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Immediate direct-to-implant breast reconstruction with acellular dermal matrix: Evaluation of complications and safety

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ABSTRACT

Objective: Immediate direct-to-implant breast reconstruction with acellular dermal matrix (ADM) is the method of choice for many plastic surgeons and patients, but the use of ADM remains a controversial subject in the literature.
This study aimed to investigate complications, reconstructive failure and possible risk factors in direct-to-implant breast reconstruction with ADM (primarily Strattice™).
Methods: We retrospectively examined all patients undergoing immediate direct-to-implant breast reconstruction with ADM, during a five-year period (2014–2019) at a university clinic. Study outcomes were all complications and explantations. Complications were stratified within and after 6 months postoperatively and subcategorized by type of intervention. Explantations were subcategorized into loss of implant or salvage with immediate insertion of a tissue expander, the same or a new implant.
Results: We included 154 patients and 232 breasts. Complications within 6 months per patient included hematoma (4%), seroma (8%), infection (9%), necrosis, wound dehiscence and delayed wound healing (19%). The total complication rate per patient was 34%. Explantation occurred in 20 patients (13%) of which 9 (6% of all) had implant loss. Preoperative radiotherapy was a significant predictor of explantation (adjusted OR 4.9, 95% confidence interval (CI), 1.0–23.5; p = 0.045), and smoking was also associated with risk of explantation, although only borderline significant (adjusted OR 4.0, 95% CI, 1.0–15.8; p = 0.050).
Conclusion: This study demonstrates acceptable rates of re-operations and implant loss compared to other studies but highlights the importance of proper patient selection with regards to risk factors to minimize complications.

1. Introduction

Immediate direct-to-implant (DTI) breast reconstruction has become a popular method of breast reconstruction following mastectomy for breast cancer, since the introduction of acellular dermal matrix (ADM) in 2005 [1–7]. A report from the American Society of Plastic Surgeons showed that ADM was used in >60% of all breast reconstructions performed in the USA in 2018 [8]. Breast reconstruction performed in one stage offers significant psychological and practical benefits for the patients and ADM plays a pivotal role in increasing the number of eligible patients [4,9]. In DTI breast reconstruction with submuscular implant placement, ADM provides coverage of the lower and lateral part of the implant and initial strengthening between the skin and the implant. Among reported benefits of ADM are reduced risk of implant exposure and migration, a more satisfying definition of the inframammary fold, reduction in postoperative pain by increasing the implant-pocket volume and eliminating the need for coverage from surrounding muscles (i.e. serratus anterior, rectus abdominis) or fascia [10–12]. More studies have reported a decreased risk of capsular

Abbreviations: Immediate direct-to-implant, DTI; acellular dermal matrix, ADM; nipple-areola complex, NAC; randomized controlled trial, RCT; indocyanine green fluorescence, ICG.

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contracture, which is otherwise a common complication in implant reconstruction. However, this has to our knowledge not been tested in randomized studies [13,14].

The use of ADM is still controversial with conflicting outcomes in regard to postoperative complications [2,13,15]. Previous studies are heterogeneous in the reconstructive procedures, mesh/ADM types, definition of complications etc. [15–17]. The interpretation of benefits and risks of DTI with ADM are thus challenging [4,10], and there is wide agreement on the lack of evidence [2,9,12,13,15,18,19].

In our center, a tertiary university hospital with tax-funded health care, ADM is used in almost every DTI breast reconstruction. Several breast and plastic surgeons, including supervised trainees, are involved in the procedures, but the surgical techniques, postoperative regime and products used are very uniform. This retrospective single-center observational study was initiated as an internal quality assurance. However, we regard our results interesting and useful for professionals involved in breast reconstructive surgery.

2. Material and methods

2.1. Design

All women having immediate DTI breast reconstruction with ADM at Herlev and Gentofte University Hospital, from August 1, 2014 to July 31, 2019, were identified. We had permission for data retrieval for this period, which also excluded the learning periods for most of the involved senior surgeons since members of the senior staff took up this procedure during 2012 and gradually all in the team had adopted the technique. Data were managed using the Research Electronic Data Capture (REDCap) [20,21], and the follow-up period was calculated from date of DTI breast reconstruction until end of data collection (May 20, 2020). Breasts were excluded if the reconstruction was assisted by a flap or a tissue expander or a combined expander-prosthesis was inserted as the primary implant. A smoker was defined as a patient smoking within 6 weeks before surgery.

All patients consented to the study, and data were handled as per The Danish Data Protection Agency. Approval from the Scientific Ethical Committee was not required.

2.2. Surgical technique and perioperative regime

The surgical techniques and perioperative regimes were standardized. Breast surgeons performed the mastectomy (two surgeons for bilateral mastectomies), and the plastic surgeon, or the resident supervised by the specialist, performed the reconstruction. Mastectomy incision was marked by the plastic surgeon and approved/modified by the breast surgeon. In most cases of in situ or invasive breast cancer, the nipple-areola complex (NAC) was excised and most often preserved in risk-reducing skin-sparing mastectomy; in both scenarios in accordance with the patient.

In skin-sparing mastectomy with excision of the NAC, an ellipsoidal periareolar incision was generally used. For nipple-sparing mastectomy an inframammary incision, or an incision along the lower half of the areola extending laterally was generally used; the latter was preferred in breasts with volumes >400–500 mL. In selected patients with large or very ptotic breasts a Wise-pattern incision was applied [22].

Intravenous antibiotics were used routinely: dicloxacillin 2 g at the beginning of the procedure and repeated in half dose after 3 h. In case of suspected allergies, cefuroxime 1.5 g was used. Antibiotics were in general not administered after the procedure, except in cases with extended drainage (see below).

Following mastectomy, the breast tissue was weighed, marked and submitted for routine histopathology. The subcutaneous cavity was irrigated twice with sterile saline, and the surgical field re-sterilized and re-draped prior to the reconstructive procedure. Implants were placed submuscularly by elevating the pectoralis major muscle from its insertion at the lower ribs and medially to about 4 o'clock/8 o'clock for the right/left breast, respectively. The ADM was washed twice in sterile saline and sutured to the lower and lateral border of the pectoralis muscle and to the inframammary fold, usually with a long-lasting absorbable suture. Most surgeons used the ADM to cover the implant lateral to the pectoralis major muscle, while some surgeons also incorporated the lower corner of the serratus muscle or fascia in the pocket.

Implants were irrigated in vancomycin 1 g in 20 mL sterile water, and the remaining solution was instilled in the implant pocket. Two drains were used routinely: one in the implant pocket and one in the subcutaneous cavity. Drains were generally removed when the daily production was $\leq$30 mL in the deep drain, and $\leq$20 mL in two consecutive days in the subcutaneous drain. In case of drainage >1 week, oral antibiotics, mostly dicloxacillin/flucloxacillin, were prescribed until drain removal.

3. Outcomes

All complications throughout the study period were categorized into conservatively treated or surgery-requiring. Complications treated with surgery were subcategorized into those with explantation and re-implantation of an expander, the same or a new implant (salvage procedures), and those causing implant loss (reconstructive failures). Early and late complications were defined as within or after 6 months of the breast reconstruction.

Seromas were recorded when clinically suspected or identified with ultrasonography after drain removal and were either self-limiting or aspirated. Infection was recorded when meeting the clinical criteria of infection or by a positive bacteria cultivation and ranged from involving the skin/wound or the implant pocket. Treatment of infection varied from oral to intravenous antibiotics with or without need of surgery with entrance to the implant cavity. Necrosis or impaired wound healing was categorized as one (assuming a similar underlying cause of compromised tissue vascularization) and included obvious necrosis (usually at the edge of the mastectomy flap), wound dehiscence and delayed wound healing.

Any complication constituted the total number of patients who had one or more complications. If complications evolved in respect to its category, only the most serious or the primary complication was registered, e.g. if a patient presented with skin necrosis and then developed infection, this was categorized as necrosis.

3.1. Statistical analyses

Descriptive statistics were applied for patient demographics and study outcomes per patient and per breast. The correlations between the outcomes and the variables were determined by multiple logistic regression with variables entering a multivariable model if the variable's significance by univariable logistic regression was $p < 0.05$. All continuous variables were prior converted to categorical variables by median split. Correlations were presented using estimated odds ratio (OR) and 95% confidence interval (95% CI). A p-value of <0.05 was considered statistically significant in the regression models.

All statistical analyses were performed using IBM SPSS Statistics 25.0 (IBM Corporation, Armonk, NY).

4. Results

4.1. Demographics and surgical technique

Out of 167 eligible patients, 154 consented to participate in the study, comprising 232 breasts with ADM assisted DTI breast reconstruction. Median follow-up was 3.1 years (range 0.8–5.7). Demographic and procedure-related data are shown in Table 1. Two patients had cancer-related surgery after their breast reconstruction.

Fourteen breast surgeons, 10 plastic surgeons, and a higher number of plastic surgery residents undertook the procedures.

Strattice™ Tissue Matrix was used in 95% of the patients and Meso BioMatrix® in the remaining 5%. Mentor® implants were used in 96% of the patients and breasts (anatomical shape in 218 breasts and round shape in 5 breasts), and the remaining 4% of the breasts were reconstructed with either Allergan shaped implants (n = 3), Motiva® Round Ergonomix implants (n = 5) or Sebbin anatomical implants (n = 1). Submuscular implant placement was used in all but one procedure. Two drains were placed in 98% of the breasts. Submuscular drains were in place median 6 days (99.6% Charierre 14) and subcutaneous drains median 7 days (47% Charierre 10 and 53% Charierre 14). Prophylactic oral antibiotics were prescribed to 44% of the patients due to prolonged drainage (data not shown).

Prior to the mastectomy, 56 patients had a lumpectomy. The subsequent mastectomy was in general due to a later finding of genetic disposition for breast cancer or patient deselection of post-lumpectomy radiotherapy. Eight patients received preoperative radiotherapy, all as part of their prior post-lumpectomy adjuvant treatment. The time period from preoperative radiotherapy to DTI breast reconstruction ranged from 0 to 15 years (median 3.5). Only radiotherapy received against the included breast was reported (Table 1).

Table 1
Health related and reconstructive characteristics per patient and breast for patients undergoing immediate direct-to-implant breast reconstruction with ADM.

	Patients (n = 154)	Breasts (n = 232)
Age at surgery, years, median (range)	47 (20–72)	
Follow-up, years, median (range)	3.1 (0.8–5.7)	
BMI, kg/m^2, n (%)		
Underweight (≤18.5)	3 (2)	
Normal (18.5–24.9)	99 (64)	
Overweight (25–29.9)	42 (27)	
Obese (≥30)	6 (4)	
Missing	4 (3)	
Smoking, n (%)		
Current	7 (5)	
Previous	58 (38)	
Never	89 (58)	
Comorbidity, n (%)		
Diabetes	2 (1)	
Hypertension	12 (8)	
Connective tissue disorder	5 (3)	
Comorbidity (any)[a]	37 (24)	
Breast reconstructive procedure, n (%)		
Unilateral	76 (49)	76 (33)
Bilateral	78 (51)	156 (67)
Type of mastectomy, n (%)		
Skin-sparing mastectomy	113 (73)	162 (70)
Nipple-sparing mastectomy	42 (27)	70 (30)
Incision type[b], n (%)		
Periareolar incision	109 (71)	157 (68)
Wise/vertical incision	9 (6)	14 (6)
Inframammary incision	38 (25)	61 (26)
Removed breast tissue[c], g		
Median (range)	296 (60–1725)	347.5 (56–1725)
Missing	3 (2)	4 (2)
Implant size, cc, median (range)	330 (140–685)	353.7 (140–685)
Surgical indication[d]		
Invasive breast cancer	67 (44)	71 (31)
Breast cancer in situ	31 (19)	31 (13)
Risk-reducing	57 (37)	130 (56)
Chemotherapy, n (%)		
Preoperative	52 (34)	
Neoadjuvant	9 (6)	
Adjuvant	44 (29)	
Postoperative	9 (6)	
Radiotherapy, n (%)		
Preoperative	8 (5)	8 (3)
Postoperative	6 (4)	6 (3)
Previous operation to the breast, n (%)		
Lumpectomy	56 (36)	58 (25)
Any previous operation to the breast	64 (42)	71 (31)
Axillary lymph node surgery, n (%)		
Sentinel node biopsy (simultaneous)	15 (10)	15 (7)
Dissection (simultaneous)	1 (1)	1 (0.4)
Drain duration, days, median (range)[e]		
Submuscular position	6 (1–20)	
Subcutaneous position	7 (1–23)	
Total	8 (3–23)	

[a] Including multiple sclerosis, osteoporosis, psoriasis, diabetes mellitus, connective tissue disorder, hypo- or hyperthyroidism, cardiovascular-, inflammatory bowel-, haematological-, CNS-, and restrictive lung diseases.
[b] Two patients had different incisions on each breast.
[c] Calculated for heaviest breast tissue per patient.
[d] Per patient by most severe disease, six patients and breasts operated for in situ carcinoma turned out to have invasive breast cancer and were categorized as such.
[e] Calculated for drain of longest duration per patient (missing n = 2).

5. Complications

Within 6 months after the DTI breast reconstruction, 52 of the patients (34%) developed one or more complications (Table 2). The most common complication was necrosis/impaired healing seen in 30 patients (19%) and 39 breasts (17%) of whom 16 patients and breasts required surgery. Fourteen patients (9%) developed infection of whom 5 required surgery, 12 patients (8%) had seroma (none required surgery) and 6 patients (4%) had hematomas (one required surgery).

Late complications (≥6 months) were seen in 8 patients, including seroma formation up until 3 years and infection up until 1.5 years postoperatively (Table 2). All patients with late seroma were treated with aspiration (≥1 times). None of the patients with late seroma were diagnosed with Anaplastic Large-Cell Lymphoma, and none had early complications. One patient with late infection had an early seroma. All three patients with necrosis/impaired healing after 6 months had similar problems in the early phase, treated with debridement.

5.1. Re-operations

Fifty-six patients (36%) were re-operated after the DTI breast reconstruction (not including NAC-reconstructions) (Table 2). The total number of re-operations was 125 of which 76% were performed under general anesthesia and 24% in local anesthesia; median number of re-operations was null (range 0–6). Fig. 1 shows the distribution of all re-operations by main indication.

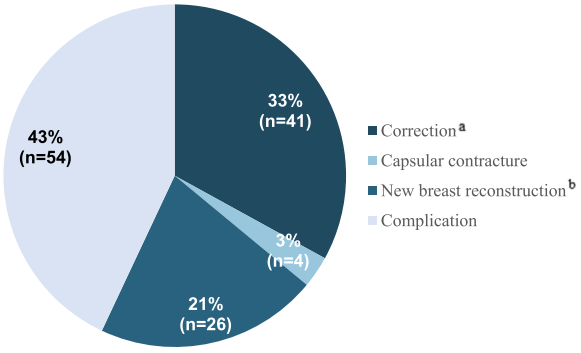
6. Explantations

Twenty patients (13%) needed explantation after the DTI breast reconstruction due to hematoma, deep infection or necrosis/impaired healing, with equal distribution among the three causes (Table 3). The reconstruction was salvaged in half of the cases (n = 11, 7% of all), the remaining (n = 9, 6% of all) had implant loss and thus reconstructive failure. Six percent (n = 9) of the salvage procedures and 3% (n = 4) of the implant losses occurred already

Table 2
Complications and re-operations (during median 3.1 years follow-up) after direct-to-implant breast reconstruction with ADM, patients (n = 154) and breasts (n = 232).

Complications	Operated		Treated conservatively		Total	
	Patients n (%)	Breasts n (%)	Patients n (%)	Breasts n (%)	Patients n (%)	Breasts n (%)
<6 months						
Hematoma	5 (3)	5 (2)	1 (0.6)	1 (0.4)	6 (4)	6 (3)
Seroma	0	0	12 (8)	12 (5)	12 (8)	12 (5)
Infection	5 (3)	5 (2)	9 (6)	10 (4)	14 (9)	15 (6)
Necrosis/impaired wound healing[a]	16 (10)	16 (7)	19 (12)	23 (10)	30 (19)	39 (17)
Systemic[b]	0		3 (2)		3 (2)	
Total complications	25 (16)	25 (11)	37 (24)	42 (18)	52 (34)	63 (27)
≥6 months						
Seroma	0	0	3 (2)	4 (2)	3 (2)	4 (2)
Infection, deep	2 (1)	2 (0.9)	0	0	2 (1)	2 (0.9)
Necrosis/impaired wound healing[a]	3 (2)	3 (1)	0	0	3 (2)	3 (1)
Re-operations[c]	0	1	2	≥3	Total	
	n (%)	n (%)	n (%)	n (%)	Median (range)	
Patients	98 (64)	56 (36)	31 (20)	18 (12)	0 (0–6)	

[a] Necrosis, wound dehiscence and delayed wound healing.
[b] Two general infections and one urinary tract infection.
[c] Reconstruction of the nipple-areola complex are not included.



[a]Including corrective surgery of the reconstructed breast to obtain better symmetry or shape.
[b]Patients undergoing a new breast reconstruction after direct-to-implant breast reconstruction with ADM.

Fig. 1. All re-operations (n = 125) after direct-to-implant breast reconstruction with ADM (during median 3.1 years follow-up), distributed by primary indication of surgery. Only surgeries of the included breasts are included in this figure. Patients can have one or more re-operations within the categories. [a]Including corrective surgery of the reconstructed breast to obtain better symmetry or shape. [b]Patients undergoing a new breast reconstruction after direct-to-implant breast reconstruction with ADM.

within 3 months after DTI breast reconstruction (data not shown).

6.1. Association between risk factors and complications

Table 4 lists possible risk factors and their associations with complications. Risk of complications was higher among older women, smokers, comorbid individuals, those with previous radiotherapy, postoperative chemotherapy, bilateral procedures and Wise/vertical skin incisions. The strongest associations were seen between infection and postoperative chemotherapy (adjusted OR 11.7, 95% CI 2.5–53.9; p = 0.002) and between necrosis/impaired healing and bilateral procedure (adjusted OR 5.1, 95% CI 1.9–13.8; p = 0.001). Additionally, the associations between any complication and bilateral procedure (adjusted OR 2.4, 95% CI 1.2–5.0; p = 0.02) and Wise/vertical incision (adjusted OR 9.6, 95% CI 1.8–50.1; p = 0.008), respectively, remained significant in the multivariate analysis (Table 4).

We did not find a statistically significant association between complications and BMI >25, preoperative chemotherapy, postoperative radiotherapy, indication for mastectomy, breast size, implant size, nipple-sparing mastectomy, prior breast surgery or

Table 3
Explantations after direct-to-implant breast reconstruction with ADM, patients (n = 154) and breasts (n = 232).

	<6 months		≥6 months		Total	
	Patients n (%)	Breasts n (%)	Patients n (%)	Breasts n (%)	Patients n (%)	Breasts n (%)
Explantation	15 (10)	15 (6)	5 (3)	5 (2)	20 (13)	20 (9)
Loss of implant	6 (4)	6 (3)	3 (2)	3 (1)	9 (6)	9 (4)
Salvage of breast reconstruction[a]	9 (6)	9 (4)	2 (1)	2 (0.9)	11 (7)	11 (5)
Cause of explantation						
Hematoma	5 (3)	5 (2)	0	0	5 (3)	5 (2)
Infection	5 (3)	5 (2)	2 (1)	2 (0.9)	7 (5)	7 (3)
Necrosis/impaired wound healing[b]	5 (3)	5 (2)	3 (2)	3 (1)	8 (5)	8 (3)

[a] Salvage with insertion of an expander, the same or a new implant.
[b] Necrosis, wound dehiscence and delayed wound healing.

Table 4
Uni- and multivariate analyses of potential risk factors for complications within 6 months after direct-to-implant breast reconstruction with ADM, expressed as OR, by patient (n = 154). Only variables that showed statistical significance in the analyses are displayed.

	Any complication (n = 52)		Hematoma (n = 6)		Seroma (n = 12)		Infection (n = 14)		Necrosis/impaired wound healing[d] (n = 30)	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age >47										
Univariate[e]	1.3 (0.7–2.6)	0.43	1.0 (0.2–4.9)	0.95	1.4 (0.4–4.5)	0.61	3.9 (1.0–14.5)	0.04	0.6 (0.3–1.3)	0.17
Multivariate[f]							3.8 (1.0–14.6)	0.05		
Smoking[a]										
Univariate[e]	2.1 (0.6–6.8)	0.22	2.5 (0.3–23.2)	0.42	1.1 (0.1–9.2)	0.94	0.9 (0.1–7.6)	0.92	3.3 (1.0–11.4)	0.05
Multivariate[f]									2.3 (0.6–8.6)	0.20
Comorbidity (any)										
Univariate[e]	1.1 (0.5–2.4)	0.84	0.6 (0.1–5.5)	0.67	3.6 (1.1–11.9)	0.04	0.9 (0.2–3.2)	0.81	1.5 (0.6–3.6)	0.40
Multivariate[f]					3.5 (1.0–11.6)	0.05				
Postoperative chemotherapy										
Univariate[e]	1.6 (0.4–6.3)	0.49	0	1	1.5 (0.2–13.3)	0.70	10.8 (2.5–46.7)	0.001	0.5 (0.1–4.2)	0.52
Multivariate[f]							11.7 (2.5–53.9)	0.002		
Bilateral procedure[b]										
Univariate[e]	2.3 (1.2–4.5)	0.02	5.7 (0.7–50.2)	0.12	0.5 (0.1–1.8)	0.30	0.6 (0.2–1.8)	0.34	5.9 (2.3–15.5)	0.000
Multivariate[f]	2.4 (1.2–5.0)	0.02							5.1 (1.9–13.8)	0.001
Wise or vertical incision[c]										
Univariate[e]	7.8 (1.6–39.9)	0.01	3.5 (0.4–33.6)	0.28	1.5 (0.2–13.3)	0.70	6.1 (1.3–27.7)	0.02	3.7 (0.9–14.6)	0.07
Multivariate[f]	9.6 (1.8–50.1)	0.008					5.4 (1.1–26.4)	0.04	6.9 (1.3–36.6)	0.02

[a] Patients who had smoked within 6 weeks of surgery.
[b] Reference: unilateral. Four patients with bilateral reconstruction at two different dates are categorized as unilateral.
[c] Reference: all other types of incisions (i.e. skin-sparing mastectomy with periareolar incision and the incisions in nipple-sparing mastectomies).
[d] Necrosis, wound dehiscence or delayed wound healing.
[e] OR and confidence interval (CI) for the variables with p-value <0.05 considered significant.
[f] OR mutually adjusted for age (continuous), smoking[a] and bilateral procedure[b].

Table 5
Uni- and multivariate analyses by patient (n = 154) for the risk of explantation (n = 20) after direct-to-implant breast reconstruction with ADM, expressed as OR.

		Univariate analysis[a]			Multivariate analysis[b]		
	n	OR	95% CI	p	OR	95% CI	p
Smoking	12	3.9	1.1–14.6	0.040	**4.0**	**1.0–15.8**	**0.050**
Preoperative radiotherapy	8	4.6	1.0–20.8	0.050	**4.9**	**1.0–23.5**	**0.045**
BMI >25	48	1.9	0.7–5.0	0.186	1.7	0.6–4.6	0.307
Age (continuous)		1.0	0.9–1.0	0.468	1.0	0.9–1.0	0.657

[a] Crude OR and confidence interval (CI) for the variables, with p-value <0.05 considered significant.
[b] OR mutually adjusted for smoking and preoperative radiotherapy which were found significantly associated with explantations, and age (continuous variable) and BMI >25 which clinically was suspected to be a risk factor.

drain duration (stratified by submuscular, subcutaneous and all drains). However, several OR estimates were increased.

Explantation was strongly associated with preoperative radiotherapy (adjusted OR 4.9, 95% CI 1.0–23.5; p = 0.045) and smoking (adjusted OR 4.0, 95% CI 1.0–15.8; p = 0.050), although only borderline significant (Table 5). When restricting to explantation with implant loss, the association of previous radiation therapy was much stronger (adjusted OR 28.3, 95% CI 4.1–194.3; p = 0.001) (data not shown). Of the eight patients with preoperative radiotherapy, three had uneventful postoperative courses. The remaining five had complications requiring operation; three lost their implant (one necrosis, two infections), one had necrosis but the reconstruction was salvaged, and one had infection with implant loss after corrective revision surgery.

7. Discussion

In this study of ADM assisted DTI breast reconstruction we found 13% of the patients underwent explantation due to complications. The reconstruction could be salvaged in a little more than half of those cases while the other half corresponding to 6% of all the patients had reconstructive failure, with infection as the main cause. Preoperative radiotherapy or smoking increased the risk of explantation, although only borderline statistically significant. For the group who lost their implant, the same association was strong and statistically significant.

Due to the absence of a control group, all the comparisons are made with other studies. This must be done with precautions, as studies differ in aspects of study designs, definitions of complications etc. For a more detailed analogy, we chose to compare with the two existing randomized controlled trials (RCT) testing Strattice™ [17,18].

A Dutch multicenter RCT randomized 142 women to DTI breast reconstruction with ADM or two-staged implant-based reconstruction without ADM [17]. They found high complication rates in the ADM group with explantation in 11% vs. 4% in the non-ADM group. Wound infection was seen in 8% vs. 2% of the patients, skin necrosis in 12% vs. 1%, and wound dehiscence in 9% vs. 0%, respectively. The authors advocated for improved understanding of patient selection, risk factors, surgical and post-surgical procedures. Our rate of implant loss (6%) was almost half the size of the Dutch RCT (11%). The remaining outcomes were similar and with an overall high risk of complications, although most were managed and implants saved.

A Swedish-UK multicenter RCT analyzed early complications (<6 months) in patients randomized to immediate implant-based breast reconstruction, with or without ADM [18]. Four of 64 patients reconstructed with ADM (6%) and 4 of 65 without ADM (6%) had explantation due to complications, which is similar to our findings. This is despite their exclusion of patients who had risk factors such as preoperative radiotherapy, smoking, neoadjuvant chemotherapy etc. Furthermore, they had shorter follow-up and included some expander reconstructions, which are regarded safer

than using permanent implants due to reduced pressure on the mastectomy flaps [18]. In their study, 22% of the patients developed seroma, in contrast to our 8%, and 6% (n = 4) had infection, with three causing implant loss, and 14% had infection treated outside hospital. This contrasts with our total infection rate of 9% that ranged from minor infection to treatment in hospital with intravenous antibiotics and re-operation with explantation. Our rate of necrosis/impaired healing (19%) was higher compared to the Swedish-UK RCT with wound dehiscence in 9% of the patients and nipple necrosis in 3%. The authors mentioned that cases of necrosis or wound dehiscence commonly progressed to re-operation, and early intervention may decrease failure rates. Our results support that statement and is one of our lessons learned.

Our study revealed a few late seromas and cases of late infection, and the risk of this should be kept in mind. We did not have any cases of red breast syndrome; a problem presumably related to a reaction towards the ADM [13,18,23].

Legal aspects and price influence the choices of ADM, and human ADM is still the most researched type [13,16,24]. Porcine ADM has been shown to share important similarities with human ADM regarding histological structure and biocompatibility, and has the advantage of greater availability and lower cost [24,25]. When comparing this study to similar studies using mainly Strattice™, some showed higher rates of explantation [17,24,26,27], others lower rates [10,12,28]. Notably, this study presents a low rate of seroma compared to many studies of Strattice™ [18,24,25,27], which might be explained by our strict drainage regime. We did not use intraoperative evaluation of skin perfusion with intravenous indocyanine green fluorescence (ICG), which could potentially have saved us from some cases of necrosis/impaired healing; some of the patients with questionable skin perfusion might have been deemed unfit for one-stage reconstruction with ADM and re-directed to two-stage reconstruction with expander. A recent meta-analysis document that the risk of major complications and implant loss can be lowered significantly with the use of ICG [29].

Immediate breast reconstruction is an acknowledged part of breast cancer treatment and considered oncologically safe. A study has found correlation between breast cancer recurrence and complications after mastectomy [30] and two smaller studies have found a similar association in patients undergoing immediate breast reconstruction [31,32]. The latest study of 438 patients undergoing mastectomy and immediate reconstruction reported recurrence in 16.7% of patients with breast complications vs. 5.9% without complications, p = 0.002. These findings support the importance of proper patient selection for immediate breast reconstruction.

Strengths of this study are the uniform surgical regimes, ample information about potential risk factors including the oncological treatment and the length of follow-up.

Limitations of this study include its retrospective design and limited cohort size; we chose to conduct the analyses per patient to create the most realistic interpretive outcomes, also intended for patient information. This could adversely weaken the results, as analyses per breast might reveal a stronger correlation between risk factors and complications. The included patients, all judged eligible to undergo DTI breast reconstruction, compose a selected cohort, although individual risk profiles differ. The possible difference in how the surgeons perceived and registered complications could have biased the strict categorization of complications, although predefined criteria were developed and discussed extensively.

The information from the surgical reports was not detailed enough to stratify results on the level of expertise/training of the involved residents. The results reflect every-day life in a university clinic and are likely to be highly referable, but surgical expertise is key in reducing complications, and unfortunately our data did not allow to adjust for this.

Patients were followed for median 3.1 years, but it is well known that the number of re-operations increase with extended follow-up, especially for capsular contracture and asymmetry [33].

8. Conclusion

This study demonstrates acceptable rates of re-operations and implant loss in ADM (almost exclusively Strattice™) assisted DTI breast reconstruction. Preoperative radiotherapy and smoking are high-risk factors for the most severe complications causing implant loss. Proper patient selection is crucial, especially since emerging evidence stresses a higher risk of recurrence of breast cancer after complicated breast surgery. Further reduction of complications should be aimed at, and we are now prospectively monitoring our surgical activity. Larger prospective studies with longer follow-up, detailed information on patient-related factors, surgery, complications, and cancer recurrence are needed to further evaluate risk factors and safety.

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Declaration of competing interest

The authors have no financial conflicts of interest to report.

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