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Original Article

Immediate prepectoral breast reconstruction using bovine pericardium matrix

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ABSTRACT

INTRODUCTION. Immediate, implant-based breast reconstruction has become increasingly popular as a single-stage procedure with prepectoral placement of the implant following the introduction of biologic matrices. Only a few studies have described the use of bovine pericardium matrixTutomesh, a xenograft derived from bovine pericardium – and the use of laser-assisted indocyanine green angiography (ICG-A) to assess skin flap perfusion.

METHODS. All patients who underwent a mastectomy followed by immediate reconstruction using prepectoral direct-to-implant with bovine pericardium from July 2019 to June 2021 were included. Complications were registered using the Clavien-Dindo classification. Postsurgical complications were analysed with multivariate logistic regression and feature selection.

RESULTS. A total of 81 prepectoral breast reconstructions were performed in 56 patients. The overall complication rate was 38.2%, and 14.3% required reoperation. Implant loss occurred in 3.7%. Multivariate logistic regression analysis demonstrated a statistically significant association between the risk of skin necrosis and previous breast surgery ($p = 0.020$) along with an increasing risk of implant rotation with increasing age ($p = 0.010$). The median follow-up was 9.9 months, and 11.1% of the breast reconstructions required postsurgical aesthetic correction.

CONCLUSIONS. Bovine pericardium may be used in prepectoral breast reconstruction with a good outcome. Careful patient selection is crucial, and ICG-A is helpful in reducing the risk of post-surgical complications.

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Implant-based breast reconstruction (IBBR) is increasingly used to restore the breast mound after mastectomy, accounting for 75% of the cases in the US [1]. Traditionally, IBBR involves inserting the implant into a subpectoral pocket by elevating the pectoralis major muscle and parts of the serratus muscle.

Biologic matrixes were introduced in IBBR in the 2000s and were used to create a hammock to augment the inferior-lateral part of the sub-pectoral pocket for the implant. This allowed a one-stage, direct-to-implant (DTI) breast reconstruction.

With the proven safety and widespread use of biologic matrices [2-5], surgical techniques have been optimised, including using laser-assisted indocyanine green angiography (ICG-A) to evaluate the blood supply to the

mastectomy skin flaps. Therefore, the previously abandoned prepectoral breast reconstruction approach has regained popularity as complication rates compared well to the subpectoral method [3, 6, 7].

Several types of meshes (i.e. allograft, xenograft and synthetic) and acellular dermal matrix have been used to facilitate prepectoral IBBR, including preshaped biologic matrices that fully or partially cover the implant, and which are secured to the chest wall [2, 8, 9]. The question of which DTI technique is superior remains a topic of debate. This uncertainty arises from heterogeneous study designs, a lack of randomized control trials directly comparing subpectoral and prepectoral matrix-assisted IBBR and inconsistency in how complications are registered and reported.

Additionally, studies most frequently report the use of human-derived biological mesh. Bovine pericardium matrix Tutomesh (RTI Surgical, Alachua, FL, US) is an avital, acellular, xenogeneic, non-crosslinked, fenestrated collagen matrix derived from bovine pericardium. Only a few studies have investigated the application of Tutomesh in IBBR [10-12].

The present study aimed to evaluate the surgical outcome, risk of complications and surgical interventions in patients undergoing prepectoral IBBR DTI using Tutomesh. The secondary outcome was the incidence of revised aesthetic procedures and length of hospital stay.

Methods

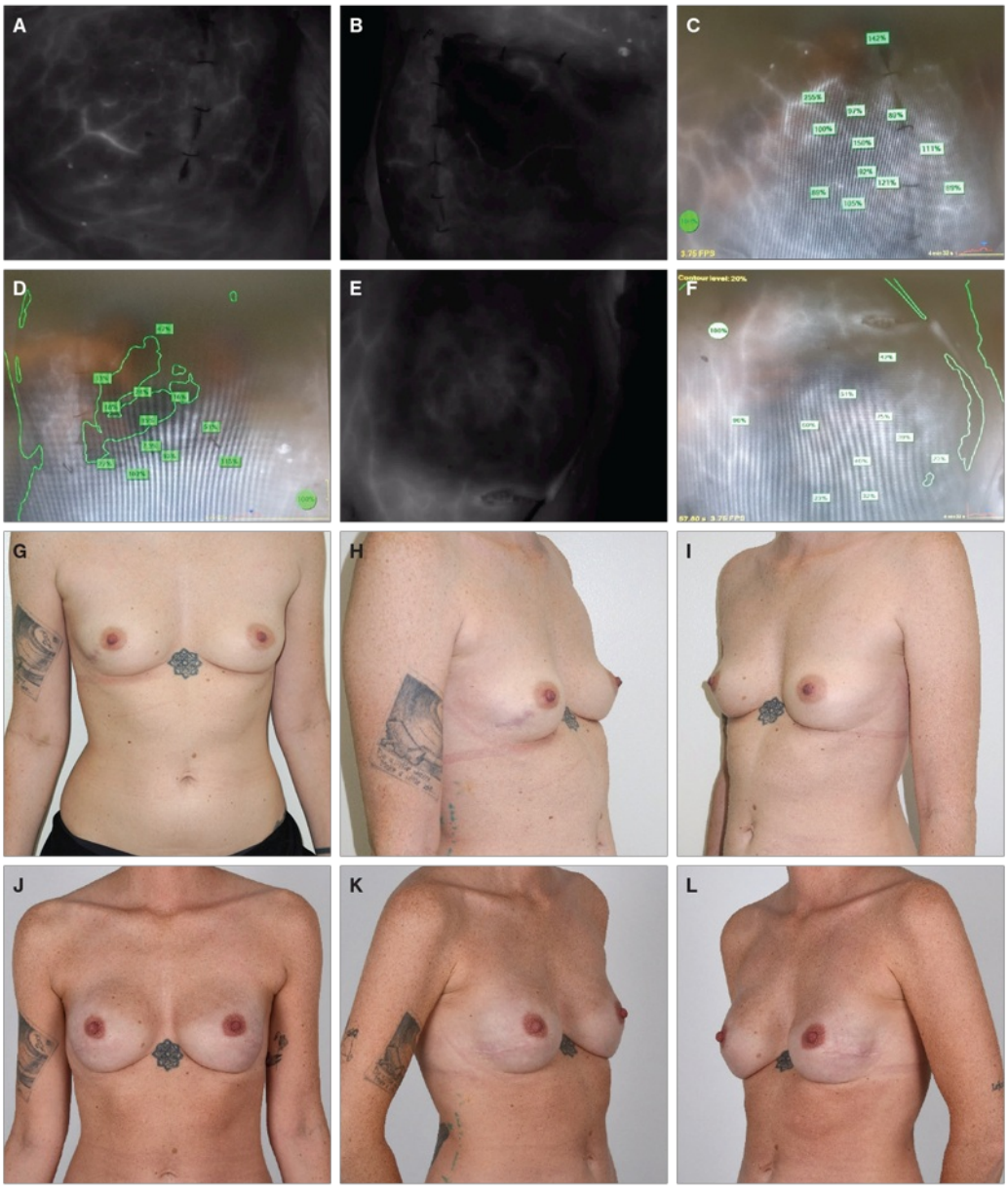
Patients undergoing prophylactic or therapeutic prepectoral DTI between 1 July 2019 and 31 June 2021 were identified through the electronic health record Sundhedsplatformen (Epic Systems Inc.), and data were collected retrospectively.

Patient demographics, including age, BMI, smoking history, comorbidities, breast cancer history, including chemotherapy and radiotherapy along with gene mutations and surgical technique (nipple sparing/skin sparing mastectomy, implant size) were registered at the time of the surgery. Furthermore, mastectomy specimen weight, tumour size, implant size and length of follow-up period were recorded.

Absolute contraindications for IBBR were locally advanced breast cancer or inflammatory breast cancer. Relative contraindications included patient age > 65 years, BMI > 30 kg/m^2, breast volume > 500-600 ml, uncontrolled diabetes, active smoking, hypertension, chronic immunosuppression and a history of radiotherapy. However, the surgeon could opt to perform the surgery despite the relative contraindications if it seemed safe. Danish national guidelines do not recommend IBBR if the patient has more than two relative contraindications [13]. A DTI prepectoral IBBR was selected if the thickness of the skin flaps was ≥ 10 mm.

Breast surgeons performed the mastectomy, after which a team of plastic surgeons assessed the vascularity of the skin flaps as an initial step. A sizer of the appropriate volume was inserted, and blood perfusion assessment was conducted using ICG-A (SPY Elite System; Stryker Inc., Michigan, US), which helped to determine the safest implant size and establish which IBBR procedure should be performed. If the average mastectomy flap blood perfusion score was > 33%, the surgeon would proceed with the DTI (**Figure 1**). A sheet of 0.5 mm thick perforated Tutomesh was soaked in saline and tailored to cover the anterior surface of the implant. The mesh was sutured with a 2-0 Maxon (Medtronic Inc.) to the inframammary fold, thoracic fascia, anterior serratus muscle and pectoralis major muscle. The implant (Mentor Breast Implants) was rinsed in gentamicin 3 mg/ml. Twelve patients with 17 breast reconstructions were also enrolled in the randomised BREAST-AB trial comparing three-substance antibiotics (gentamicin, vancomycin and cefalozin) or a placebo saline solution [14].

FIGURE 1 Indocyanine-green angiography technique (**A-F**) and clinical pictures of skin-sparing breast reconstructions before (**G-I**) and after (**J-L**) surgery in a young patient. A-F depicts the angiography, including quantitative perfusion assessment (C + D + E). The perfusion is deemed sufficient (white-grey areas) when the relative perfusion is above 33% (marked in green).



Two drains were inserted into the breast cavity and were removed once daily seroma output decreased to < 30 ml after the first post-operative day. Patients were given prophylactic intravenous antibiotics just before surgery and on the first post-operative day.

Complications

All post-operative complications, length of stay and secondary aesthetic procedures were recorded using the Clavien-Dindo classification system (**Table 1**), which was originally designed for abdominal surgery but has been adopted in other surgical specialities [2, 15]. Surgical complications included infection, haematoma, seroma requiring aspiration, skin necrosis, wound dehiscence, capsular contracture (Baker grade III or IV), rippling,

implant rotation and implant loss. Standard follow-up included outpatient visits after three weeks, three months and one year.

TABLE 1 Clavien-Dindo classification of surgical complications.

Grade	Definition
I	Any deviation from the normal post-operative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions Acceptable therapeutic regimens: drugs such as antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy This grade also includes wound infections opened bedside
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic or radiological interventions
III-a	Intervention not under general anaesthesia
III-b	Intervention under general anaesthesia
IV	Life-threatening complication, including CNS complications[a] requiring IC/ICU-management
IV-a	Single-organ dysfunction, including dialysis
IV-b	Multi-organ dysfunction
V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge, the suffix "d" is added to the respective grade of complication This label indicates the need for a follow-up to fully evaluate the complication

"d" = "disability"; CNS = central nervous system; IC = intermediate care; ICU = intensive care unit.
a) Brain haemorrhage, ischaemic stroke, subarachnoid bleeding, but excluding transient ischaemic stroke.

Statistics

Complication rates and surgical outcomes are presented using simple descriptive statistics such as range, mean, median and standard deviation. Logistic regression was used for multivariate analysis to assess associations between potential risk factors and surgical complications. Features were chosen using forwards-and-backwards selection and to estimate uncertainty. Each operation was assumed independent, even in patients undergoing a bilateral procedure. The χ^2-distribution was used for feature selection. All statistical analyses were performed with R version 4.4.1 (2024), R studio 2024.04.2+764.

Ethics

The study was conducted in accordance with the Helsinki Declaration.

The study was approved by the Institutional Board Research Council at the Department of Plastic Surgery and Burns Treatment, Rigshospitalet, Copenhagen University Hospital.

Trial registration: not relevant.

Results

A total of 81 breast reconstructions were performed in 56 women. One patient was lost to follow-up. Patient characteristics are shown in **Table 2**. The duration of drainage was missing for two patients.

TABLE 2 Patient characteristics and treatment details.

	n (%)	Median (min.-max)	Mean ± SD
Patients			
Patients, total	56		
Procedures, total	81		
Laterality:			
Unilateral	31 (55.4)		
Bilateral	25 (44.6)		
Former smoker	19 (33.9)		
Hypertension	4 (7.1)		
Gene mutation:			
BRCA	25 (44.6)		
BCRA1	16 (28.6)		
BRCA2	9 (16.1)		
TP53	1 (1.8)		
PALB2	1 (1.8)		
Subtotal, gene mutation	27 (48.2)		
Previous lumpectomy	22 (39.3)		
Neoadjuvant chemotherapy	9 (16.1)		
Adjuvant chemotherapy	19 (33.9)		
Adjuvant antihormone therapy	21 (37.5)		
Age, yrs		41 (25-63)	42.6 ± 9.8
BMI, kg/m²		22.6 (18.4-36.0)	23.3 ± 2.9
Length of hospital stay, days		3 (2-9)	3.9 ± 1.8
Length of drain in situ, days		7 (3-26)	7.8 ± 4.3
Weight of breast tissue removed, g		316 (124-950)	343.6 ± 182.3
Volume of breast implant, ml		315 (175-685)	321 ± 112.6
Follow-up period, mos.		9.9 (0.6-25.6)	9.3 ± 5.9
Operations			
Indication for surgery:			
Therapeutic	45 (55.6)		
Prophylactic	36 (44.4)		
Nipple-sparing mastectomies	38 (46.9)		
Skin-sparing mastectomies	43 (53.1)		
Breasts receiving fat grafting procedure(s)	9 (11.1)		

BRCA = breast cancer gene; PALB2 = partner and localiser of BRCA2; TP53 = tumour protein 53.

Complications were noted in 31/81 breast procedures (38.2%) and in 26/56 patients (46.6%), as specified in **Table 3**. Eight patients scored Clavien-Dindo grade IIIb or greater. The remaining patients scored Clavien-Dindo Grade I. Four patients had skin necrosis (superficial 5.4%; full thickness 1.8%). Three patients needed removal of the implant – the first patient due to full-thickness skin necrosis and subsequent infection. The second patient experienced partial skin necrosis and haematoma. The third patient had a partial skin necrosis and wound dehiscence, and opted not to receive a new implant. Rippling was the most frequent complication, with a rate of 14.3% in eight patients. Revised aesthetic procedures with fat grafts were performed in nine breasts (11.1%), whereas three patients received two fat graft procedures to correct contour irregularities.

TABLE 3 Complications and multivariable logistic regression and feature selection per breast and per patient.

	Complications, n (%)	
	breasts (N_b = 81)	patients (N_p = 56)
Seroma	0	0
Skin necrosis		
Superficial	4 (4.9)	3 (5.4)
Full thickness	1 (1.2)	1 (1.8)
Subtotal	5 (6.1)	4 (7.2)
Infection	3 (3.7)	3 (5.4)
Haematoma	2 (2.5)	2 (3.6)
Wound dehiscence	1 (1.2)	1 (1.8)
Capsular contracture Baker grade III or IV	0	0
Rippling	11 (13.6)	8 (14.3)
Implant rotation	6 (7.4)	5 (8.9)
Implant loss	3 (3.7)	3 (5.4)
Total complications	31 (38.2)	26 (46.6)

Discussion

Prepectoral breast reconstruction was introduced in 1971 [16]. However, due to high complication rates and poor aesthetic outcomes, it was not widely adopted until the introduction of biologic matrices. For decades, the prepectoral method was preferred owing to the less traumatic approach to the pectoral major muscle, the anatomically correct placement, faster recovery, reduced need for post-operative analgesics and a lower risk of animation deformity. A disadvantage of prepectoral placement is the risk of rippling. Biologic matrices offer a reduced risk of capsular contracture, improved control of the implant pocket and mechanical support for recreating a more naturally looking breast mound and ptosis. However, none of the methods has been established as superior [3, 6, 7].

Bovine pericardium made its first appearance in IBBR in 2011 with the use of Veritas (Synovis Surgical Innovation, St Paul, MN) [17], followed by Tutomesh. Its advantage over Strattice (Lifecell Corp., Branchburg, NJ) is its fenestrations and thinner profile, which facilitate fluid outflow from the implant pocket while preserving the anti-inflammatory properties of the graft. Three studies, all with small sample sizes, have

described the use of Tutomesh with overall complication rates varying from 31% to 60%, including a notable incidence of red breast syndrome and skin redness [10-12].

The overall complication rate (Table 3) was 38.2% per breast and 46.6% per patient. This is similar to the findings of other studies [2, 4, 6, 8, 18], regardless of differences in how complications are subdivided into major and minor categories. Chandarana et al. reported an overall complication rate of 28.6% in 496 breast reconstructions but did not report data for rippling, implant rotation and implant loss [2]. Kim et al. compared a subpectoral group to a prepectoral group, finding an overall complication rate of 41.2% and 37.7% per patient, but also did not report data on implant rotation and rippling [6].

In a study using ICG-A in 73 breast reconstructions in 50 patients, complications were reported in 35.2% with no skin necrosis [8]. In a large multicentre cohort with a 22.7-month median follow-up period, an overall complication rate of 43.5% was reported in 1,450 prepectoral breast reconstructions [4]. Khan et al. reported an overall complication rate of 33.3% per breast procedure, but complications such as erythema, skin and nipple necrosis were divided into several subcategories, and data on rippling and implant rotation were not reported [18].

This lack of consensus on the grading and reporting of post-operative complications challenges comparisons. The Clavien-Dindo classification system is an excellent and easily applicable tool offering a high accuracy in ranking post-operative complications. This facilitates consistent and accurate documentation of post-operative parameters. In the present study, 8/56 patients (14.3%) scored Clavien-Dindo grade IIIb requiring post-operative intervention under general anaesthesia due to full or partial skin necrosis, wound dehiscence, haematoma or implant rotation. Another study applied the Clavien-Dindo classification and reported a Clavien-Dindo grade IIIb rate of 15.3% [2].

In our study, the incidence of skin flap necrosis was 6.1% (superficial 4.9%; full thickness 1.2%) per breast, which is similar to results previously published [2, 4, 18]. Multiple logistic regression analysis demonstrated a statistically significant correlation between skin necrosis and previous breast surgery (per breast; $p = 0.020$ and per patient; $p = 0.035$). Skin flap quality is commonly assessed by gross clinical inspection, which is quite unreliable. IGA provides real-time visualisation of skin flap perfusion during surgery [19]. Harless et al. demonstrated an 86% reduction in mastectomy flap necrosis before and after implementing ICG-A in SBBR [20]. A meta-analysis comparing studies with and without ICG-A demonstrated an overall risk reduction of 47% for major complications with the use of ICG-A [19]. The skin flap necrosis rate was relatively high, which might reflect a learning curve, encouraging the consistent use of ICG-A to further improve results.

In the present study, 14.3% of the patients experienced rippling. Furthermore, in 5/56 patients, implant rotation occurred with a statistically significant association with age (per breast; $p = 0.010$ and per patient; $p = 0.047$). This may be explained by the effect of ageing on collagen deposition in the skin. Secondary interventions, such as fat graft transfer, may be used to fill contour irregularities. A secondary fat grafting procedure was needed in nine breasts (Figure 1), which is in line with the literature [3, 18].

In the present study, a 3.7% incidence of implant loss was noted, which is lower than reported elsewhere, varying from 4.5-7.5% [2, 4, 18]. Implant malposition constitutes the most common reason for reoperation, and this was seen in 8.9% of patients.

Smooth round implants with higher cohesiveness in breast reconstruction have become increasingly popular due to these implants' ability to minimise rippling and wrinkling. Our institution used Mentor CPG cohesive III anatomical implants and Mentor Siltex round moderate plus profile cohesive I or II (smooth or microtextured) implants. In cases with implant rotation, all patients had the Mentor cohesive III anatomical implants.

None of the patients experienced seroma or capsular contracture. The median follow-up period was only 9.9

months, and capsular contracture events rarely occur during the first two years.

This study has some limitations, including its retrospective design, a relatively short median follow-up period of 9.9 months and possible selection bias from being conducted at a single centre. Another limitation is the lack of a comparison group, i.e. patients undergoing subpectoral IBBR. Large randomised controlled trials with more collaborating institutions are needed to compare various prepectoral techniques and different types of biologic matrices to confirm the long-term outcome.

Conclusions

This study demonstrated that prepectoral IBBR using a Tutomesh is a safe method, which yields a good aesthetic outcome without increasing the risk of post-operative complications. Careful patient selection and choosing the accurate implant size are crucial in lowering the risk of complications. ICG-A is a most useful tool for improving peroperative skin-flap assessment, thereby minimising the risk of complications. To harmonise reporting of post-operative complications, using the standardised Clavien-Dindo grading system is highly recommended.

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