ORIGINAL

The perifascial areolar tissue and negative pressure wound therapy for one-stage skin grafting on exposed bone and tendon

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Abstract : Background : Factors such as exposed bones or tendons can inhibit wound healing and make it a lengthy process unless aggressive debridement or vascularized flap surgery are performed. We have developed a new procedure involving simultaneous application of a skin graft and perifascial areolar tissue (PAT) and negative pressure wound therapy. Methods : Of 8 patients with wounds, bones, tendons, and thick fascia were exposed in 4, 2, and 2 cases, respectively. These wounds were adequately covered with PAT, and split-thickness skin grafts were applied simultaneously on the PAT with a VAC® device. Results : In 6 of 8 cases, the skin graft and PAT were successful, and epithelialization was achieved within 4 weeks. PAT adapted but skin graft was unsuccessful in one case, and both the skin graft and PAT failed to adapt of a pressure ulcer. Using the PAT to overlap more than 400% of the exposed areas resulted in better adaptation. Conclusions : This procedure contributed to reducing the burden on the patients because we were able to use a skin graft on the exposed areas, without the need for removal of bone or tendons. This potentially means patients avoid loss of function in the affected areas and achieve better outcomes. J. Med. Invest. 65 : 96-102, February, 2018

Keywords : *Wound Healing, Negative-Pressure Wound Therapy, Skin Transplantation, Diabetic Foot*

INTRODUCTION

Two therapeutic strategies are required for treatment of refractory skin ulcers when bones, tendons, or thick fascia are exposed. One is pedicled or free vascularized tissue transplantation on the exposed bone, tendon, or fascia. The other is skin grafting on the granulation tissue or conservative treatment after removal of the exposed areas. Using this method may cause considerable functional disabilities due to the removal of bones or tendons, and wound healing becomes a long process.

Although artificial dermis or perifascial areolar tissue (PAT) (1-3) can be effective as scaffolds for granulation tissue, two-staged surgery is required and we need to allow adequate time for granulation tissue to form. To offset these disadvantages and minimize the burden on the patient, we have developed a new procedure for skin grafting using simultaneous PAT and negative pressure wound therapy (NPWT) for refractory skin ulcers. The aim of the present study was to reveal the effectiveness of this new procedure.

PATIENTS AND METHODS

The present study included 8 patients (Table 1). The study group comprised 6 men and 2 women ; their mean age was 62.3 years. Five patients had refractory diabetic foot ulcers, including 3 with neuropathic ulcers and 2 with severe peripheral arterial disease. Two had extensive skin pressure ulcers ; one was on the lower leg and the other was on the sacrum. One had a skin defect on her back due to resection of a malignant melanoma. Two patients had osteomyelitis and in 1 patient, a pressure ulcer on the sacrum became infected just before surgery. Five of 8 cases were treated with NPWT pre-operatively to prepare the wound bed.

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Operative procedure

After sufficient debridement of the wound, the size of the exposed area was measured and the required PAT size was determined. In the present study, PAT was harvested from the external abdominal oblique muscle. A skin incision was made approximately 2 cm above the full thickness inguinal graft along the skin wrinkle line. After dissecting the area between the subcutaneous fat tissue and the external abdominal oblique muscle fascia, a thin membrane including tiny vessels was detected just above the external abdominal oblique muscle fascia (Fig. 1A, B). After additional dissection of the subcutaneous tissue horizontally, the PAT was

Table 1. Patient Demographics

Case No.	Age	Sex	Lesion	Wound Site	vascular disease or infection	pre-operative NPWT
1	82	M	DM Ulcer	Dorsal Foot	PAD, osteomyelitis	Applied
2	59	M	DM Ulcer	Dorsal Foot		Applied
3	42	F	DM Ulcer	Calcaneus	PAD	Applied
4	88	M	Pressure Ulcer	Lower Leg		Applied
5	28	M	DM Ulcer	Lower Leg		Not Applied
6	44	M	DM Ulcer	Dorsal Foot	osteomyelitis	Not Applied
7	82	F	Malignant Melanoma	Back		Not Applied
8	73	M	Pressure Ulcer	Sacrum	wound infection	Applied

DM, diabetes mellitus ; PAD, peripheral artery disease ; NPWT, negative pressure wound therapy harvested to the required size (Fig. 1C). To assist with the revascularization from the granulation tissue into the PAT, a wide overlap of the area between the PAT and the exposed area was needed (Fig. 1D). The exposed part that was inhibiting wound healing was covered with the harvested PAT, which was sutured with absorbable threads. A meshed split-thickness skin graft (STSG) made from harvested full-thickness skin and dermatome was applied to the PAT with simultaneous use of a VAC® (Vacuum-Assisted Closure by KCI, San Antonio, TX) device using 50 to 75 mmHg continuous negative pressure (Fig. 1E). In patients with uneventful post-operative periods, the VAC® device was applied for 5-7 days. After removal of the device, hydrophilic ointments or wound dressings were applied every day or every 2 days, depending on the amount of wound discharge.

Measurement of the overlapping area between the PAT and the exposed area

A wide overlap with PAT on the exposed area, such as tendons, bones, and thick fascia, is essential for good adaptation. The overlapping area between the PAT and the exposed area was measured with Image J (version 1.48, Wayne Rasband, National Institutes of Health, USA), counting the number of pixels on the photographs. The ratio between the size of the PAT area and that of the exposed area was calculated.

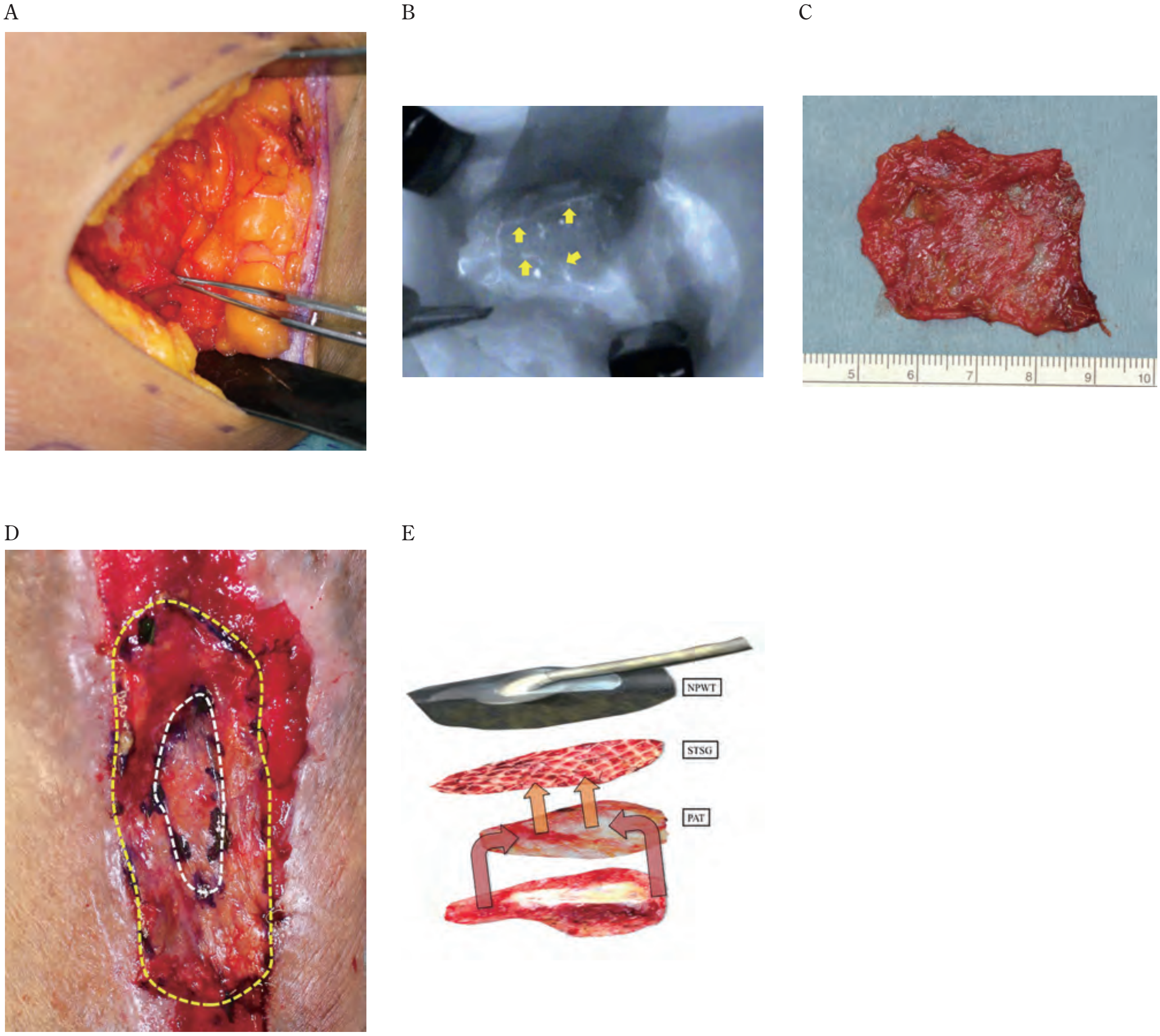

Fig. 1 Operative procedure
A : The intraoperative procedure harvesting the perifascial areolar tissue (PAT) from the external abdominal oblique muscle.
B : The vascular network (yellow arrows) in the PAT is shown with indocyanine green fluorescence angiography. A rubber sheet is inserted under the elevated PAT.
C : The harvested PAT at the required size.
D : A wide overlap of the area between the PAT (outer yellow dots) and the exposed area (inner white dots) is required to promote revascularization from the granulation tissue into the PAT.
E : The schema of the procedure is shown ; split-thickness skin graft (STSG) combined PAT with negative pressure wound therapy (NPWT). The primary revascularization from the granulation tissue into the PAT (pink arrows) and secondary revascularization into the STSG via the PAT (orange arrows) are indicated.

RESULTS

Results are shown in Table 2. Of the 8 wounds in this study, bones, tendons, and thick fascia were exposed in 4, 2, and 2 cases, respectively. In 6 of 8 cases, adaptation of the skin graft and PAT was successful, and epithelialization was achieved within 4 weeks of surgery. In 1 case where the procedure had been applied immediately after ablation of a malignant melanoma on her back, only the PAT adapted but the skin graft failed to adapt. Both the skin graft and the PAT failed to adapt in a case with an extended pressure ulcer on the sacrum, malnutrition, and difficultly maintaining an off-loading posture.

The mean ratio of PAT to the exposed area was 578% in the both PAT and skin graft adapted cases, but was lower in those in with failed adaptation ; these were 345% and 210%, respectively. A ratio of PAT to the exposed area of more than 400% resulted in better adaptation of both the PAT and skin graft.

Case reports

Case 4 : The patient was an 88-year-old man who had pressure ulcer at the lower leg. Since the fibula was exposed and a fistula extended proximally toward the ulcer, a fistula incision was made by a previous doctor. Although wound bed preparation was performed with VAC®, the fibula was still exposed without granulation tissue. Therefore, additional operative treatment applying STSG, PAT, and NPWT was performed. The area of exposed fibula measured 2.5 × 1.5 cm (Fig. 2A), and a 5 × 3 cm PAT was applied (Fig. 2B) with an overlaying meshed STSG (Fig. 2C). The ratio of PAT to the exposed area was 401%. The VAC® device was used with 50 mmHg of pressure. One month post-operatively, both the PAT and skin grafts had achieved good adaptation (Fig. 2D).

Case 6 : The patient was a 44-year-old man who had a DM ulcer with neuropathy and osteomyelitis at the first metatarsal bone. Since the extensor hallucis longus tendon was exposed and a fistula extended proximally toward the ulcer, a fistula incision was made at the first visit. After conventional treatment with antibiotics and wound toilet, additional operative treatment applying STSG combined with PAT and NPWT was performed. The area of exposed hallucis longus tendon measured 2.5 × 1 cm (Fig. 3A), and a 3.5 × 3 cm PAT was applied (Fig. 3B) with an overlying meshed STSG (Fig. 3C). The ratio of PAT to the exposed area was 447%. The VAC® device was used with a pressure of 50 mmHg (Fig. 3D). One month post-operatively, both the PAT and skin grafts had achieved good adaptation (Fig. 3E).

DISCUSSION

Flap coverage is the ideal method in the presence of exposed bones, tendons or thick fascia that inhibit wound healing. Technically less demanding and speedier options might be considered for small shallow wounds, for wounds with adjacent tissue loss precluding pedicled local flaps, or for healthy recipient vessels with free flap impairment. Moreover, the extensive local flap or free flap procedure is sometimes significantly invasive for elderly patients or those in poor general condition. When the bone, tendon, or thick fascia is exposed, there is generally one method used to heal these wounds : the resection of the whole exposed area with additional skin grafting. However, this may cause severe disabilities due to the resection of the functional bones or tendons post-operatively. Although NPWT is a well-established method to promote wound healing (4-6) and its efficacy is largely accepted by many clinicians, it is often used as a bridging device for closure of a skin graft or a skin flap. Therefore, a longer period is required for producing the vascularized granulation tissue on those exposed areas and this process can be a burden on patients.

Kouraba *et al.* (3) first described PAT as a useful autologous material to cover exposed areas such as bones and tendons that inhibit wound healing. Perifascial areolar tissue is located under the deep adipofascial layer and directly adhered to the innominate fascia in the lower abdomen or the temporal region. It is a loose connective tissue and part of a group of structures known as the lubricant adipofascial system reported by Nakajima *et al.* (7, 8) Perifascial areolar tissue is mainly composed of gelatinous matrix and a few cells, such as fibroblasts, macrophages, plasmacytes, adipocytes, and mastocytes ; it also contains collagen and elastic fiber. Because it forms a meshwork of sparse collagen and elastic

Table 2. Applications and Assessments of PAT Skin Grafts and NPWT

Case No.	Exposed Are Interfering with Wound Healing	Size of the Exposed Area (cm)	Size of the PAT Graft (cm)	Ratio of PAT to Exposed Area (%)	Assessment
1	navicular bone	1 × 1	4 × 2	790	Both PAT and SG adapted
2	4th & 5th metatarsal bones	1.5 × 1	3 × 2	547	Both PAT and SG adapted
3	calcaneus	3 × 2	7 × 5	649	Both PAT and SG adapted
4	fibula	2.5 × 1.5	5 × 3	401	Both PAT and SG adapted
5	tendon of short peroneal muscle	1 × 0.5	2 × 2	513	Both PAT and SG adapted
6	extensor hallucis longus tendon	2.5 × 1	3.5 × 3	447	Both PAT and SG adapted
7	fascia of trapezius muscle	3 × 2	5 × 4	345	PAT : adapted SG on the PAT : failed
8	thoracolumbar fascia	5 × 3	7 × 5	210	Both PAT and SG failed

NPWT, negative pressure wound therapy ; PAT, perifascial areolar tissue ; SG, skin graft

Fig. 2 Case 4 : An 88-year-old man
A : After the surgical debridement, the area of exposed fibula measures 2.5 × 1.5 cm.
B : A 5 × 3 cm perifascial areolar tissue (PAT) is applied to the exposed fibula and adjacent granulation tissue. The ratio of PAT to the exposed area is 401%.
C : An overlaying meshed STSG is applied on the PAT and surrounding granulation tissue.
D : One month post-operatively, both the PAT and skin graft achieve good adaptation.

fibers, it is suitable as a vascular growth scaffold. Because of its rich vascular network, PAT is able to transplant a vascular bed onto an area of poor vascularity. Moreover, because of its thin and pliable membrane, PAT can be transplanted onto an irregular wound surface (1, 2).

Other possible alternative materials for vascular scaffolds mentioned in previously published reports include various artificial dermis (9, 10), acellular dermis (11), and collagen cell carriers (12). Although there are some reports that these materials improve the grafted skin quality when placed under the STSG, the efficacy and outcome of these materials are still under debate. In addition, these alternatives have no vascular structures and only angiogenesis could be expected using these materials on the wound bed. Perifascial areolar tissue contains tiny vessels and linking these vessels between the wound bed and the PAT could possibly accelerate formation of non-vascularized grafted PAT into the

Fig. 3 Case 6 : A 44-year-old man
A : The area of the exposed hallucis longus tendon measures 2.5 × 1 cm.
B : A 3.5 × 3 cm perifascial areolar tissue (PAT) graft is applied to the exposed hallucis longus tendon and adjacent granulation tissue. The ratio of PAT to the exposed area is 447%.
C : An overlaying meshed split-thickness skin graft (STSG) is applied on the PAT and surrounding granulation tissue.
D : A VAC® device simultaneously delivers NPTW with 50 mmHg of pressure .
E : One month post-operatively, both the PAT and skin graft achieve good adaptation.

vascularized wound bed. Therefore, care and precision are required when harvesting the PAT to prevent impairment of the tiny vessels involved.

Hachiya *et al.* (13) reported the histologic outcomes after placement of a strip of PAT into rabbit vocal folds. According to their report, PAT gradually lost its original architecture and a greater deposition of collagen in the implanted vocal folds than in the control group was detected. Hayashi *et al.* (14) also reported the pathological findings from the granulation tissue after grafting PAT. They found that the tissue from ulcers with a PAT graft developed a thick collagen layer and large, mature vessels grew toward the surface of the wound. This did not occur for wounds without a PAT graft. Our findings suggest that skin grafts on the well-vascularized granulation tissue can lead to considerably good adaptation when PAT is placed between the skin graft and the granulation tissue. Perifascial areolar tissue was able to function as a good scaffold to provide vascularized material to the skin grafts.

When using PAT as a rich vascular plexus scaffold for the skin graft, it should overlap well beyond the exposed area to extend to the area adherent to the vascularized granulation tissue. Previous report on PAT without NPWT has harvested PATs 2-3 times wider than the defect (14). We recommend a PAT overlay of at least 400% of the exposed area, as this resulted in better adaptation of both the PAT and the skin graft in our cases.

This new skin grafting procedure combining PAT and NPWT is supported by several advantages. It is well-known that NPWT contributes to wound healing by inducing mechanical stress as macrodeformations and cellular stimulation as microdeformations (4-6). The main effects contributing to successful treatment using this procedure include firm adherence to the wound surface and excretion of redundant exudate. Because of accelerated revascularization in the PAT from the granulation tissue, this method can aid in providing a bridging vascular bed on avascular tissue. Moreover, because of the rapid angiogenesis in the grafted skin via the granulation tissue, this method can aid in epithelial growth toward the grafted skin on the PAT.

It is well-known that negative pressure increases the blood-flow in both the subcutaneous and muscular tissue (5, 15), while impairing the blood-flow in the adjacent wound edge when NPWT is applied with high-pressure values (16-18). Therefore, pressure values in the present study were set between 50 and 75 mmHg, which are relatively low-pressure values compared to that used for wound bed preparation prior to surgery. In addition, to avoid significant decrease in blood-flow and prevent collapse of the tiny vascular cavities in the PAT, the VAC® device should be used with low-pressure values. Negative pressure wound therapy with low-pressure values may be just as effective for vascular growth and excretion of redundant exudate as described in previous reports (16, 19). There were no significant differences in PAT and skin graft adaptation for the two pressure values (50 and 75 mmHg) in the present study.

According to a previous report describing PAT grafting of a 3 cm exposed Achilles tendon, the PAT did not take (14). Therefore, they concluded that exposed tendons with widths under 2 cm may have been successful as the PAT overlap would have been larger. However, they did not use PAT grafts on exposed tendons with NPWT. They only used PAT grafts with or without skin grafts. When using NPWT on exposed tendons, the PAT grafting should be extended because of the benefits to wound healing as mentioned above.

With respect to exposed bone ulcers, a previous report has suggested that grafting bone ulcers is more difficult than exposed tendon ulcers, even in cases of exposure widths as narrow as 1 cm (14). Although 2 of 4 cases with grafted PAT on an exposed bone were unsuccessful in that report, 4 of 4 cases were successful in our study where the skin grafts were overlaid on the PAT simultaneously. Our combined NPWT, PAT, and skin grafting procedure may not have been the only reason for success. Sufficient debridement on the exposed cortex until slight bleeding and the exposure of some degree of bone marrow may have also contributed. By exposing the bone marrow, which contains multipotent stem cells differentiated to macrophages, pericytes, and fibroblasts, revascularization into the PAT and wound healing was supposedly accelerated.

We experienced 2 cases of unsuccessful adaptation of the PAT or skin graft on exposed thick fascia. In 1 case, only the PAT adapted and the skin graft failed to adapt. Insufficient granulation tissue surrounding the fascia was supposedly one of the reasons, because immediate reconstruction had been performed after skin cancer ablation. In that case, revascularization to the grafted PAT may have been less than sufficient ; therefore, the PAT had not worked as a well-vascularized scaffold for the skin graft. The other case had both PAT and skin grafts that failed to adapt. The patient was malnourished due to disuse syndrome, and had an extended pressure ulcer with exposed thick fascia on the sacrum. It was difficult for him to maintain an off-load posture and the shear stress between the wound bed and the applied PAT or skin graft supposedly resulted in poor adhesion post-operatively. In addition, infected granulation also resulted in poor adhesion despite the sufficient surgical debridement and toileting performed during the operation. A common reason for STSG failure is infection and the presence of shear stress significantly reduces the success rate of STSG with traditional bolster dressings. Perioperative NPWT application to the STSG is one of the established methods to improve the success rate of STSG in cases with a contraindication to skin graft adaptation (20-22). Moreover, a temporal immobilization around the operation site with or without a plastic brace should be taken into consideration, even when applying the NPWT.

CONFLICT OF INTEREST

The authors have no financial interest in any medical device, product or procedure mentioned in this article.

This study was approved by the Research Ethics Board at Tokushima University and informed consent was obtained.

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