The use of dermal templates in dermato-surgery and patient perspectives

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Abstract

Acellular dermal matrices currently represent a useful reconstructive method in onco-dermatologic surgery. Nevertheless, they have some limitations, especially in terms of costs and outpatient post-operative wound care. While some studies on their cost-to-benefit ratio in breast surgery have already been issued, evidence is currently lacking in onco-dermatological surgery. The aim of this study was to evaluate the clinical outcomes perceived by patients who had undergone onco-dermatologic surgery in which either acellular dermal matrices or skin grafts had been used as reconstructive methods. A study population of 150 patients was identified retrospectively and patients' degree of satisfaction was assessed through the Global Aesthetic Improvement Scale and the Patient Scar Scale Questionnaire. Despite similar scores among the study groups, slightly better results were appreciable after single-stage grafting. However, to what extent these variations really represent a significant difference from a clinical point of view remains to be determined. Moreover, other potential bias in the interpretation of our results may reside in differences in terms of age, body location and baseline tumor size among the study groups. Therefore, further research is needed.

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Key words: acellular dermal matrices; dermatologic surgery; dermato-oncology; reconstructive surgery; clinical outcomes.

Contributions: AP, conceptualization; SM, AP, formal analysis; SM, Aal, AAc, CB, CF, FG, investigation; CR, MF, BF, data curation; SM, writing-original draft preparation; AP, writing-review and editing; CM, supervision. All the authors read and approved the final version to be published.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Ethical approval and consent to participate: all the procedures in the present study were performed in accordance with the principles of the Helsinki's Declaration. The present study was approved by the local Research Ethics Committee (Comitato Area Vasta Emilia Nord, CE 426/2022/OSS/AOUMO SIRER ID 4558).

Availability of data and material: data are available from the authors upon reasonable request.

Informed consent: the data was collected retrospectively, and no consent was required.

Received: 19 January 2024.
Accepted: 4 February 2024.

Licensee PAGEPress, Italy
Dermatology Reports 2024; 16:9941
doi:10.4081/dr.2024.9941

Introduction

In onco-dermatologic surgery, there are a variety of reconstructive methods for covering tissue defects, including primary closure, flaps, grafts and dermal substitutes.[1]

The use of cutaneous flaps is sometimes limited by tumor and subsequent wound size, and therefore skin grafts are considered as the reconstructive technique of choice for larger wounds.[2] Moreover, grafts are also indicated when tumor margins are not clearly definable with non-invasive methods, such as dermoscopy, confocal microscopy and Optical Coherence Tomography (OCT) and/or Mohs surgery is not feasible. However, poor functional and aesthetic results are sometimes achieved due to excessive scar contraction and depression of the grafted area.[3] For these reasons, bioengineered skin equivalents, also called acellular dermal matrices (ADMs), are currently employed as alternative and/or complementary reconstructive methods for full-thickness wounds.[3-5]

ADMs consist of biomedical scaffolding materials that can be used to cover large surgical defects and provide a provisional template for the host's cells migration and proliferation, therefore supporting tissue regeneration.

Two main acellular dermal substitutes are currently in use at our center and probably represent the most commonly used dermal templates worldwide: Integra (Integra Life Sciences, Palinsboro, NJ, USA) and Matriderm (MedSkin Solution Dr Souwelack AG, Billerbeck, Germany).

Integra skin substitute exists in two possible versions: double layered, composed of 2mm thick collagen, glycosaminoglycan and chondroitin-6-sulfate matrix and a superficial silicon coverage, and single-layer, deprived of the outer silicon coating.[4-8]

Matriderm is an acellular single laminar dermal template, composed of bovine-derived collagen and elastin hydrolysate, which create a highly porous membrane providing a 3D scaffold

to promote tissue regeneration and modulating scar formation.[5] Matriderm skin substitute is available as 1 and 2-mm thick sheets.

While the recently released single layer Integra and 1-mm Matriderm allow a single-stage reconstructive procedure, combining the template placement with a skin graft to obtain immediate closure,[4] dual layer Integra as well as 2-mm Matriderm require two-step surgery for tissue reconstruction.[4,8] Once the templates are applied to the wound bed, they act as a vector for the host's fibroblasts and endothelial cells to produce the so called *neodermis*, with the deposition of newly formed collagen and subsequent vascularization and granulation tissue formation.[4] After approximately 3-4 weeks, the silicone layer is removed and the neodermis is covered using a split-thickness skin graft (0.2-0.4 mm).

Although current bioengineered skin substitutes provide useful reconstructive alternatives in onco-dermatologic setting, they have some shortcomings that may limit their use, such as high costs, storage, risk of immune rejection or foreign-body reaction, infections, and the need of professional outpatient wound-care in the first weeks after their positioning.[7] Moreover, recent studies on acellular dermal matrices use in breast surgery opened a new scenario on possible pros and cons of their application.[9-12]

Evidence is currently lacking in the setting of reconstructive onco-dermatological surgery.

The aim of the present study was to evaluate the aesthetic and functional outcomes perceived by patients who had undergone dermatologic surgical procedures in which either bioengineered acellular skin substitutes or skin grafts had been used as reconstructive methods after excision, in order to assess whether the costs of dermal templates and/or two-step surgery were justified by patient satisfaction.

Materials and Methods

Between November 2022 and May 2023, a monocentric, observational study was conducted at the Dermatologic Surgery Unit of Modena University Hospital, as previously authorized by the local Research Ethics Committee (Comitato Area Vasta Emilia Nord, CE 426/2022/OSS/AOUMO SIRER ID 4558).

The study population was identified retrospectively. To be eligible for the inclusion in this study, patients had to be aged over 18 and had to have gone through surgery at our center in the past ten years. Skin lesions excision had to be followed by either two-step (use of acellular dermal matrix followed by subsequent skin autograft) or one-step (skin grafts only or acellular dermal matrix positioning followed by wound secondary healing) reconstructive procedures.

Patients who underwent primary suture or cutaneous flaps after tumor excision were excluded. Deceased patients or patients uncapable of understanding and willing were also not included in the study.

Afterwards, selected patients were asked to a series of questionnaires regarding their level of satisfaction after surgery. Patients' degree of satisfaction with the aesthetic outcome was assessed through the Global Aesthetic Improvement Scale (GAIS) and the Patient Scar Scale Questionnaires (Tables 1 and 2).[13-16] The GAIS is a five-point Likert scale, ranging from *much improved* to *much worse*. On the contrary, the results of the Patient Scar Scale questionnaire range from a minimum of 6 up to a maximum of 60 points, with lower scores being associated with higher satisfaction.

Demographic (sex, age) and anamnestic (comorbidities, tumor histology, single or two-step surgery) data were also collected. Data from the study population were collected in Case Report CRFs). Results from the surveys submitted to the patients were expressed in numeric scores. Multivariate statistical analysis was performed in order to evaluate possible significant associations among the parameters taken into examination. The Student T-test was used to define significant differences among the three analyzed groups. The statistical analysis was carried out by means of the STATA version 17 software (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX; USA: StataCorp LLC).

Table 1. Patient Scar Scale questionnaire.

No, no complaints	1	2	3	4	5	6	7	8	9	10	Yes, worst imaginable
Is the scar painful?											
Is the scar itching?											
No, as normal skin	1	2	3	4	5	6	7	8	9	10	Yes, very different
Is the color of the scar different?											
Is the scar more stiff?											
Is the thickness of the scar different?											
Is the scar irregular?											
Total score Patient Scar Scale											

Adapted from Draaijers *et al.*[14]

Table 2. Global Aesthetic Improvement Scale score.

1	Very much improved
2	Much improved
3	Improved
4	Not changed
5	Worsened

Results

A total of 150 patients were enrolled in the present study (Table 3). ADMs were used in the majority of cases (n=81).

Of these, 2-step surgery based on the use of dermal substitutes followed by subsequent skin autograft was used in 67 cases, while ADMs positioning was followed by secondary wound healing in 14 cases. On the contrary, 69 subjects underwent single stage surgery with skin removal immediately followed by skin graft.

Age significantly differed between the three groups, with acellular dermal matrices being generally employed in younger subjects. On the contrary, direct skin grafting turned out to be the reconstructive method of choice in older patients.

No specific differences in terms of comorbidities or voluptuary habits were detected. Despite small statistically significant differences between the 3 groups, mean GAIS score was approximately 3 in all the study subpopulations, therefore indicating similar results in terms of esthetic improvement are perceived by patients in all the study conditions. As for patient evaluation of residual scarring after surgery, with all the scores ranging from 10 to 20. Despite not being adjusted according to baseline lesion and/or patient characteristics, slightly better results were appreciable after single-stage grafting.

When stratifying for the type of lesion, however, no statistical differences in terms of GAIS and/or Patient Scar Scale, were found between the three reconstructive techniques in the case of basal cell carcinomas and squamous cell carcinomas. On the contrary, when dealing with melanoma, patient healed by secondary intention had less satisfactory results in terms of scarring (mean PSS 38, p=0.0173), while only borderline statistical significance was reached for differences in the GAIS scores. Therefore, most of the differences were due to all the other forms of skin lesions. In particular, dermatofibrosarcoma protuberans had the highest GAIS scores (mean 3.9).

Discussion and Conclusions

A recent study by Lohmander *et al*. aimed at assessing the differences between breast reconstruction with and without the use of ADMs.[9,10,17] Published results reveal no significant differences in the two possible reconstructive strategies after mastectomy (immediate implant-based *vs* use of ADMs) in terms of need for reintervention, surgical complications, patient quality of life or aesthetic outcome. To date, however, it is impossible to draw similar conclusions on the use of skin substitutes for post-oncological surgery skin wound healing.

Most of the available literature on clinical studies based on the use of bioengineered skin templates in the dermatological setting is focused on surgical treatment of burn wounds.[8,18]

With regards to this, a recent prospective randomized controlled clinical trial published by Corrêa and collaborators compared the efficacy of skin grafts and dermal matrices in the treatment of burn contractures.[19] Interestingly, patients treated with skin graft only, without previous skin substitute positioning, displayed lower rates of wound contraction. No significant differences were detected between Integra® and Matriderm® templates.

These results are in line with our data in the dermato-oncological setting. However, to what extent a variation of 9 points on a 60-point scale really represents a significant difference from a clinical point of view remains to be determined. Moreover, another possible bias in the interpretation of our results resides in the different ages of the three study populations, since generally younger patients have higher esthetic standards in terms of final clinical outcomes. Lastly, the retrospective nature of our patient selection did not allow us to have homogeneous population in terms of tumor size and location or possible strategies. If on the one side, for example, direct skin graft in a single surgical intervention is the preferred choice in older patients, the reconstruction of specific defects necessarily requires the use of dermal templates (*e.g*. surgical treatment of epidermolysis Bullosa patients; scalp neoplasms involving the periosteum; etc.). Moreover, retrospec-

Table 3. Patient characteristics and questionnaire scores.

	Total	ADM templates + skin graft	Skin graft	ADM templates + secondary healing	p
Patients	150	67 (44.7)	69 (46)	14 (9.4)	
Gender					
F	48 (32.2)	21 (31.3)	21 (30.9)	6 (42.9)	0.654
M	101 (67.8)	56 (68.7)	47 (69.1)	8 (57.1)	
Age, mean±SD (range)	78.0±15.3 (23-97)	76±15.8 (23-97)	82.8±9.5 (44-97)	66.0±26 (23-97)	*0.001*
Smoker (1/0)	33 (22.1)	13 (19.4)	17 (25.0)	3 (21.4)	0.644
Diabetes (1/0)	21 (14.1)	10 (14.9)	11 (16.2)	0 (0.0)	0.280
CVD (1/0)	30 (21.1)	16 (23.9)	13 (19.1)	1 (7.1)	0.344
CTD (1/0)	4 (2.7)	1 (1.5)	3 (4.4)	0 (0.0)	0.475
Age at surgery, mean±SD (range)	76.9±14.9 (22-96)	75.2±15.7 (23-95)	81.0±8.0 (51-95)	65.3±26.1 (22-96)	*<0.001*
GAIS					*0.025*
1	19 (12.7)	2 (3)	16 (23.2)	1 (7.1)	
2	39 (26)	17 (25.4)	19 (27.5)	3 (21.4)	
3	35 (23.3)	20 (29.9)	10 (14.5)	5 (35.7)	
4	34 (22.7)	16 (23.9)	16 (23.2)	2 (14.3)	
5	22 (14.7)	12 (17.9)	7 (10.1)	3 (21.4)	
GAIS, mean±SD	3.0±1.2 (1-6)	3.2±1.1 (1-5)	2.7±1.4 (1-6)	3.2±1.2 (1-5)	*0.039*
Patient Scar Scale	14.3±10.3 (3-52)	16.0±10.6 (6-52)	11.6±8.4 (3-45)	19.6±13.5 (6-44)	*0.005*

ADM, acellular dermal matrix; SD, standard deviation; CVD, cardio-vascular disorders; CTD, connective tissue disorders; GAIS, Global Aesthetic Improvement Scale. P-values in *italics* are significant.

tive selection does not take into account that acellular dermal matrices were certainly chosen as reconstructive technique for deeper wounds, therefore the results being possibly biased by baseline differences in tumor size and/or thickness. Prospective evaluation of patients with similar baseline characteristics (age, wound size) is mandatory in the next future to confirm our findings. In conclusion, more data are currently needed to determine the real cost-to-benefit ratio of acellular dermal matrices use in the dermatological setting.

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