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ORIGINAL ARTICLE
Reconstructive

The Benefits of Using Platelet-rich Plasma with Dermal Substitutes for Extremity Posttraumatic Skin Defects: A Short-term Outcome

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Background: Skin injuries are very common. Skin grafting is an ongoing wound management procedure. The artificial dermis, PELNAC, has been considered in the treatment of several acute and chronic skin injuries. Platelet-rich plasma (PRP) is blood plasma with a platelet count higher than the baseline. It is presumed to act in a synergetic pattern to promote the healing of wounds. This study was conducted to assess the potential benefit of adding PRP to PELNAC as adjuvant therapy in treating posttraumatic skin.

Methods: In this study, adult patients who were admitted to the hospital with extremity traumatic skin and soft tissue defects with exposed bare bone, exposed tendons, or exposed cartilage in the period between October 2019 and March 2021 were allocated to either being managed with dermal substitute (PELNAC) together with PRP (group I) or PELNAC alone (group II).

Results: Patients in group I showed a higher mean graft take rate and a lower mean time for neovascularization of the acellular dermal matrix, with a statistically highly significant difference. The Vancouver Scar Scale values showed no significant difference in either group. The PRP-treated group showed statistically significant shorter hospital stays.

Conclusions: The addition of PRP to the treatment protocol showed better outcomes in terms of graft take rate, time for neovascularization of acellular dermal matrix, and length of hospital stay, with no side effects. The present study findings emphasize the promising outcome of PRP in addition to the standard treatment of complex wounds to achieve rapid and safe healing. *(Plast Reconstr Surg Glob Open 2024; 12:e5492; doi: 10.1097/GOX.0000000000005492; Published online 29 January 2024.)*

INTRODUCTION

Skin, being the outermost organ that covers the entire surface of the human body, is very commonly inured. Epidermal and dermal layer integrity loss can be subsequently complicated by many adverse events that may eventually cause death. Therefore, early initiation of wound management is mandatory to reduce morbidity and mortality.[1]

Skin grafting is an ongoing wound management procedure. Nevertheless, several disadvantages related to skin grafting were documented. These include creation of secondary wound sites and limitation of donor site in patients with extensive skin injury.[2]

It is well-established that flap surgery is the basis of tissue reconstruction in the field of plastic surgery.[3] However, skin substitutes are currently playing an important role in wound management, and sometimes, they are the best or even the only choice. The introduction of skin substitutes was driven by the crucial necessity for early management and coverage of extensive burn injuries in patients who have no sufficient sources of skin for autologous grafting and in patients whose ability to heal is compromised.[2,4,5]

Skin substitutes are diverse types of materials that are used for wound coverage. They provide several benefits,

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Received for publication January 3, 2022; accepted October 24, 2023.

DOI: 10.1097/GOX.0000000000005492

Disclosure statements are at the end of this article, following the correspondence information.

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such as the rapid coverage of the minimally vascularized wound bed, the increase of the healed wound's dermal component, and the decrease of scarring.[6]

PELNAC (Gunze Co., Ltd., Kyoto, Japan) was manufactured and allowed for clinical use in 1996. It is formed of two layers: a 3-mm-thick sponge layer of atelocollagen that is derived from porcine tendon and a superficial layer of reinforced silicone film.[7]

PELNAC was originally developed to induce dermal regeneration for the treatment of extensive burn injuries. Recently, it has been considered in the treatment of several acute and chronic skin injuries.[8]

Platelet-rich plasma (PRP) is blood plasma with a platelet count higher than the baseline.[9] Platelets are a mainstay in the process of wound healing owing to their well-known hemostatic properties and the presence of growth factors and cytokines. PRP can produce several growth factors through the degranulation of platelet alpha granules.[10] Growth factors are signaling polypeptides that stimulate the regeneration of epithelial and endothelial cells and promote the synthesis of collagen, angiogenesis, hemostasis, and soft tissue healing.[11–15]

The role of accompanying PRP with different types of dermal substitutes is still not fully elucidated. This study was conducted to assess the potential benefit of adding PRP to PELNAC dermal substitute as adjuvant therapy in treating posttraumatic skin.

PATIENTS AND METHODS

This is a prospective randomized study conducted at Kasr Al-Aini Hospital's department of plastic and reconstructive surgery after obtaining regional research ethics committee approval. Adult patients who were admitted to the hospital with extremity traumatic skin and soft tissue defects with exposed bare bone, exposed tendons, or exposed cartilage, and who were not eligible for flap surgery in the period between October 2019 and March 2021, were eligible for the study. Patients with clinically infected wounds or those with hypersensitivity to proteins of animal origin were excluded.

Randomization

Patients were allocated to either being managed with dermal substitute (PELNAC) together with PRP (group I) or dermal substitute alone (group II) by sealed envelope randomization in the absence of the study clinical investigator to achieve blinding.

The sample size required for the study was calculated according to Marck et al, based on which the mean healing rate in the PRP-treated group would be 18 days compared with 20 days in the non-PRP-treated group. With a confidence level of 0.95, the least required sample size was 52 patients.[16] Accordingly, in this study, 30 patients were allocated to each group. A written consent form was signed by each patient or their legal representative after explaining the existing problem and the management plan.

Preparation of PRP

The PRP gel formation steps are seen in Supplemental Digital Content 1 (**See graphic, Supplemental Digital Content 1**, which displays the PRP gel formation steps. http://links.lww.com/PRSGO/C977.) The whole blood was obtained from the patient by venipuncture and placed in an anticoagulated tube (usually with sodium citrate solution). The blood was centrifuged with double spin centrifugation: the first was for 15 minutes at 1500 rpm and the second was for 7 minutes at 3500 rpm, and then the platelet-poor plasma was removed via the side port. The PRP is formed by the re-suspension of the concentrated platelets on top of the floating buoy and is obtained from a specialized side port. This was then mixed with calcium and thrombin and subsequently coagulated to create PRP gel.[17]

Takeaways

Question: This study was conducted to assess the potential benefit of adding PRP to PELNAC as an adjuvant therapy in treating skin defects.

Findings: Adult patients having exposed bare bone or cartilage were allocated to either being managed with dermal substitute with PRP (group I) or PELNAC alone (group II). Patients in group I showed higher graft take and lower time taken for neovascularization of ADM.

Meaning: The study emphasizes the good outcome of PRP in addition to the standard treatment of complex wounds to achieve rapid healing.

After proper assessment and management of serious injuries, patients were transferred to the operating room. The surgery was conducted under general or spinal anesthesia. The affected limb was positioned according to the area to be reconstructed, and then povidone-iodine solution was used for sterilization of the whole limb.

Patients underwent reconstruction for the raw area in three stages: debridement in the first 8 hours of the trauma; then dermal matrix application after the wound bed is ready; and finally, autologous split-thickness skin graft (STSG) after the formation of dermal-like granulation.

First Stage

After the management of vascular and orthopedic injuries, debridement of necrotic tissue until viable bleeding tissue was reached was performed within the first 8 hours after trauma, and then the wound was rinsed with hydrogen peroxide (3%) and normal saline. Slight drilling into the surface of the exposed bone was performed using a Kirschner wire to induce punctate bleeding. Meticulous hemostasis was achieved without excessive cauterization so as not to devascularize the bed.

Second Stage

For patients in group I, PRP (0.1 mL/cm^2) was injected into the wound bed and edges. This step was omitted in patients in group II. The dermal substitute was prepared according to the guidelines of the manufacturer; the dermal matrix PELNAC was placed in sterile saline with Garamycin for about 20 minutes until it was fully moistened.

Adequate hemostasis was ensured before dermal substitute application; dermal substitute PELNAC was

adjusted regarding size and shape to provide a closure that is tension-free. The collagen side of PELNAC limitation was opposed to the wound surface, and then interrupted absorbable stitches or staples were taken to fix the artificial dermis to the surrounding skin.

Stabbing of the overlying silicon layer was carried out using a no. 11 scalpel blade to facilitate effusion drainage. Nonadherent silver antimicrobial dressings such as Silvercel or Acticoat were placed above the silicone layer of the dermal matrix PELNAC to act as a barrier to bacterial penetration. Vacuum-assisted closure therapy (VAC) was applied with a continuous negative pressure of 100 mm Hg to decrease closure time, prevent seroma or hematoma, control bacterial growth, and reduce shearing forces.

Every 4 days, observation of the wound bed through the silicone layer for proper granulation tissue formation was performed with a VAC dressing. VAC was sustained until the proper neovascularization and dermis-like tissue formation were indicated by the alteration of the color of the tissue deep to the silicone layer from white into pink and the silicon layer peeling off.

Third Stage

The silicon layer was discarded. Autologous STSG was harvested from the patient's thigh by an electric-powered dermatome or Humby knife and applied to the dermal-like granulation for final coverage of the wound. VAC was applied to the graft. In cases where it was applied to flexible areas such as a joint, it was firmly fixed by a splint. The first graft check was done after 4 days, and a light dressing was used.

Postoperative Management

Patients were instructed to take bed rest and elevate their limbs over pillows. Good postoperative hydration was achieved with IV fluids. Broad-spectrum antibiotics, analgesics, and anti-edematous drugs were prescribed, and anticoagulants were given for bedridden patients.

Follow-up

The graft site was examined in the outpatient clinic on days 7, 14, and 21 after surgery. The primary outcome of this study was the time taken for neovascularization of the acellular dermal matrix (ADM) and the graft take rate. Graft take rate was calculated in this study as the percentage of the graft that was viable, pink, and adherent to the wound bed on day 14 postoperatively. The secondary outcomes were scar appearance at 1, 3, and 6 months postoperatively using the Vancouver Scar Scale (VSS), as well as the length of hospital stay and surgery complications. VSS is a scale that assesses four parameters: scar height and thickness, pliability, vascularity, and pigmentation. The score ranges from 0 to 13 points; the lower the score, the better the scar appearance. The consort flow diagram is presented in Figure 1.

Statistical Analysis

Tabulation and analysis of the patients' data were conducted with the use of SPSS (Statistical Package for Social Science), version 22. Quantitative data were expressed as mean ± SD, and qualitative data were expressed as frequency and distribution. Independent *t* tests, chi-square tests, and Fisher exact tests were used for comparing the two groups as appropriate. The level of significance in this study was considered to be 0.05.

RESULTS

This study was conducted on 110 patients with posttraumatic extremity skin defects. The study patients were classified into two groups: those who were managed with dermal substitute (PELNAC) together with PRP (group I) and those who were managed with dermal substitute application only (group II). Patients' demographic data and basal clinical criteria are demonstrated in Table 1. No significant difference was demonstrated regarding age, gender, mode of trauma, location of the injury, exposed structures, wound dimensions (cm), and size of exposed structures (cm).

There was a statistically highly significant reduction in the time taken for neovascularization of the ADM in group I compared with group II. A statistically significant increase in graft take rate was found in group I compared with group II.

No significant differences were found in the rehabilitation time or the functional outcome (range of motion of the affected joint) for either group, with the sessions continuing for 10.5 ± 2.2 weeks in group I and 10.9 ± 2.8 weeks in group II. The affected joints were full range in 12 (40%) patients, decreased by a quarter in 10 (33.3%) patients, decreased by half in four (13.3%) patients, and decreased to a quarter in four (13.3%) patients of group I. In group II, the affected joints were full range in 11 (36.7%) patients, decreased by a quarter in 10 (33.3%) patients, decreased by half in six (20%) patients, and decreased to a quarter in three (10%) patients.

At 6 months postoperatively, some cases dropped out, and only 25 patients in group I and 28 patients in group II had a VSS assessment. In group I, VSS ranged from 3 to 5, with a mean of 3.6 ± 0.74. In group II, VSS ranged from 3 to 6, with a mean of 3.73 ± 1.3. No statistically significant difference was noted (Table 2).

Length of Hospital Stay and Complications

Hospital stay length showed a statistically highly significant reduction in group I (18.73 ± 2.37), compared with group II (31.68 ± 5.55). The main complications were rash [two cases (6.7%) in group I and four cases (13.3%) in group II] and secondary infections [two cases (6.7%) in each group], with a nonsignificant difference between both groups. No graft failure was encountered. No limb contracture or recurrent ulcer was detected during the study follow-up period. Figure 2–5 are examples of managed cases.

DISCUSSION

An incompletely understood complex panel of intracellular and extracellular reactions mediates the hard and soft tissue healing processes. However, a considerable role in this process is certainly mediated by platelets.[18]

The role of accompanying PRP with different types of dermal substitutes is still not fully elucidated. Available

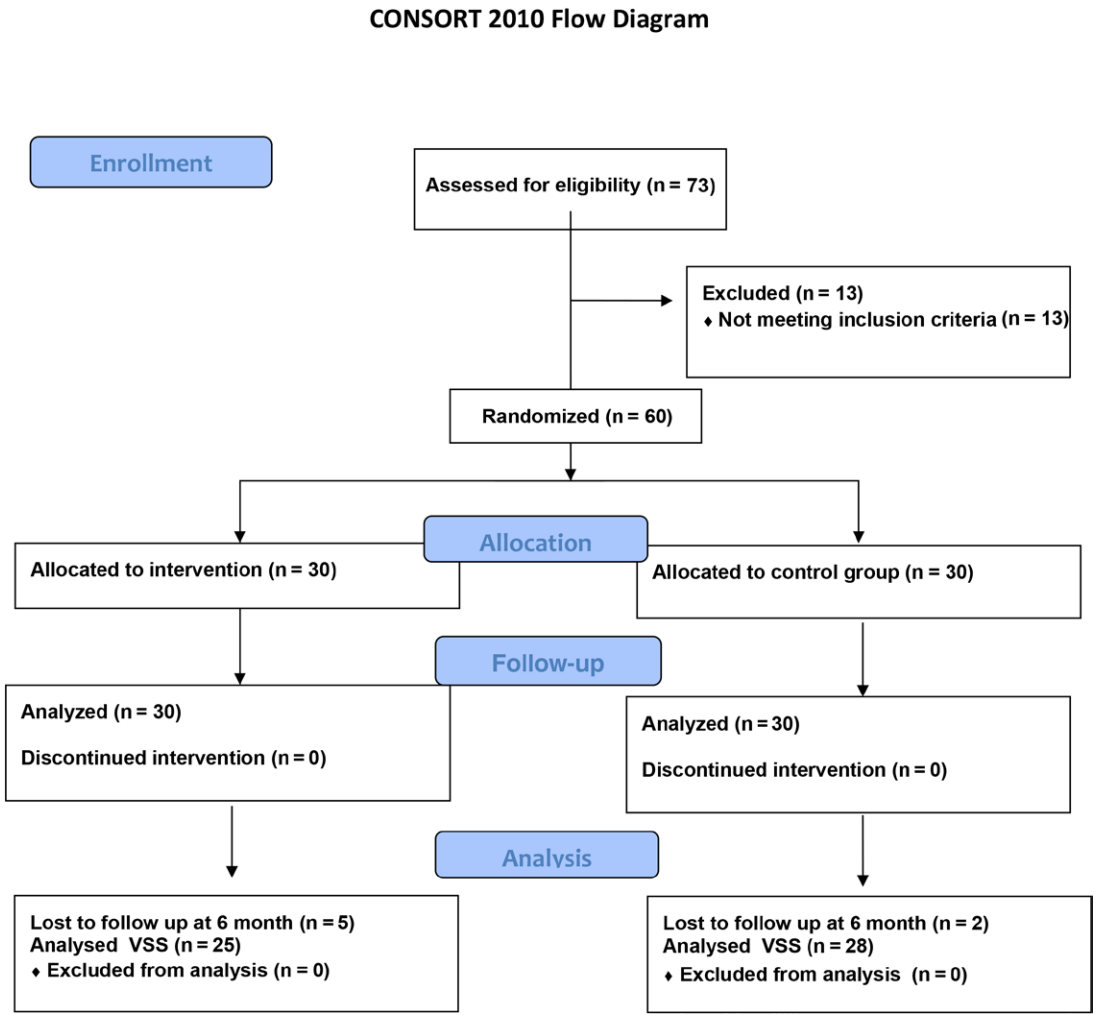

Fig. 1. The consort flow diagram.

data suggest the use of PRP for healing traumatic wounds, diabetic vascular and chronic ulcers, and open and chronic ankle wounds.[19,20]

This study was conducted to assess the potential benefit of PRP to PELNAC dermal substitute as adjuvant therapy in treating posttraumatic skin. PELNAC decreases disability and scar contractures, and also improves the cosmetic appearance by providing a result that finally mimics endogenous dermis.[21]

The mean time taken for neovascularization of ADM in the current study was significantly lower in group I (with PRP). Patients in group I also showed a higher mean graft take rate with a statistically highly significant difference. These findings confirm the beneficial effects of PRP.

Several RCTs comparing PRP with standard treatment for chronic wounds have been published. The results of the most recent study by Liu et al are in harmony with the present study findings. They carried out an RCT study that involved 102 patients to evaluate the value of PRP gel in the treatment of refractory pressure injuries and whether it affects the time of wound healing. They reported that adding PRP gel to the standard therapy can promote wound healing and reduce healing time without increasing complications.[22]

Knighton et al found that lower extremity ulcers showed accelerated reepithelialization when they were treated with platelet-derived healing formula.[23] Similarly, Babaei et al reported that, after topical application of PRP, healthy granulation tissue creation and rapid total wound closure were noted in 150 patients with ulcers of the diabetic foot.[24] Minamimura et al observed that PRP-impregnated collagen matrix used in the treatment of 16 chronic limb ulcers led to successful healing.[25]

Furthermore, a meta-analysis was conducted by Xia et al to assess the role of PRP in nonhealing ulcers compared with the traditional therapy of wounds. They came to the conclusion that PRP is a simple, valuable, and safe treatment for chronic wounds.[26] Other meta-analysis studies also concluded that PRP enhances the healing of acute and chronic wounds.[27,28] In an experimental study, the authors found that using a PRP-hydrogel, combined treatment compared with either treatment individually resulted in a decrease in wound size and a shorter healing period.[29] Also, in a study performed by Hahn et al,

Table 1. Comparison between the Study Groups in regard to Demographic and Basic Clinical Data

	Group I	Group II	Total	Test	
Age					
Mean ± SD	35.2 ± 17.9	32.4 ± 19.5	33.8 ± 18.4	$t = 0.58$	0.56
Sex					
Male	20 (66.7%)	22 (73.3%)	42 (70%)		0.78*
Female	10 (33.3%)	8 (26.7%)	18 (30%)		
Mode of trauma					
Road traffic accident	24 (80%)	23 (76.7%)	47 (78.3%)		1.00*
Isolated trauma	6 (20%)	7 (23.3%)	13 (21.7%)		
Location of injury					
Upper extremities	13 (43.3%)	16 (53.3%)	29 (48.3%)		0.61*
Lower extremities	17 (56.7%)	14 (46.7%)	31 (51.7%)		
Exposed structures					
Tendon	6 (20%)	8 (26.7%)	14 (23.3%)	$X^2 = 0.44$	0.8
Bone and tendon	10 (33.3%)	10 (33.3%)	20 (33.3%)		
Bone	14 (46.7%)	12 (40%)	26 (42.4%)		
Wound dimensions (cm)					
Length (mean ± SD)	12.6 ± 5	15.80 ± 11.6	—	$t = 1.39$	0.17
Width (mean ± SD)	7.53 ± 2.9	6.73 ± 2	—	$t = 1.24$	0.22
Size of exposed structures (cm)					
Length (mean ± SD)	3.33 ± 1.496	4.02 ± 2.7	—	$t = 1.22$	0.23
Width (mean ± SD)	1.73 ± 0.46	1.7 ± 0.53	—	$t = 0.23$	0.82

* Fisher exact test

X^2, chi-square test; $P > 0.05$, nonsignificant; $P < 0.05$, significant; $P < 0.001$, highly significant.

Table 2. Time Taken for Neovascularization of ADM, Graft Take Rate (%), and VSS in the Study Groups

Group	Group I	Group II	*t* Test	*P*
Time taken for neovascularization of ADM (d)				
Mean	10.8	19.13	14.29	<0.001
SD	1.57	2.78		
Graft take rate (%)				
Mean	98.2%	92.78%	4.25	<0.001
SD	1%	9.5		
VSS				
Mean	3.60 (n = 25)	3.73 (n = 28)	0.58	0.57
SD	0.74	0.88		

$P > 0.05$, nonsignificant; $P < 0.05$, significant; $P < 0.001$, highly significant.

the PRP associated healing rate was more accelerated.[30] Another experimental study demonstrated that administering PRP resulted in increased composite graft viability, a higher graft survival rate, and revascularization.[31]

Despite literature evidence about the role of PRP in healing enhancement, a few studies, have failed to demonstrate PRP's better effect. This could be attributed to devices or study design variations. Marck et al reported results that were contradictory to the current study findings. Their study included 52 patients with regions ranging from deep dermal to full-thickness burns. Comparable regions A and B were addressed and either managed with an STSG alone or with an STSG and PRP. They found no statistically significant difference between either group in the mean graft take rates.[16] However, their rates were reported on days 5–7, and this may partially explain the cause of the discordant findings.

The present study displayed comparable rehabilitation periods and functional outcomes for both groups. This is consistent with the previously published evidence. It was found that, despite the theoretical proposal that PRP use improves bone healing, there is no consensus supporting the use of PRP for bone healing enhancement.[32] A recent review highlighted three randomized controlled trials that could not demonstrate a beneficial effect of PRP on functional outcomes.[33]

Some studies claim that an enhanced inflammatory reaction is exhibited due to the leukocytes in PRP.[34] This could theoretically worsen the quality of the final scar. Moreover, it was assumed that certain platelet-derived growth factors in PRP are chemotactic and induce chronic inflammation that may result in a hypertrophic scar.[35]

In the present study, no significant differences were depicted concerning the VSS values, denoting comparable scar quality in both groups. Also importantly, despite being statistically nonsignificant, fewer scores were obtained in group I denoting better scar quality, ensuring that PRP did not worsen the scar quality. This finding is in line with what was reported by Marck et al, that at 3, 6, and 12 months, there was no significant difference in the scar quality between the PRP and standard-managed regions.[16]

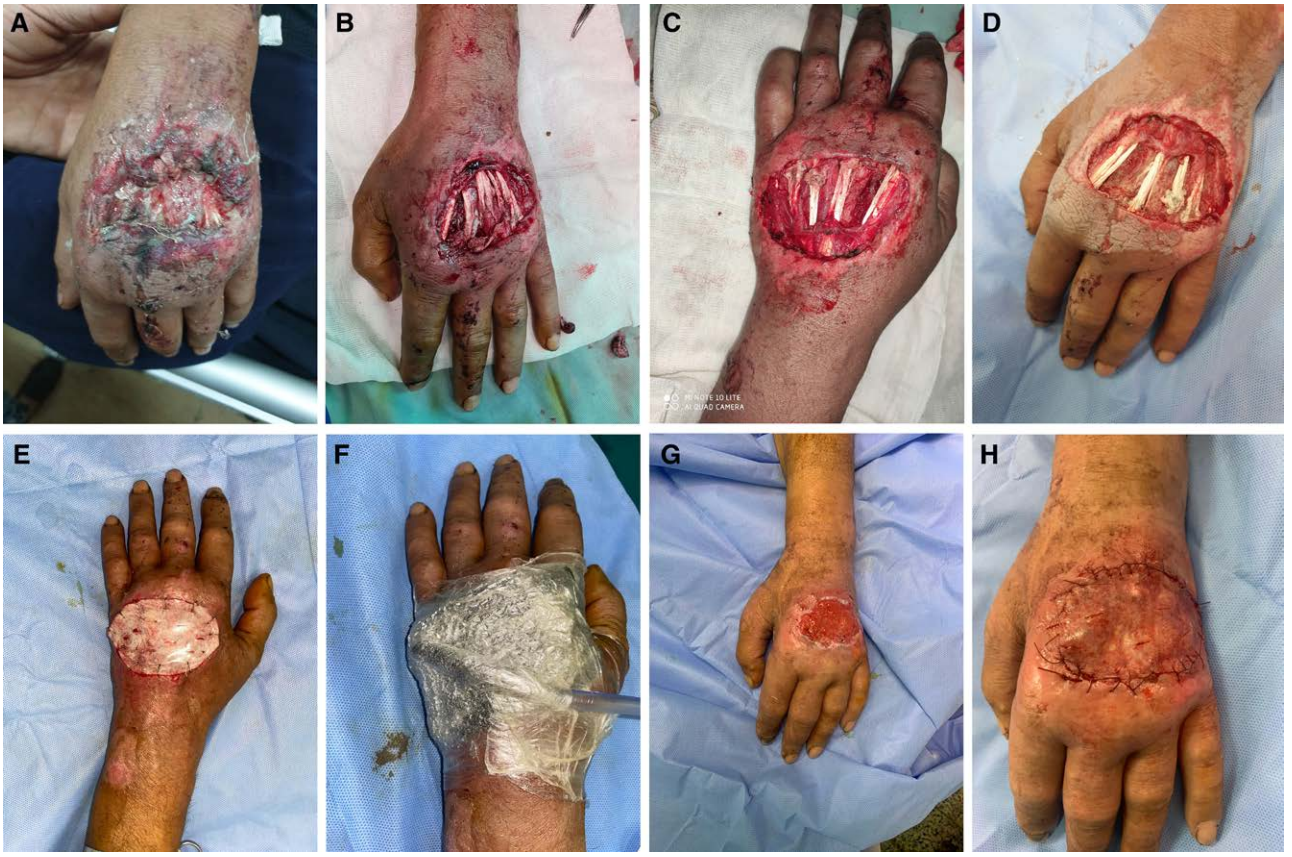

Fig. 2. A 53-year-old man had a left hand injury in a road traffic accident with full-thickness skin defect (9 cm × 6 cm); there were exposed tendons and extensor digitorum communis tendons cut of the index, middle, ring and little finger as well as extensor indicis tendon cut. A, Post traumatic skin loss before debridement. B-C, Wound lavage and debridement were done and tendons were repaired. D–F, PELNAC artificial dermis and VAC was applied. G-H, After 22 days and formation of dermal-like granulation tissue, skin graft harvested and applied on the newly formed granulation tissue.

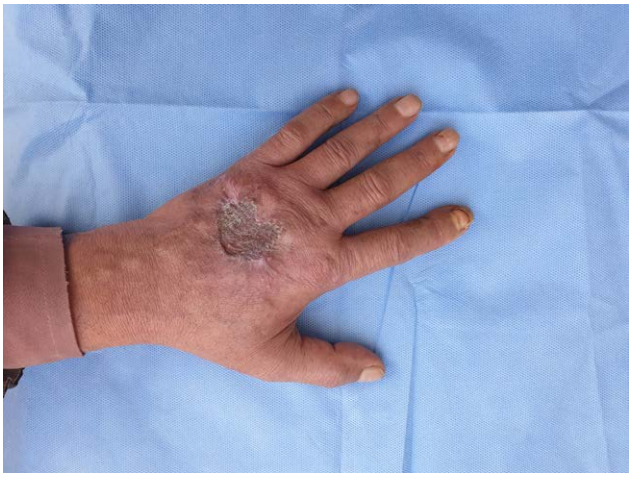

Fig. 3. Follow-up is shown. The patient obtained a satisfying appearance and functional recovery.

Concerning hospital stay length, the PRP-treated group showed a statistically significant shorter hospital stay, reflecting overall more rapid healing and less morbidity. Few studies have assessed the difference in hospital stay length. The Uçar and Çelik study reported, in agreement with the present study, that adding PRP to the treatment protocol significantly shortened the hospital stay length.[36]

PRP is immunologically neutral. It is mandatory to follow sterile techniques at every stage of PRP preparation and application, particularly in patients who are highly at risk of infection. Some medical conditions are reported to contraindicate PRP use, including critical thrombocytopenia, sepsis, hemodynamic instability, anticoagulation therapy, and chronic liver disease.[37]

In the present study, no severe complications attributed to PRP use were addressed. This is in agreement with multiple studies.[16,21,38] The encountered complications, such as the rash or the secondary infection, were nonsignificantly different in both groups.

Indeed, before the adoption of PELNAC with PRP for routine use in patients with posttraumatic skin defects, economic aspects should be addressed. Skin substitutes generally necessitate a higher cost, expertise, and experience. Adding the cost of PRP augments such costs. However, we think that when the learning curve increases, such novel methods may be cost-effective. They speed up the healing of wounds and shorten the hospital stay. Further studies

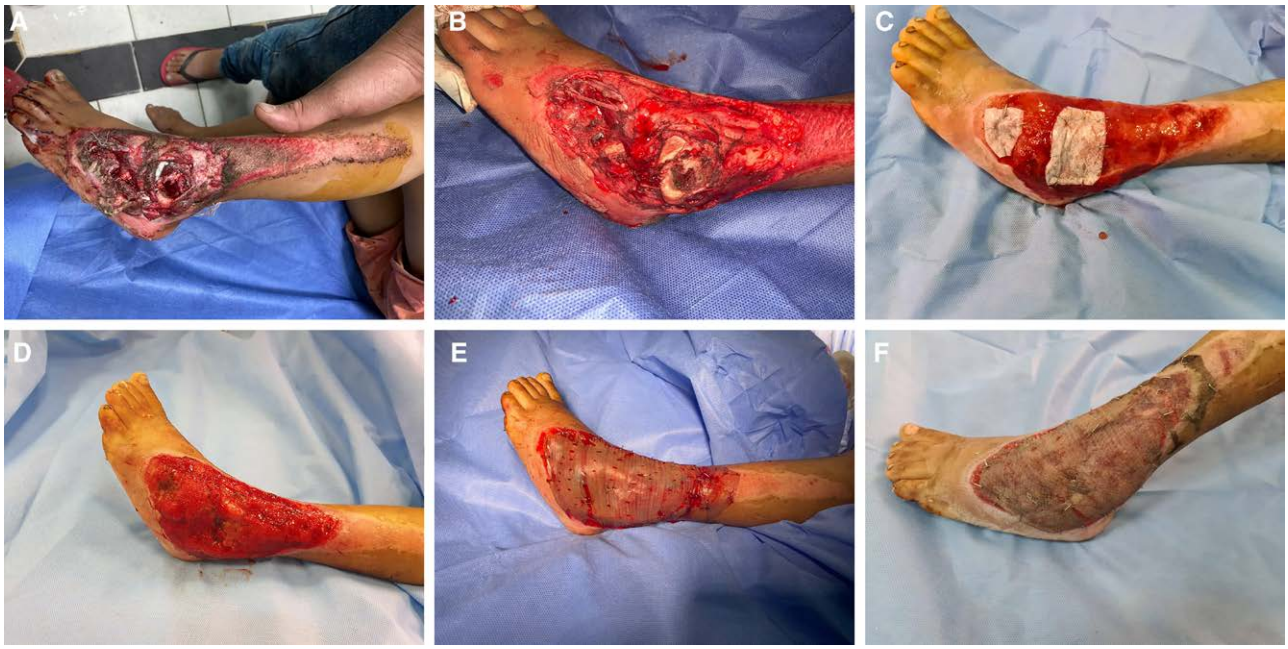

Fig. 4. A 19-year-old woman sustained a road traffic accident injury with soft tissue loss (30 cm × 6 cm) and exposed lateral malleolus, cuboid and fifth metatarsal bone, and extensor digitorum longus tendons. A-B, Posttraumatic skin loss with exposed bone and tendon in the left foot before and after debridement. C, PELNAC dermal substitute was applied after PRP injection. D, After removal of silicon layer and formation of dermal-like granulation tissue on the thirteenth day. E, Autologous STSG harvested and applied. F, First graft check showing good take.

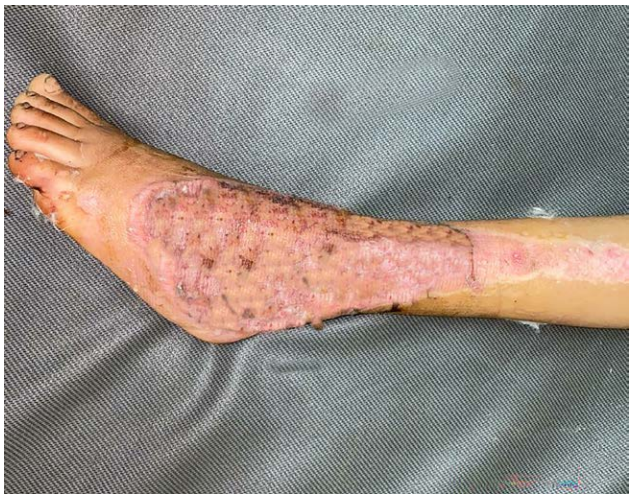

Fig. 5. Follow-up is shown. The patient achieved a satisfying scar appearance and functional recovery.

focusing on the financial evaluation of using PELNAC with PRP are, however, recommended.

The strength points of this study are its prospective randomized design and being one of the few pieces of evidence that investigated the effect of PRP as an adjuvant therapy to PELNAC in the treatment of road traffic accident patients' deep skin injuries. The study is, however, limited by the number of dropped outpatients, the short-term follow-up, and the subjective determination of vascular ingrowth using the VSS.

Overall, although flap reconstructive surgery is the basic management procedure for deep wounds, the current work demonstrates that management with skin substitutes could be an excellent alternative in cases not eligible for flap surgery, especially when PRP is added.

CONCLUSIONS

PRP, in addition to the treatment protocol, showed better outcomes in terms of graft take rate, time for neovascularization of ADM, and length of hospital stay, with no side effects. The present study findings emphasize the promising outcome of PRP in addition to the standard treatment of complex wounds to achieve rapid and safe healing.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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