Case Series

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Early complications in cases series in implant-based immediate breast reconstruction with a biological acellular matrix during the learning curve of this technique and using 3 different matrices: a case series of 84 breasts

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Introduction: We present our experience in implant-based immediate breast reconstruction (IBIBR) with biological acellular matrix during our learning curve and compare the complications with the use of three different matrices.

Materials and methods: We did a retrospective study on patients who underwent an IBIBR with acellular matrix after skin sparing mastectomy with or without nipple-areolar complex preservation at the Breast Pathology Unit at University Hospital Vall d'Hebron, Barcelona (Spain) between July 2011 and December 2014.

Results: A total of 84 breasts were reconstructed in 71 women. A therapeutic mastectomy was performed in 55 of them (65.5%) and a prophylactic mastectomy in 29 (34.5%). The total rate of complications was 41.67% (35 patients): we found 11 cases of erythema (13.1%), 19 cases of seroma (22.62%), 9 cases of hematoma (10.71%), 17 cases of wound dehiscence (20.24%), 11 cases of skin flap necrosis (13.1%), and 10 cases of reconstruction failure (11.9%). The probability of reconstruction failure was higher in smokers and former smokers ($P = 0.0011\%$). There were more complications with the Protexa matrix than with the other 2, Strattice and Tutomesh ($P < 0.001$) and a higher risk of reconstruction failure as well ($P = 0.03$).

Conclusions: In our experience the use of acellular matrix in IBIBR can have a high rate of complications, especially during the learning curve. Therefore, the selection of suitable patients and the better matrix is an issue of great importance to achieve favorable results.

Keywords: Breast Cancer, Reconstruction, Implant, Dermal matrix

Introduction

Implant-based breast reconstruction is the commonest method of reconstruction after mastectomy. In some series, it represents the technique selected for immediate reconstruction after mastectomy in 37% of cases in the United Kingdom[1]. Implant-based breast reconstruction has evolved from a complete retromuscular placement of the implant to a dual plane position. The introduction of acellular matrix in implant-based breast reconstruction has provided benefits and complications[1,2] but there is contradictory data in literature about the rate of complications with this technique.

The aim of this work is to present the experience of our Plastic Surgery Unit at the University Hospital Vall d'Hebron of Barcelona (Spain) with implant-based immediate breast reconstruction (IBIBR) with support of acellular matrix during our learning curve with this technique in order to show the rate of complications and reconstructive failure (exposure of the implant leading to its removal) and its association to possible known risk factors and the different acellular matrices used.

Materials and methods

The study is a retrospective case series and it was performed including all the consecutive patients who underwent an IBIBR assisted with acelular matrix after skin or nipple-sparing mastectomy at the Breast Pathology Unit of University Hospital Vall d'Hebron (single center) of Barcelona (Spain), between July 2011 and December 2014. This study was approved by the Research Ethics Committee at our hospital and it has been reported in line with the PROCESS criteria[3].

We reviewed the computerized clinical records of these patients and analyzed the epidemiological data, the presence of

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possible known risk factors (smoking, radiotherapy, mastectomy skin incisions, size of initial implant inserted), the type of acellular matrix used, and early complications (adverse event occurring within 30 d of surgery as a direct result of the procedure). The complications identified were erythema (red breast), seroma (a subcutaneous collection of fluid judged to be significant by a surgeon), hematoma (a subcutaneous collection of blood), wound dehiscence, mastectomy skin flap necrosis and reconstructive failure due to implant exposure leading to removal of implant.

Statistical analysis was performed. The Fisher exact test was used when comparing categorical data between groups that might be plotted in a contingency table such as: complications and reconstruction failure, risk factors and reconstruction failure, radiotherapy and reconstruction failure, and choice of acellular dermal matrix (ADM) and presence of complications. Mann-Whitney *U* test was used to compare sample means when no assumptions can be made on the distribution, in this particular case it was used to compare patient's mean age and reconstruction failure. Kruskal-Wallis test was used for initial implant volume for each choice of ADM since it presented >2 sample groups and the inability to make assumptions regarding distribution warrants the use of a nonparametric test.

During this period of time we used 3 different types of acellular matrices. Straticce (LifeCell), which is a 1-mm thick porcine dermis matrix; Protexa (Tecnoss, Italy), a 1.4-mm thick porcine dermis as well; and Tutomesh (Tutogen, Germany), which is made of bovine pericardium and it is a 0.5-mm thick and fenestrated matrix. Before using, we rehydratated them in sterile saline solution following the manufacturers recommendations (20 min for Protexa, 2 min for Straticce, and 5 min for Tutomesh). These matrices are gradually reabsorbed while acting as a guide or scaffold to form new endogenous connective tissue. They have been used in recent years for other surgical procedures, such as abdominal wall reconstruction for abdominal hernia repair[4], and more recently for breast reconstruction.

At our center, all the patients who are going to receive a skin sparing mastectomy followed by breast reconstruction are discussed in a multidisciplinary meeting. If we decide to perform an IBIBR assisted with an acellular matrix, the patient is informed of the possibility of a tissue expander–based reconstruction or even a delayed reconstruction based on surgeon criteria according to the mastectomy skin flaps viability.

Smokers are specifically informed about the high risk of skin flap necrosis, implant exposure, and breast reconstruction failure if they decide this reconstruction technique. They will only be considered to this surgery provided they understand and assume the greater risk of complications.

In patients with large breasts we only perform this technique provided they accept a contralateral breast reduction therefore smaller breast size is going to be achieved. Literature describes an increase in complication risks in patients with a BMI >30[5], and a greater infection rate in patients whose mastectomy specimen weight was >600 g[6]. These recommendations are similar to those published in other literature reviews[7,8].

Surgical technique

After skin-sparing mastectomy (with or without nipple areola complex preservation), the pectoral major muscle origin is sectioned at ribcage level from the 5 to 8 o'clock position if we visualize an analogical clock, and dissect a subpectoral pocket. The muscle will cover the 2 upper thirds of the implant. The sternal origins of the pectoral major muscle are only partially sectioned to achieve correct midline projection while avoiding the possibility of a symmastia. Next the ADM is fixed to the fascia at submammary fold level via single resorbable stitches. Next the implant or expander is inserted below the muscle and matrix. Possible matrix surplus is resected along the edges and then continuous resorbable suture of the lower edge of the pectoral major muscle with upper matrix edge. Finally, any possible lateral surplus of the matrix is cut away and the lateral edge adjusted with single resorbable stitches to the serratus fascia, so the matrix also acts as a lateral support to prevent lateral displacement of the implant. During this procedure we insert a subcutaneous aspiration drainage catheter and another submuscular/submatrix. The least productive drainage catheter is removed at 3 days (usually the subcutaneous one), and the other from day 5 if drainage is under 40 mL in 24 hours.

All surgeries were performed by 2 plastic surgeons skilled in breast reconstruction that are part of the Breast Pathology Unit. These were their first breast reconstructions using acellular matrix. The review of the computerized clinical records was performed by a third plastic surgeon in order to reduce interoperator or intraoperator variation.

Results

Over 3 year 6 month period between July 2011 and December de 2014, 71 women underwent skin-sparing mastectomies with or without nipple areola complex preservation and IBIBR with acellular matrix. A total of 84 breasts were reconstructed, representing 58 unilateral and 13 bilateral reconstructions. Therapeutic mastectomy was performed on 55 breasts (65.5%) and prophylactic mastectomy on 29 breasts (34.5%). The mean patient age was 44.3 years (range, 27–78 y).

The initial mean implant volume used was 333.3 mL (range, 80–640 mL). Eleven breasts (13.1%) were reconstructed with a tissue expander, and the remaining 73 breasts (86.9%) were reconstructed with a definitive anatomic breast implant.

The postoperation follow-up reviewed was 30 days in all cases in order to detect early complications. In total, 35 breast of the 84 breasts reconstructed had early complications (41.67%): 11 cases of erythema (13.1%), 19 cases of seroma (22.62%), 9 cases of hematoma (10.71%), 17 cases of wound dehiscence (20.24%), 11 cases of skin flap necrosis (13.1%), and 10 cases of reconstruction failure (11.9%). The descriptive analysis between the presence of complications and reconstruction failure showed that 28.57% of patients with complications finished with a reconstruction failure. Furthermore, reconstruction failure and seroma ($P<0.001$), wound dehiscence ($P<0.001$) and skin flap necrosis ($P<0.001$) are associated; although not in the other cases.

Regarding descriptive analysis between the presence of possible risk factors (patient's age, smoking, radiotherapy, mastectomy approach, and initial size of implant) and that of any complication no statistically significant associations were found. However, on performing descriptive analysis between the presence of these risk factors and reconstruction failure, it was noted that:

- The probability of reconstruction failure is greater among smokers (40%) and former smokers (37.5%) than in nonsmokers (4.69) ($P=0.0011$).

- On average patients suffering from reconstruction failure are younger than those who do not (40.40 vs. 47.03 y) ($P = 0.035$).
- Reconstruction failure occurred in 33.33% of patients who received presurgery radiotherapy, 18.18% of patients who received postsurgery radiotherapy and 10% of patients who did not receive radiotherapy. These differences were not statistically significant ($P = 0.296$).
- There were no association between reconstruction failure and initial size of inserted implant ($P = 0.084$), or different mastectomy approaches used ($P = 0.737$).

Regarding the biological matrix, Strattice was used in 44 reconstructions (52.38%); Protexa was used in 16 cases (19.05%); and Tutomesh in 24 breasts (28.57%). The selection of each biological matrix depended on the availability and surgeon's preferences. If we assess the onset of any complication taking into account the matrix used (excluding postsurgical hematomas since these are more attributable to the surgical technique than material used), we observed statistically significant differences ($P < 0.001$). Twelve cases (75%) presented complications in reconstructions using the Protexa matrix, 13 cases (29.55%) using the Strattice matrix, and 3 cases (12.5%) using the Tutomesh matrix. The assessing of the complications one by one according to the matrix used is collected in **Table 1**.

Given the type of biological matrix used seems to be a risk factor, the presence of possible risk factors were analyzed per type in order to detect possible confusion factors. We analyzed the presence of: smoking, radiotherapy, mastectomy approach used, patient's age, and initial size of inserted implant per group according to biological matrix used. Statistically significant differences were found for the following parameters:

- Smoking. The Protexa group presented a higher percentage of smokers (18.75%) and ex-smokers (31.25%) than the Strattice (13.64% and 2.27%, respectively) and Tutomesh (4.17% and 8.33%, respectively) ($P = 0.012$).
- Initial implant size. The Protexa group presented an initially higher mean implant volume (411.56 mL; range, 170–640 mL), than the Strattice (340.45 mL; range, 100–595 mL) and Tutomesh (263.33; range, 80–445 mL) group, $P = 0.001$. However, initial implant size was not associated with the possibility of having a complication or reconstruction failure in our series.

Discussion

The evolution toward implant position from a total retropectoral positioning to a dual plane, where only the upper thirds are covered by muscle, has enabled a decrease in operating time, greater comfort for the patient during expansion and less morbidity to the chest wall. However, this technique presents less control over the Inframammary fold position and has been associated with a complication rate close to 40%, including extrusion and loss of implant, implant displacement and rotation, capsular contracture and rippling[2,9].

Use of an acellular matrix has 3 obvious theoretical advantages. First, a dermal matrix fixed to the inframammary fold enables better control of its position. Second, the additional cover from the lower third of the implant reduces risk, while enabling greater control of the lower pole with greater expansion and a better esthetic result with fewer skin wrinkles. And third, the matrix creates a hammock effect supporting implant weight and avoiding the implant from resting directly against the fine skin cover. Despite this, there is contradictory data in literature. A lot of studies found no significant ADM effects on complications in immediate expander/implant breast reconstruction using ADM[7,10,11], although, others conclude that this technique presents a greater risk of some complications such as seroma, infection, and reconstruction failure than muscle-fascial flap-assisted implant breast reconstruction[5]. Our case series presented a higher rate of complications, with a global complication rate per breast of 41.67% (13.1% erythema, 22.62% seroma, 10.71% hematoma, 20.24% wound dehiscence, 13.1% skin flap necrosis, and 11.9% reconstruction failure). This analysis varies when observing the complications depending on the matrix used (**Fig. 1**). Thus, we can see the greatest number of complications was found in reconstructions which used Protexa ADM. We believe this has been influenced by 2 factors. One the one hand, this group has a large percentage of smokers and ex-smokers. Smoking is a known risk factor, and in our series we found association between smoking and reconstruction failure. And on the other, the matrix type and its properties. Although, Potter et al[12] no found significant differences in the rate of complications between ADM-assisted implant-based reconstruction with Protexa and standard expander-implant procedures. Furthermore, the fact that this matrix is thicker than the others (1.4 mm against 0.9 mm and 0.5 mm) may involve a greater foreign body reaction, and not being fenestrated can lead to worsen the seroma management. We think that the ADM could play a fundamental role in the formation of seroma, acting as a foreign body until it is integrated in the organism; and the double dead space secondary to the lack of coincidence between skin wrapping and underlying volume. Furthermore, the seroma volume has a mechanical tension effect on the skin flaps already weakened in this kind of surgery. This increase in tension on the mastectomy flap might worsen vascularization of the skin flaps favoring necrosis and/or wound dehiscence. Therefore, we believe it is essential to know this fact to identify seromas as soon as possible to resolve them. Probably, as Tutomesh matrix is perforated, it enables communication between the subpectoral pocket and subcutaneous dissection, what we believe it hinders the seroma formation, facilitating their evacuation via the aspiration drainage catheters inserted. Even so, the seroma incidence with Tutomesh did not particularly differ from that observed with Strattice which is a nonperforated matrix, but it is permeable. Nevertheless, remember we always use 2 aspiration drainage catheters (one subcutaneous and the other submuscular/submatrix) in all cases, and theoretically Protexa ADM and Strattice ADM are permeable.

Some patients subjected to ADM-assisted breast reconstruction develop a postsurgery erythema supra-adjacent to the dermal matrix. It can be easily confused with an infection process. This phenomenon is now known as red breast syndrome (RBS). This erythema responds poorly to antibiotics and occasionally

Table 1

Complications according to the matrix used and *P*-value.

	Biological Matrix [n (%)]			
	Protexa	Strattice	Tutomesh	*P*
Complication				
Erythema	6 (37.50)	4 (9.09)	1 (4.17)	0.007
Seroma	11 (68.75)	5 (11.36)	3 (12.50)	< 0.001
Wound dehiscence	8 (50.00)	8 (18.18)	1 (4.17)	0.002
Skin flap necrosis	3 (18.75)	8 (18.18)	0	0.048
Reconstruction failure	5 (31.25)	4 (9.09)	1 (4.17)	0.030

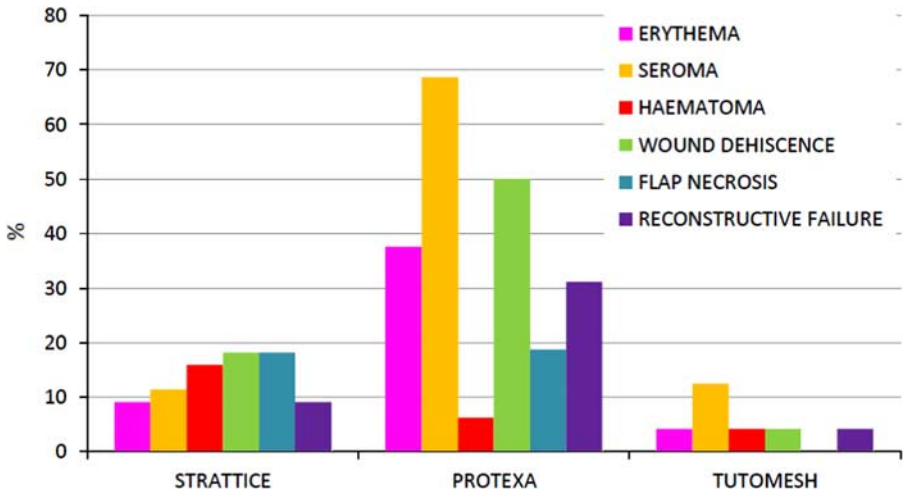

Figure 1. Complications depending on acellular matrix used. Observe a great concentration of complications with Protexa ADM.

responds to corticoids[13]. Etiology of this phenomenon has been explained as a late hypersensitivity reaction (type IV or cell mediated)[13,14]. We appreciated erythema in 11 cases (13.1%). Out of these cases 6 were Protexa (37.5%), 4 Strattice (9.09%), and 1 Tutomesh (4.17%). The fact this erythema is not statistically significant associated with reconstruction failure unlike seroma or wound dehiscence allows us to think that not all the erythema cases correspond to a skin inflammatory response due to a wound dehiscence causing infection or a seroma causing tension in skin flaps and hindering their vascularization. We therefore consider an appreciable percentage of these erythemas might really correspond to RBS. The type of material the matrix is made off and processed thereof (how cells are removed from the acellular matrix, artificial *crosslinking* and sterilization process) may determine a different cellular response in the host once the acellular matrix is implanted[15]. For example, in a comparison between porcine and bovine acellular dermal matrices in IBIBR, the porcine matrix was associated with higher rates of skin erythema postoperatively[16]. A possible explanation is that in our series it seems that the dermal matrices have a greater tendency to generate erythema than the bovine pericardium one, may be due to the type of material or processing the bovine pericardium matrix undergoes is less immunogenic than the dermal ones. The differences between the 2 dermal matrices (Strattice and Protexa) may be due to different processing and even different physical characteristics. In this sense we think more prospective and comparative studies are required to clarify these doubts.

Some patients after the surgery required adjuvant radiotherapy (even though before surgery was unlikely to be needed), in the case of complications this adjuvant treatment could be delayed. Furthermore, postsurgery radiotherapy is associated with an increase in complications, by up to 4 times[7]. In our series the presence of presurgery radiotherapy tripled the percentage of reconstruction failure (33.33% vs. 10%) and the presence of postsurgery radiotherapy doubled the risk of reconstruction failure (18.18% vs. 10%). Although, these differences were not statistically significant ($P = 0.296$).

The cases who had already received radiotherapy underwent this surgical technique because their skin presented good characteristics and did not want an autologous reconstruction. This makes us think that even in cases which seem favorable, radiotherapy is always a bad travelling companion for the plastic surgeon. Those cases who received postsurgery radiotherapy had opted for this reconstruction technique because at the time of surgery, the possibility of requiring radiotherapy was deemed very scarce. Moreover, postsurgery radiotherapy increases the risk of capsular contracture[7] in both cases using ADM and those which did not. Despite this, the use of ADM may reduce the severity of capsular contracture[17].

Obviously, our study had limitations. It was a case series with a retrospective design (low evidence level), and also the groups were not cent per cent equipped (Protexa group had a large percentage of smokers). However, from this study we can obtain certain conclusions and learning.

Conclusions

Our case series of IBIBR with acellular matrix showed a high complications rate. However, we should not put this technique to one side but rather endeavor to find out the reasons why. In our learning journey with this technique, we have reached the conclusion that IBIBR with acellular matrix has a place in the plastic surgeon's arsenal; furthermore, they must be extremely meticulous when choosing patients and matrix type used. Strict selection of patients to undergo this type of breast reconstruction is probably one of the major critical factors for the success. As to the acellular matrix, the growing number of possibilities in the market hinders the knowledge acquisition process regarding this technique, as, although the products are similar, they are not identical, which may cause different responses in the organism. Therefore, further research is needed with new studies with more evidence level in order to compare different matrices.

Ethical approval

The Clinical Research Ethics Committee with drugs from the University Hospital Vall d'Hebron certified that this work is adequate from an ethical and scientific point of view (act number 246).

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Author contribution

All authors read and approved the manuscript.

Conflict of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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