# The Role of Dermal Regeneration Templates in Severe Soft Tissue Defects. Management of "Critical Zones". Case Series

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## ABSTRACT

**Introduction:** The aim of this study is to report outcomes and complications in a series of patients suffering soft tissue defects in critical areas treated using an acellular dermal matrix. **Materials and Method:** A retrospective review of patients with soft tissue coverage deficits in critical areas treated with acellular dermal matrix in our center over a five-year period was conducted. The preoperative variables analyzed were: age, sex, comorbidities, number of previous surgeries, size and characteristics of the critical area and cause of the coverage defect. The intraoperative variables analyzed were: size of the dermal substitute used, surgical time and complications. The postoperative variables were: incorporation of the dermal substitute, time elapsed until the placement of the skin graft, and postoperative complications. **Results:** The initial diagnoses were tumor (3 patients), acute trauma (3 patients) and sequelae of compartment syndrome (2 patients). The soft tissue defect was located in the leg (3 cases), in the hand (2 cases), in the thigh (1 case), in the forearm (1 case) and in the foot (1 case). In 5 cases the critical zone was characterized by tendon exposure with loss of peritenon; in one case bone exposure and loss of periosteum; in one case exposure of nerve graft and in one case exposure of osteosynthesis material. Three complications were recorded. Two patients required placement of a new template; in another patient an internal saphenous neurocutaneous flap was performed due to failure of coverage with membrane. **Conclusion:** Dermal substitutes are characterized by their versatility. This technique can provide protection in situations of bone exposure, in addition to providing a gliding plane in case of tendon exposure. In addition, using a dermal matrix saves on the use of flaps.

**Key words:** Dermal substitute; acelullar dermal matrix; soft tissue coverage; reconstructive surgery.

**Level of Evidence:** IV

## Uso de la matriz dérmica acelular para el tratamiento de zonas críticas en defectos de cobertura. Serie de casos

## RESUMEN

**Introducción:** El objetivo de esta serie de casos es describir resultados y complicaciones de pacientes con heridas graves con defecto de cobertura en zonas críticas tratadas mediante el empleo de matriz dérmica acelular. **Materiales y Métodos:** Se realizó una revisión retrospectiva de los pacientes con déficit de cobertura en zonas críticas tratados con matriz dérmica acelular en nuestro centro. Definimos como zona crítica al déficit de cobertura que no pueda ser tratado solo con injerto de piel. Evaluamos variables preoperatorias, intraoperatorias y postoperatorias. **Resultados:** Tres pacientes presentaron diagnóstico inicial de tumor, 3 pacientes trauma agudo y 2 pacientes secuela de síndrome compartimental. En 3 casos el defecto de cobertura se localizó en pierna, en 2 casos en mano, en un caso en muslo, en un caso en antebrazo y en un caso en pie. En 5 casos la zona crítica se caracterizó por exposición tendinosa con pérdida de peritenon, en un caso exposición ósea y pérdida de periostio, en un caso exposición de injerto de nervio y en un caso exposición de osteosíntesis. Se registraron 3 complicaciones. Dos pacientes requirieron una nueva colocación de matriz y en otro paciente se realizó un colgajo neurocutáneo de safeno interno por fracaso de la cobertura con membrana. **Conclusión:** Los sustitutos dérmicos se caracterizan por su fácil uso y versatilidad. Esta técnica otorga protección en situaciones de exposición ósea, además de proveer un plano de deslizamiento en caso de exposición tendinosa. El uso de matriz dérmica permite, además, ahorrar la necesidad del empleo de colgajos.

**Palabras clave:** Sustituto dérmico; matriz dérmica acelular; defecto de cobertura; cirugía reconstructiva.

**Nivel de Evidencia:** IV

Received on May 14th, 2020. Accepted after evaluation on September 9th, 2020 • MARIANO O. ABREGO, MD • mariano.abrego@hospitalitaliano.org.ar https://orcid.org/0000-0001-9783-7373

**How to cite this article:** Abrego MO, Sánchez Saba J, Zaidenberg EE, Rellán I, Donndorff A, Gallucci G, De Carli P, Boretto JG. The Role of Dermal Regeneration Templates in Severe Soft Tissue Defects. Management of "Critical Zones". Case Series. *Rev Asoc Argent Ortop Traumatol* 2021;86(2):167-174. https://doi.org/10.15417/issn.1852-7434.2021.86.2.1117

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## INTRODUCTION

Surgical reconstruction of soft tissue defects continues to be a challenge for the orthopedic surgeon. In certain situations, the use of skin flaps or grafts does not represent the solution to the problem, either due to a contraindication or a technical impossibility. Under these circumstances, dermal substitutes have gained ground, becoming a resource within the surgeon's therapeutic arsenal.

A dermal regeneration template is a type of synthetic skin substitute composed mainly of bovine collagen and chondroitin sulfate.[1] It has a double layer of matrix that stimulates fibroblast and endothelial growth through a process of imbibition, neovascularization and remodeling.[2] Originally described by Burke et al., the use of dermal regeneration templates for neodermis development has been extensively studied in soft tissue coverage deficits in full-thickness burns.[1]

Over time, the indication for the use of dermal regeneration templates has broadened.[3] In recent years, satisfactory results have been reported with the use of dermal substitutes in severe injuries secondary to trauma, both in acute disease and in chronic soft tissue defects.[4-7] The aim of this consecutive case series is to describe the outcomes and complications in patients with severe wounds with soft tissue defects in critical areas treated using a dermal regeneration template.

## MATERIALS AND METHODS

A retrospective review of patients with soft tissue coverage deficits treated with a dermal regeneration template was conducted in our center, by the same surgeon (JB), during a period of five years (2014-2019). The information of the patients was extracted from the electronic health records of our institution.

We included patients—regardless of gender or age—with a soft tissue defect of the lower or upper limb in "critical areas" treated with the placement of an Integra® dermal regeneration template (Integra Life Sciences Corporation, Plainsboro, NJ, USA) and subsequent reconstruction with skin graft. "Critical area" is defined as a soft tissue deficit that cannot be treated with a skin graft alone, such as bone exposure without periosteum or tendon exposure without peritenon. Patients in whom the dermal substitute had been used in non-critical areas were excluded.

Preoperative, intraoperative and postoperative variables were analyzed. The preoperative variables analyzed were: age, sex, comorbidities, number of previous surgeries, size and characteristics of the critical area and cause of the soft tissue defect. The intraoperative variables analyzed were: size of the dermal substitute used and complications. The postoperative variables were: incorporation of the dermal substitute, time elapsed until the placement of the skin graft and complications. In addition, we describe the surgical technique for the placement of the dermal substitute and the evolutionary stages.

### Surgical technique

In the first surgical stage, the objective is to place the dermal substitute in the area of the defect. Measurement of the defect is essential for preoperative planning and thus requesting the appropriate dermal substitute size.

All procedures were performed in the operating room and under sterile technique, after asepsis and antisepsis. Debridement of the wound is essential before placing the dermal substitute. Thorough bed hemostasis is essential before placing the dermal matrix. This favors the contact of the membrane with the bed and reduces the formation of bruises.

The collagen bilayer is placed on the bed, fixing it at its edges, either with clips or non-absorbable sutures. Periodic dressing changes are performed, which depend on the wound exudate or the use of a negative suction system for an average period of three weeks. If a negative-pressure wound therapy (NPWT) system is placed, dressings must be changed in a sterile way, in the operating room, every week. During this period, vascular regeneration begins in the bed. After seven days, the color of the membrane changes due to cellular infiltration. At 14 days, the matrix turns orange, indicating neovascularization.

At approximately three weeks, the neodermis reaches its adequate degree of revascularization. These synthetic bilayers feature a removable silicone covering, which must be removed to place the partial-thickness skin graft.

## FINDINGS

We identified eleven patients in whom a dermal substitute was used for the management of soft tissue defects during the studied period (Table). Eight patients met the inclusion criteria (2 women and 6 men). All the patients included in this study had undergone previous surgeries for their underlying disease (tumors) or in the context of an emergency (trauma, compartment syndrome).

**Table.** Characteristics of the sample.

| Case | Age (cx) | Comorbidities | Follow-up (months) | Pathology | Cause of defect | Location | Previous procedures | Defect size (cm) | Defect characteristics | Dermal substitute complications | Treatment of the complication |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 38 | Smoking | 22 | Severe bone marrow aplasia | Compartment syndrome | Hand | Fasciotomy / VAC / lipotransfer | 9X10 | Tendon exposure | No | - |
| 2 | 41 | No | 51 | High-grade myxofibrosarcoma | Oncologic resection | Leg | Latissimus dorsi flap | 20x25 | Tendon exposure | Yes | Integra membrane replacement |
| 3 | 38 | No | 16 | Grade 2 chondrosarcoma | Oncologic resection | Leg | Tumor resection alloprosthesis | 2x2 | Exposure of osteosynthesis material | Yes | Internal saphenous neurocutaneous flap |
| 4 | 62 | Smoking / Type II Diabetes | 20 | Trauma | Compartment syndrome | Forearm | Fasciotomy / VAC | 10x20 | Tendon exposure | No | - |
| 5 | 85 | No | 18 | Trauma | Foot degloving | Foot | VAC | 10x20 | Bone exposure | No | - |
| 6 | 4 | No | 36 | Trauma | Severe injury with arterial lesion | Thigh | Latissimus dorsi flap | 10X25 | Nerve exposure | No | - |
| 7 | 35 | No | 38 | Monophasic synovial sarcoma | Oncologic resection | Leg | VAC | 18x12 | Tendon exposure | Yes | Integra membrane replacement |
| 8 | 58 | Smoking | 8 | Trauma | Exposed fracture | Hand | Reduction and osteosynthesis / Posterior interosseous flap | 10x20 | Tendon exposure | No | - |

VAC = vacuum-assisted closure

Three patients had a tumor diagnosis as the underlying condition: two with a histological diagnosis of soft tissue sarcoma (leg and thigh) and one with a histological diagnosis of chondrosarcoma (grade II, leg). The two patients with soft tissue sarcoma presented tendinous exposure without peritenon: one evolved with a soft tissue defect secondary to the oncological resection, while the other evolved with a soft tissue defect as a consequence of the oncological resection and the subsequent loss of the latissimus dorsi and parascapularis flap. The third patient (chondrosarcoma) presented exposed osteosynthesis material secondary to tumor reconstruction surgery.

Three patients in our series had a soft tissue defect secondary to acute trauma. One suffered a foot degloving with bone exposure and absence of periosteum. Another presented a wound with a covering defect in the thigh with tendinous exposure without peritenon and, in addition, exposure of the sciatic nerve. In the first instance, a latissimus dorsi flap reconstruction was performed, which progressed to total necrosis. The third patient had multiple open hand fractures, with tendon exposure and absence of peritenon.

The remaining two patients had a soft tissue deficit as a consequence of compartment syndrome. The first had a catheter infection in the context of severe spinal aplasia, and developed a compartment syndrome of the hand, treated with fasciotomies (bone exposure and necrosis of the extensor apparatus of the fingers in zone 6) (Figures 1 and 2). The second developed a forearm compartment syndrome as a consequence of a closed fracture in the context of polytrauma, was treated with fasciotomies, and evolved with a soft tissue deficit due to skin necrosis and tendon exposure with absence of peritenon. It should be clarified that, in this patient, despite having suffered a trauma, the soft tissue defect was the result of the surgical treatment of the compartment syndrome.

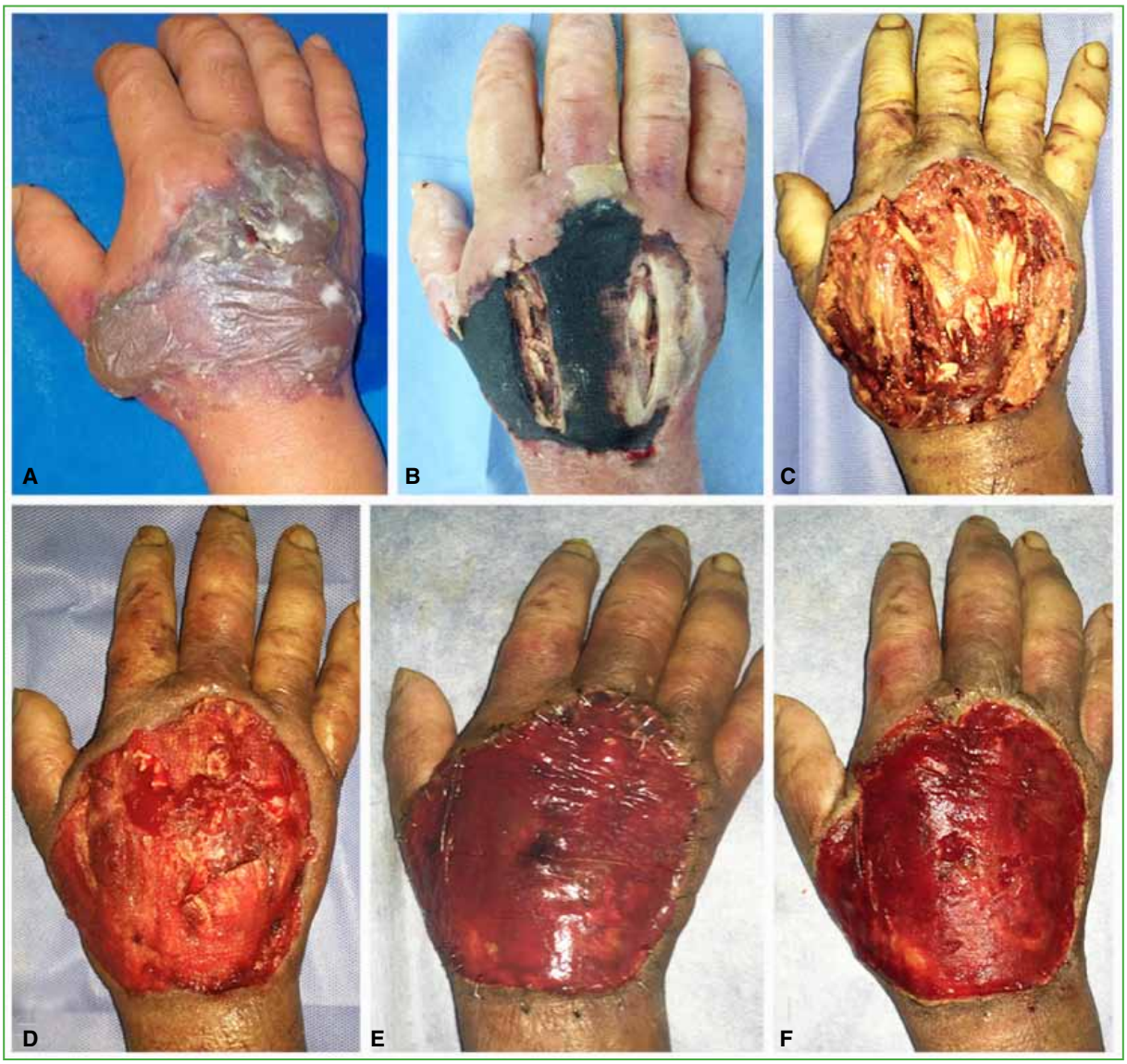


**Figure 1.** Case 1. **A.** Compartment syndrome secondary to catheter infection. **B.** Post-fasciotomy evolution. **C.** Tendon exposure. **D.** Bone exposure after tendon necrosis. **E.** Dermal substitute placement. **F.** Regenerated matrix.

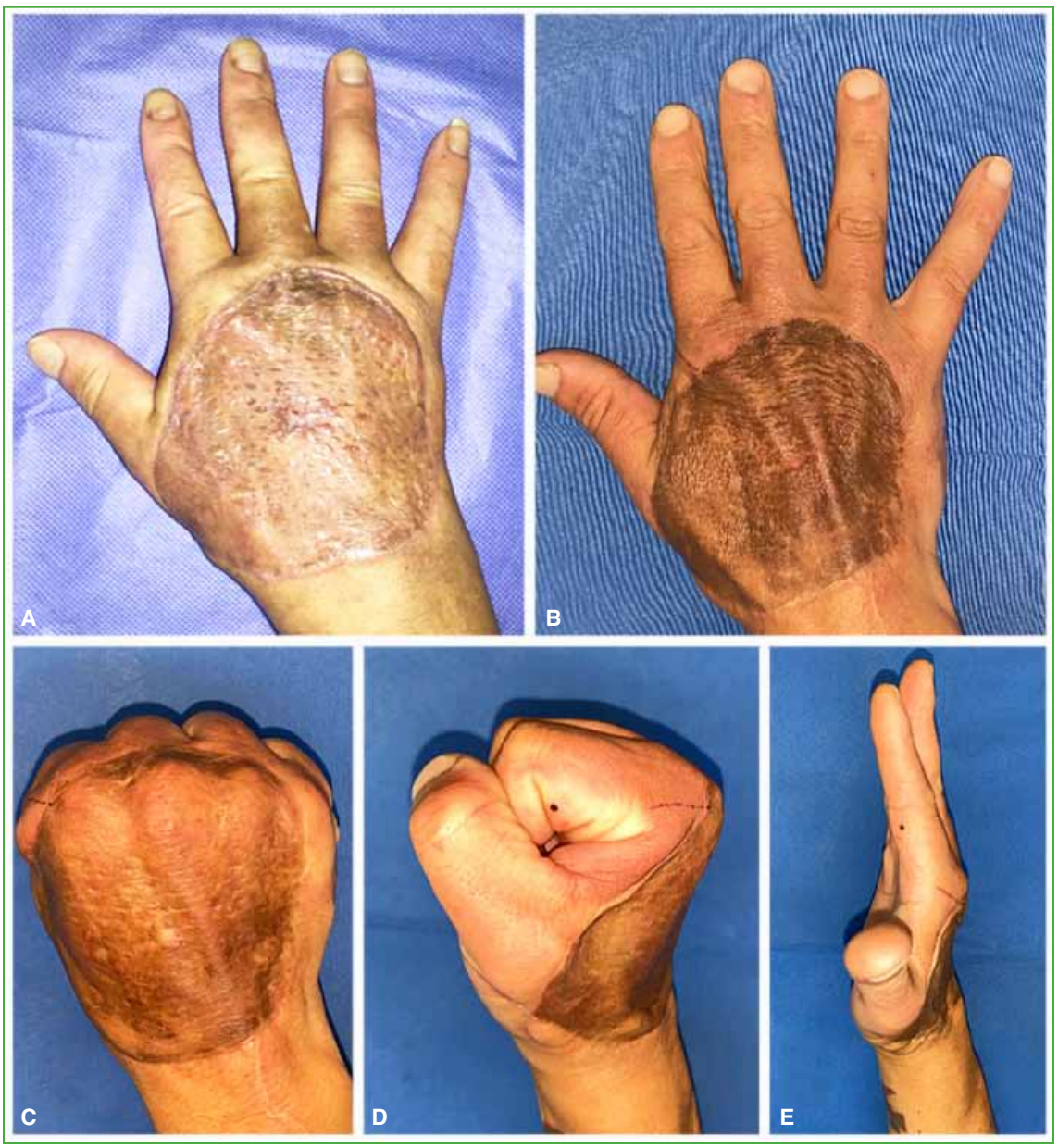


**Figure 2.** Case 1. **A.** Free skin graft placement. Early follow-up. **B- E.** Long-term follow-up after tendon reconstruction.

The average age at the time of surgery was 45 years (range 4-85). Average follow-up was 26 months (range 6–51). As relevant preoperative history, three smoker patients were registered, one of them also suffered from type 2 diabetes mellitus. The average size of the dermal substitute was 140 $cm^2$ (range 4-250).

No intraoperative complications were recorded. There were three postoperative complications. Two patients required a new placement of matrix in the area of the defect (soft tissue sarcoma) and, in another patient (chondrosarcoma grade II), a neurocutaneous saphenous flap reconstruction was performed due to failure of the membrane coverage.

## DISCUSSION

This study reports the use of a dermal regeneration template and the placement of a free skin graft in critical areas in soft tissue defects, in eight patients. In the final evaluation, the result was satisfactory in seven of the eight patients.

In the context of a severe wound with insufficient coverage, the basic therapeutic aims are: to remove contamination, to identify and classify the severity of the injury, and to perform hemostatic control, debridement, bone stabilization, restoration of circulation (direct repair or graft), nerve repair, tendon repair, and soft tissue coverage.[8]

The wound healing process involves a cascade of multiple cells (keratinocytes, endothelial cells, macrophages, platelets, fibroblasts) that leads to the inflammatory response and the subsequent formation of new tissue.[9]

Acellular dermal substitutes originate from cadaveric dermal material, which is subjected to a process of cell and antigenic material removal; as well as of infectious material.[10,11]

Dermal substitutes are characterized by their easy use and versatility. Based on the degree of complexity of the procedure, the reconstructive ladder modified by Rehim et al.[12] positions dermal substitutes between local flaps and distant pedicle flaps. The characteristics of the ideal dermal substitute have been postulated, including: resistance to infection, absence of antigenic response, durability, easy access, stability and capacity of covering a wide spectrum of wounds.[13] In recent years, the medical evidence on the use of dermal substitutes in venous ulcers and diabetic patients has increased considerably.[14,15]

Sometimes, it is not possible to treat the exposure of deep structures (tendons, bones, nerves, osteosynthesis material) with simple skin grafts.[16] In addition, the possibility of making flaps is not always available, either due to clinical comorbidity of the patient or surgical history that contraindicates it. Dermal substitutes have the ability to provide an adequate glide plane in the event of tendon exposure. However, the biological quality of reconstruction with a dermal substitute is inferior to that of flaps.

In our series, there were three complications. In two patients, the membrane had to be repositioned; both cases yielded satisfactory results. The third patient had a particular context, for which we do not recommend a new attempt with dermal matrix. As it is well known, neovascularization of the biological membrane occurs from the periphery when the bed is avascular or hypovascular. In this case, the vitality of the edges of the soft tissue defect was altered due to radiation therapy. In addition, the osteosynthesis material from this patient was exposed and fixed to an allograft bone. All this determines that the indication of dermal matrix is not adequate in case of failure in the first instance. We believe that the particular characteristics of the defect (edges altered by radiotherapy, bank bone and exposed osteosynthesis) are too unfavorable to insist on a minimally invasive treatment, such as the placement of a dermal substitute. However, we cannot say whether exposure of osteosynthesis *per se* is a contraindication.

One of the disadvantages of dermal substitutes is the high cost.[17] In addition, although there are reports of the placement of Integra® and the subsequent skin graft in a single surgical act, this procedure is usually performed in two stages and this involves two procedures, which further increases costs.[18] The formation of seromas in the postoperative period has been described; this can be controlled by piercing the membrane and thus allowing fluid to drain.[19]

Although the use of NPWT is not a mandatory indication for the use of dermal substitutes, it has been shown that they increase the rate of vascularization of the membrane.[20] NPWT tends to accelerate the process of tissue neoformation. In previous studies, the success rate with NPWT was 90% compared to membrane use without NPWT (75%). In addition, the use of NPWT would give greater stability and contact between the membrane and the bed. On the other hand, NPWT would eliminate excess exudate and, therefore, reduce the eventual proliferation of bacteria to a minimum, taking into account that dermal substitutes tend to be easily colonized.[16,21] However, the use of NPWT implies an extra cost, because the dressing changes must be made in the operating room, which increases the cost of the treatment. However, dressing changes are performed every seven days when NPWT is used and between 24 and 72 hours when it is not used. If possible, we recommend using NPWT, taking into account the extra cost and logistics involved. Nevertheless, the results without NPWT are still satisfactory. After the skin graft is placed, negative pressure therapy is repositioned for faster and more complete incorporation of the graft.

We believe—not unlike the literature—that, as indications for the use of dermal substitutes expand, the need for prospective comparative studies to evaluate the long-term benefits of the technique will grow.[12,22,23]

The most relevant limitation of this study is its retrospective characteristic, added to the low number of patients. However, in the international literature, the critical areas mentioned in our study are not accurately defined and the series are usually heterogeneous, including soft tissue defects without exposure of noble structures.

## CONCLUSIONS

The combined use of dermal substitutes and subsequent skin graft placement represents a versatile and relatively simple variant for the management of soft tissue defects. In addition, this technique may be indicated when the soft tissue defect includes critical areas (tendon exposure with absence of peritenon, bone exposure without periosteum, exposed neurovascular structures) and the direct use of skin graft is contraindicated. Dermal substitutes have to be considered a tool for the reconstruction of soft tissue defects in the extremities.

Conflict of interests: The authors declare they do not have any conflict of interests.

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