23 pts 23 b | 45 (30–55)                | 22.1 (19, 30, 9) | Included 9 pts     | —       | Prepectoral BR | Active smokers |
| Safran      | 214 pts 313 b | 48.6 (19–83)           | 25.9 (18–54) | Included 38 pts    | Included | Prepectoral DTI BR | BMI > 30 |
| Bilezikian  | 131 pts 230 b | 45 (30–47) | 27.6 (20–38) | Included 3 pts | Included | Prepectoral 2-stage BR | Lack of fat donor sites |
| Holland     | 45 pts 80 b | 50.3                      | —   | —                  | —       | Animation deformity after subpectoral BR | Poor mastectomy flap perfusion (SPY Elite System) |

*Previous or adjuvant.
ADM, acellular dermal matrix; BMI, body mass index; pts, patients; b, breasts; BR, breast reconstruction; NSM, nipple-sparing mastectomy; SSM, skin-sparing mastectomy.
Foundation, Edison, N.J.), Dermacell (LifeNet Health, Virginia Beach, Va.), and Cryoderm (CGBio Corp., Seongnam, Korea).

ADM assemblage can be executed by positioning the matrix into the subcutaneous pocket due to soft tissue support (on-label technique) creating complete anterior coverage or, by wrapping the matrix around the tissue expander or the implant before insertion into the subcutaneous pocket, creating complete anterior and posterior coverage (off-label technique). In our review, 10 articles described complete anterior coverage of the implant (180 degree wrapping), 7 studies described complete anterior and posterior implant coverage using 2 ADM sheets (360 degree wrapping). Moreover, in 2 studies, hADM support was combined with the use of a local autodermal-adipous flap harvested from the inferior and lateral pole of the breast.

Eligibility for prepectoral breast reconstruction represents a very relevant issue. Our meta-analysis exclusion and inclusion criteria resulted quite heterogeneous. All authors agreed on the need to perform an intraoperative mastectomy skin flap evaluation using perfusion assessment devices in cases of both immediate and delayed breast reconstruction. Active smokers, previous RT, and obesity represented exclusion criteria in 5, 3, and 4 articles, respectively. Most studies included obese patients and patients who had undergone previous or adjuvant radiation therapy.

Even if there is a lack of long-term outcomes in our meta-analysis (mean follow-up, 17.6 months), results with more than 2 years of follow-up are encouraging. The overall complication rate amounted to 19%, including 4.8% cases of seroma, 7.9% cases of infection, 2.8% cases of implant loss, and 3.4% cases of mastectomy flap necrosis. No authors mentioned the onset of red breast syndrome.

Capsular contracture was reported in 1.2% of patients, which was derived from local inflammation related to an exaggerated production of collagen by fibroblastic cells in contact with the breast implant.55 Our data are in line with previous literature that reported a significantly lower rate of capsular contracture in cases of ADMs compared with conventional IBR.12,43–47 In fact, clinical and experimental studies demonstrated that hADMs induce a reduction of chronic inflammation and fibroblasts’ proliferation compared with native breast capsules.48 Lately, prepectoral reconstruction in the setting of radiotherapy has become a crucial topic of interest.15,34,45 The present univariate logistic regression analysis suggests that previous or adjuvant radiation therapy should not be considered as an independent risk factor (Table 6).

Nahabedian hypothesized that the side effects of radiotherapy are more marked toward the pectoralis muscles mostly when the inferior origin has been interrupted.15 In fact, while radiotherapy, in the setting of a subpectoral device, commonly caused skin tightening and an inframammary fold elevation with a cephalad displacement of the implant, when radiation is delivered in the setting of a prepectoral device, elevation of the inframammary fold is not observed.15 Similarly, univariate logistic regression analysis investigating the subgroup of patients with a BMI greater than 30 kg/m² did not show a significant increase in overall complication rates (Table 6).

Implant rippling still remains an unwanted side effect of prepectoral breast reconstruction, with an incidence reported between 0.8% and 35%.48 Preoperative or postoperative fat graft, especially in patients with low BMI,
Table 2. Intraoperative Data

| Study            | Mastectomy Type | Time of BR | Type of BR | Implant Description | ADM | Treatment | Size | Location                        | Dermal Flap |
|------------------|-----------------|------------|------------|---------------------|-----|-----------|------|---------------------------------|-------------|
| Becker et al.    | SM (vertical incision) | Immediate | DTI        | Smooth round saline (Spectrum, Mentor Corp) | FlexHD Pliable (84% of pts) | — | Trimming | 16 × 16 cm | Complete anterior coverage | Lateral flap |
| Woo et al.       | SM              | Immediate | DTI 10%    | Silicone gel anatomical (Mentor) | AlloDerm RTU | — | — | 16 × 20 cm | Complete anterior and posterior coverage | No |
| Downs et al.     | SM              | Immediate | DTI         | — | AlloDerm 69% FlexHD 31% | — | — | 16 × 20 cm | Complete anterior or anterior and posterior coverage | No |
| Zhu et al.       | SSM 21 (42%) / SSM 29 (58%) | Immediate | Two-stage | Expander (Natrelle 133 Mx or MV) | AlloDerm (15/29 pts) | — | Not reported | 16 × 16 or 16 × 20 cm | Complete anterior coverage | Inferior flap |
| Schnarrs et al.  | SM 53 pts       | Immediate | DTI 1      | — | AlloDerm RTU 19 FlexHD 18 | — | — | 16 × 20 cm | Complete anterior coverage | No |
| Bohac et al.     | —              | Delayed 23 pts | Immediate 3 pts | Two-stage | Expander (Mentor) | AlloDerm | — | 16 × 16 cm | Complete anterior coverage | No |
| Sigalove et al.  | SM 47% / SMM 53% | Delayed    | DTI 46     | Natrelle MX/Natrelle Inspira | AlloDerm | — | — | 16 × 20 cm | Complete anterior coverage | No |
| Jones et al.     | SM 49 (94.2%) / SMM 3 (5.8%) | Immediate | DTI        | Anatomic cohesive gel full height and profile-textured surface implants (Allergan) | AlloDerm | Washing | 16 × 20 cm | Complete anterior coverage | No |
| Jones et al.     | SM 72% / SMM 28% | Delayed    | Pocket Conversion | — | AlloDerm RTU | — | — | 16 × 20 cm | Complete anterior coverage | No |
| Gabriel et al.   | SM 72% / SMM 28% | Delayed    | Pocket Conversion | Round silicone implant | AlloDerm RTU LifeCell | — | — | 16 × 20 cm | Complete anterior coverage | No |
| Lentz et al.     | —              | Delayed    | Pocket Conversion | Smooth round cohesive or responsive silicone gel (Allergan) Upsize 90ml | AlloDerm | Washing | 16 × 20 cm | Complete anterior coverage | No |
| Jones et al.     | SM 49 (94.2%) / SMM 3 (5.8%) | Immediate | DTI 19 (36.5%) | — | AlloDerm | — | — | 16 × 20 cm | Complete anterior coverage | No |
| Sigalove et al.  | SM 77% / SMM 16% | Immediate | DTI 12 (25.5%) | Textured, anatomic (Mentor or Allergan) Size: 252, 4 ml (125–440) | CryoDerm | Washing (Betadine) | 212 cm | Two crossed ADMs | Complete anterior and posterior coverage | No |
| Lee et al.       | SM 45 (14.3%) / SMM 267 (85.3%) | Immediate | DTI         | Size: 392.9 ml (229–700) | AlloDerm 215 b (77.6%) | — | — | 16 × 20 cm | Complete anterior coverage | No |
| Safran et al.    | SM 45 (14.3%) / SMM 267 (85.3%) | Immediate | DTI         | — | AlloDerm | — | — | 16 × 20 cm | Complete anterior and posterior coverage | Wise pattern |
| Manrique et al.  | SM              | Immediate | DTI        | Round, smooth, silicone, cohesive gel (Allergan) | AlloDerm | — | — | 16 × 20 cm | Complete anterior and posterior coverage | No |
| Bilezikian et al.| SM              | Immediate | DTI        | Round, smooth, SCX (Allergan) | DermaCell | — | — | 16 × 20 cm | Complete anterior coverage | No |
| Holland et al.   | SM 13 pts/20 b | Delayed    | Pocket Conversion | — | AlloDerm | — | — | 16 × 20 cm | Complete anterior, Partial posterior and inferior coverage | No |

ADM, acellular dermal matrix; BR, breast reconstruction; DTI, direct to implant; NSM, nipple-sparing mastectomy; PO, postoperative; pts, patients; SSM, skin-sparing mastectomy.
represents the most frequently used technique to repair this cosmetic complication. In 2017, Saliban recommended creating a prepectoral pocket with a smaller base than that of the prosthesis and closing the inframammary fold incision under a moderate amount of tension in leaner patients.45 In our review, only 5 studies mentioned the onset of rippling (ranging from 0.8% to 35%), and all cases were corrected by fat graft or implant exchange (upsizing or cohesive gel implant). Astoundingly, only 4 studies reported patient satisfaction scores or objective aesthetic evaluation scales. These data point out that there is still a lack of homogeneity concerning breast reconstruction outcome evaluation.

Our meta-analysis incorporated different types of breast reconstructions, including direct-to-implant, two-stage reconstruction and pocket conversion from a subpectoral to a prepectoral plane. The latter technique was described in 6 studies and requires the dissection of the plane between the pectoralis major muscle from the overlying mastectomy skin flap, the removal of the indwelling implants, the anchorage of the pectoralis muscle to the anterior chest wall, and the placement of the implant in the new prepectoral pocket. All patients who had undergone this operation reached a complete resolution of animation deformity and chronic pain. Gabriel12 compared the results of two groups of patients who had undergone a pocket conversion with or without the use of hADM, showing a significant decrease in the complication rate in the first group.

There are several limitations to the meta-analysis, such as the possible conflict of interest related to the use of ADMs and possible publication bias. Six of 18 studies had no conflicts of interest to declare.30,33,35,36,38 However, no funding or financial support was received from any company for any of the included studies. The relative small
sample size (<100 breasts) in 9 studies, the fact that many studies were set as retrospective analysis, and the lack of correction of the confounding factors limited the power of statistical analysis.

**CONCLUSIONS**

This meta-analysis includes 1425 patients who had undergone immediate or delayed IBR adopting hADMs, with the aim to provide updated information regarding complication rates related to this procedure. The overall complication rate amounted to 19%. The most frequent complication was infection (7.9%), followed by seroma (4.8%), mastectomy flap necrosis (3.4%), and implant loss (2.8%). Capsular contracture was reported in fewer than 1% of patients.

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Table 5. Aesthetic Outcomes and Revision Surgery

| Study            | Rippling | Revision | Fat Graft % | Implant Exchange | Pt Satisfaction | Aesthetic Scale |
|------------------|----------|----------|-------------|------------------|-----------------|----------------|
| Becker\(^{25}\)  | —        | Reported | 15.3%       | 14% implant exchanged for silicone implants | —               | —              |
| Woo\(^{26}\)     | —        | —        | Second stage | 0                | —               | —              |
| Downs\(^{27}\)   | 35% 14 pts | Reported | 60%–70%     | No               | —               | —              |
| Zhu\(^{28}\)     | —        | —        | 0           | 0                | —               | —              |
| Schnarrs\(^{29}\)| —        | —        | Second or third stage | 37%               | —               | —              |
| Bohac\(^{30}\)   | —        | —        | 0           | 0                | —               | —              |
| Sigalove\(^{31}\)| —        | —        | Second or third stage | 37%               | —               | —              |
| Jones\(^{32}\)   | 12% 9 pts | Reported | —           | Two patients requested upsizing to a larger, higher profile implant at 12-15 months | High | — |
| Jones\(^{33}\)   | 4.9% 7 pts | Reported | 18.3% 26    | 0.7% 1 pt requested a smaller implant size | — | Overall breast aesthetics were improved |
| Gabriel\(^{34}\) | —        | —        | —           | —                | —               | Animation deformity resolution |
| Lentzi\(^{13}\)  | —        | Reported | 21.4% (group without prior fat graft) | 38% 13.5% | — | Animation deformity resolution |
| Jones\(^{34}\)   | 15% 18 pts | Reported | 7.2% 1.8%   | —                | —               | Successful outcome was achieved in 93.3% of cases |
| Sigalove\(^{35}\)| Reported | — | 1 pt TRAM | KNUH Breast Reconstruction Satisfaction Questionnaire: high | — | — |
| Lee\(^{36}\)     | —        | —        | 1 pt latissimus dorsi flap | — | Successful outcome |
| Safran\(^{37}\)  | —        | —        | 21% 4 pts   | 0                | —               | Breast Q 84.8 |
| Manrique\(^{38}\) | —        | Reported | —           | —                | Aesthetic Items Scale mean 20.9 Likert Scale | — |
| Bilezikian\(^{39}\) | 0.8% 2b | 3% 7 breasts cosmetic revisions | 2 pts/4b | 1 larger implant 1 cohesive gel because of visible rippling | — | — |
| Holland\(^{40}\) | —        | 6.2% 4 cosmetic revision | — | — | 7 asymmetric |

Table 6. Binary Logistic and Linear Regression Models for Radiotherapy and Obesity Variables on Surgical Outcomes

| Complication | OR  | IC    | P    |
|--------------|-----|-------|------|
| RT           | 1.2163 | 0.82–1.79 | 0.32   |
| BMI > 30 kg/m\(^2\) | 1.03 | 0.75–1.43 | 0.8 |

Table 7. Binary Logistic and Linear Regression Models for Radiotherapy Variable on Seroma, Infection, Mastectomy Flap Necrosis, Implant Loss, and Capsular Contracture

| Complication                  | OR  | IC    | P    |
|-------------------------------|-----|-------|------|
| Seroma                        | 0.1296 | 0.03–0.50 | 0.0038 |
| Infection                     | 0.279 | 0.134–0.580 | 0.0006 |
| Mastectomy flap necrosis      | 0.1449 | 0.035–0.599 | 0.0077 |
| Implant loss                  | 0.4205 | 0.128–1.3766 | 0.152  |
| Capsular contracture          | 0.5252 | 0.064–4.285 | 0.54   |

Table 8. Overview on Complications by RT Exposure

| Complication                  | Radiation Therapy (no. pts.) | No Radiation Therapy (no. pts.) |
|-------------------------------|-------------------------------|---------------------------------|
| Overall patients              | 304                           | 1121                            |
| Overall complications         | 22                            | 193                             |
| Seroma                        | 2                             | 57                              |
| Infection                     | 8                             | 99                              |
| Mastectomy flap necrosis      | 3                             | 48                              |
| Implant loss                  | 2                             | 49                              |
| Capsular contracture          | 1                             | 7                               |

REFERENCES

1. Raposio E, Belgrano V, Santi P, et al. Which is the ideal breast size?: Some social clues for plastic surgeons. *Ann Plast Surg.* 2016;76:340–345.
2. Albornoz CR, BWach PB, Mehrara BJ, et al. A paradigm shift in U.S. Breast reconstruction: Increasing implant rates. *Plast Reconstr Surg.* 2013;131:15–23.
3. Cemal Y, Albornoz CR, Disa JJ, et al. A paradigm shift in U.S. breast reconstruction: Part 2. The influence of changing mastectomy patterns on reconstructive rate and method. *Plast Reconstr Surg.* 2013;131:320e–326e.
Mangialardi et al. • Prepectoral IBR Using Human ADMs

4. Leff DR, Bottle A, Mayer E, et al. Trends in immediate postmastectomy breast reconstruction in the United Kingdom. Plast Reconstr Surg Glob Open. 2015;3:e507.

5. Gardani M, Bertozzi N, Grieco MP, et al. Breast reconstruction with anatomical implants: A review of indications and techniques based on current literature. Ann Med Surg (Lond). 2017;21:96–104.

6. Sbitany H, Piper M, Lenz R. Prepectoral breast reconstruction: A safe alternative to submuscular prosthetic reconstruction following nipple-sparing mastectomy. Plast Reconstr Surg. 2017;140:432–443.

7. Highton L, Johnson R, Kirwan G, et al. Prepectoral implant-based breast reconstruction. Plast Reconstr Surg Glob Open. 2020;8,e2667.

8. Ter Louw RP, Nahabedian MY. Prepectoral breast reconstruction. Plast Reconstr Surg. 2017;140(5S Advances in Breast Reconstruction):518–598.

9. Walia GS, Anton J, Bello R, et al. Prepectoral versus subpectoral tissue expander placement: A clinical and quality of life outcomes study. Plast Reconstr Surg Glob Open. 2018;6:e1751.

10. Mangialardi ML, Barone Adesi L, Salgarello M. Delayed acellular dermal matrix assisted prepectoral breast reconstruction: Preliminary results. Breast J. 2020;26:1104–1106.

11. Hammond DC, Schmitz WP, O’Connor EA. Treatment of breast animation deformity in implant-based reconstruction with pocket change to the subcutaneous position. Plast Reconstr Surg. 2015;135:1540–1544.

12. Gabriel A, Sigalove S, Sigalove NM, et al. Prepectoral revision breast reconstruction for treatment of implant-associated animation deformity: A review of 102 reconstructions. Aesthet Surg J. 2018;38:519–526.

13. Lenz R, Alcon A, Sbitany H. Correction of animation deformity with subpectoral to prepectoral implant exchange. Gland Surg. 2019;8:75–81.

14. Rebowe RE, Allred IJ, Nahabedian MY. The evolution from subcutaneous to prepectoral prosthetic breast reconstruction. Plast Reconstr Surg Glob Open. 2018;6:e1797.

15. Nahabedian MY. The bioengineered prosthetic breast reconstruction: Advancements, evidence, and outcomes. Gland Surg. 2019;8:271–282.

16. Boháč M, Daníšová L, Koller J, et al. What happens to an acellular dermal matrix after implantation in the human body? A histological and electron microscopic study. Eur J Histochim. 2018;62:2873.

17. Cheng A, Saint-Cyr M. Clin comparison of different ADM materials in breast surgery. Plast Surg. 2012;59:167–175.

18. Breuing KH, Warren SM. Immediate bilateral breast reconstruction with implants and inferolateral AlloDerm slings. Ann Plast Surg. 2005;55:232–239.

19. Gurunluoglu R, Gurunluoglu A, Williams SA, et al. Current trends in breast reconstruction: Survey of American Society of Plastic Surgeons 2010. Ann Plast Surg. 2013;70:103–110.

20. Loo YL, Kamalathevan P, Ooi PS, et al. Comparing the outcome of different biologically derived acellular dermal matrices in implant-based immediate breast reconstruction: A meta-analysis of the literatures. Plast Reconstr Surg Glob Open. 2018;6:e1701.

21. Wagner RD, Braun TL, Zhu H, et al. A systematic review of complications in prepectoral breast reconstruction. J Plast Reconstr Aesthet Surg. 2019;72:1051–1059.

22. Bertozzi N, Pesce M, Santi P, et al. One-stage immediate breast reconstruction: A concise review. Biomed Res Int. 2017;2017:64680859.

23. Grieco MP, Simonacci F, Bertozzi N, et al. Breast reconstruction with breast implants. Acta Biomed. 2019;89:457–462.

24. Moher D, Liberati A, Tetzlaff J, et al; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. BMJ. 2009;339:b2535.

25. Becker H, Lind JG II, Hopkins EG. Immediate implant-based prepectoral breast reconstruction using a vertical incision. Plast Reconstr Surg Glob Open. 2015;3:e412.

26. Woo A, Harless C, Jacobson SR. Revisiting an old place: Single-surgeon experience on post-mastectomy subcutaneous implant-based breast reconstruction. Breast J. 2017;23:545–553.

27. Downs RK, Hedges K. An alternative technique for immediate direct-to-implant breast reconstruction—a case series. Plast Reconstr Surg Glob Open. 2016;4:e821.

28. Zhu L, Mohan AT, Abdelbarrat JM, et al. Comparison of subcutaneous versus submuscular expander placement in the first stage of immediate breast reconstruction. Plast Reconstr Aesthet Surg. 2016;69:e77–86.

29. Schnarrs RH, Carman CM, Tobin C, et al. Complication rates with human acellular dermal matrices: Retrospective review of 211 consecutive breast reconstructions. Plast Reconstr Surg Glob Open. 2016;4:e1118.

30. Bohac M, Varga I, Polak S, et al. Delayed post mastectomy breast reconstructions with allogeneic acellular dermal matrix prepared by a new decellularization method. Cell Tissue Bank. 2018;19:61–68.

31. Sigalove S, Maxwell GP, Sigalove NM, et al. Prepectoral implant-based breast reconstruction: Rationale, indications, and preliminary results. Plast Reconstr Surg. 2017;139:287–294.

32. Jones G, Yoo A, King V, et al. Prepectoral immediate direct-to-implant breast reconstruction with anterior AlloDerm coverage. Plast Reconstr Surg. 2017;140(6S Prepectoral Breast Reconstruction):318–385.

33. Jones GE, King VA, Yoo A. Prepectoral site conversion for animation deformity. Plast Reconstr Surg Glob Open. 2019;7:e2301.

34. Jones G, Antony AK. Single stage, direct to implant prepectoral breast reconstruction. Gland Surg. 2019;8:53–60.

35. Sigalove S. Prepectoral breast reconstruction and radiotherapy—a closer look. Gland Surg. 2019;8:67–74.

36. Lee JS, Kim JS, Lee JH, et al. Prepectoral breast reconstruction with complete implant coverage using double-crossed acellular dermal matrix. Gland Surg. 2019;8:748–757.

37. Safran T, Al-Halabi B, Viezela-Mathieu A, et al. Direct-to-implant, prepectoral breast reconstruction: A single-surgeon experience with 201 consecutive patients. Plast Reconstr Surg. 2020;145:686e–696e.

38. Manrique OJ, Huang TC, Martinez-Jorge J, et al. Prepectoral two-stage implant-based breast reconstruction with and without acellular dermal matrix: Do we see a difference? Plast Reconstr Surg. 2020;145:263e–272e.

39. Bilezikian JA, Tenzel PL, Bebb GG, et al. The broad application of prepectoral direct-to-implant breast reconstruction with acellular dermal matrix drape and fluorescent imaging in a community setting. Plast Reconstr Surg. 2020;145:291–300.

40. Holland MC, Lenz R, Sbitany H. Surgical correction of breast animation deformity with implant pocket conversion to a prepectoral plane. Plast Reconstr Surg. 2020;145:652–642.

41. 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 Aesthet Surg. 2015;68:162–167.

42. Liu J, Hou J, Li Z, et al. Efficacy of acellular dermal matrix in capsular contracture of implant-based breast reconstruction: A single-arm meta-analysis. Aesthetic Plast Surg. 2020;44:735–742.

43. Bernini M, Calabrese C, Cecconi L, et al. Subcutaneous direct-to-implant breast reconstruction: Surgical, functional, and aesthetic results after long-term follow-up. Plast Reconstr Surg Glob Open. 2015;3:e574.

44. Salibian AH, Harness JF, Mowlds DS. Staged supraperctoral expander/implant reconstruction without acellular dermal...
matrix following nipple-sparing mastectomy. *Plast Reconstr Surg.* 2017;139:30–39.

45. Headon H, Kasem A, Mokbel K. Capsular contracture after breast augmentation: An update for clinical practice. *Arch Plast Surg.* 2015;42:532–543.

46. Salzberg CA, Ashikari AY, Berry C, et al. Acellular dermal matrix-assisted direct-to-implant breast reconstruction and capsular contracture: A 13-year experience. *Plast Reconstr Surg.* 2016;138:329–337.

47. Sbitany H, Gomez-Sanchez C, Piper M, et al. Prepectoral breast reconstruction in the setting of postmastectomy radiation therapy: An assessment of clinical outcomes and benefits. *Plast Reconstr Surg.* 2019;143:10–20.

48. Basu CB, Leong M, Hicks MJ. Acellular cadaveric dermis decreases the inflammatory response in capsule formation in reconstructive breast surgery. *Plast Reconstr Surg.* 2010;125:1842–1847.