

# Negative-pressure wound therapy combined with artificial dermis (Terudermis) followed by split-thickness skin graft might be an effective treatment option for wounds exposing tendon and bone

## A retrospective observation study

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### Abstract

Skin grafts are not suitable for closing tendon- or bone-exposing wounds, which require flap surgery. Dermal regeneration templates have value for closing such wounds, but the disadvantages of the technique include implantation failures because of infection, hematoma formation, or inappropriate immobilization. Negative-pressure wound therapy was reported to increase graft acceptance in difficult wounds.

This retrospective case series of 65 patients evaluated negative-pressure therapy combined with artificial dermis for the treatment of acute or chronic tendon- or bone-exposing wounds. The artificial dermis was placed after adequate wound-bed preparation, with simultaneous application of a vacuum-assisted closure system. Split-thickness skin grafting was performed after the implanted artificial dermis had become established.

The overall success rate was 88.1% (59/67): 88.6% (39/44) in the chronic wounds group and 87% (20/23) in the acute-trauma group separately. The overall mean survival time of artificial dermis in success cases was  $13.24 \pm 7.14$  days. In separately, the survival time of artificial dermis had no statistically difference in chronic wound group ( $13.64 \pm 7.53$  vs  $12.60 \pm 5.86$ ,  $P = .943$ ), but had significant statistical difference in acute trauma group ( $12.45 \pm 6.44$  days vs  $23.33 \pm 4.04$  days,  $P = .018$ ). Also, comorbidity of PAOD was found a strong risk factor of failure in chronic wound group (100% vs 23.1%,  $P < 0.001$ ).

We concluded that artificial dermis combined with negative-pressure therapy followed by split-thickness skin grafting might be a reliable and effective option for surgical reconstruction of tendon- or bone-exposing wounds, and could decreasing waiting periods of autologous skin graft.

**Abbreviations:** AEBT = area of exposed bone and tendon, CAD = coronary artery disease, CHF = congestive heart failure, CKD = chronic kidney disease, CVA = cerebral vascular accident, DM = diabetes mellitus, ESRD = end-stage renal disease, HTN = hypertension, PAOD = peripheral arterial occlusive disease, STSG = split thickness skin graft, TG = time of granulation, TST = times for survival of Terudermis, VHD = valvular heart disease.

**Keywords:** artificial dermis, negative-pressure wound therapy, tendon and bone exposed wounds, terudermis, vacuum-assisted closure

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## 1. Introduction

The concept of a reconstructive ladder to achieve adequate closure of wounds was proposed using a stepladder approach from simple to complex procedures. Autograft healing is dependent on sufficient microcirculation from the underlying connective tissue layers; thus, skin grafts are not suitable to cover exposed bony or tendinous structures. The processes required to create healthy granulation tissue overlying tendons and bone are often time-consuming and not always successful. Therefore, flap surgery remains the most commonly used technique to close wounds that expose tendon or bone<sup>[1-7]</sup>

The value of dermal regeneration templates such as artificial dermis for trauma, burns, and oncological reconstruction has been demonstrated<sup>[7-13]</sup> and could be an alternative method for reconstruction in patients who are not suitable for flap surgery. However, most types of artificial dermis require a second-stage skin graft, with a 2~4 weeks waiting period, and still have a lower acceptance rate because of mechanical weakness, infection, or formation of hematoma or seroma.<sup>[14]</sup> Several studies have reported that negative-pressure wound therapy (NPWT) accelerated the incorporation of Integra over the wound bed,<sup>[6,15,16]</sup> but few studies have investigated the use of Terudermis (Terumo

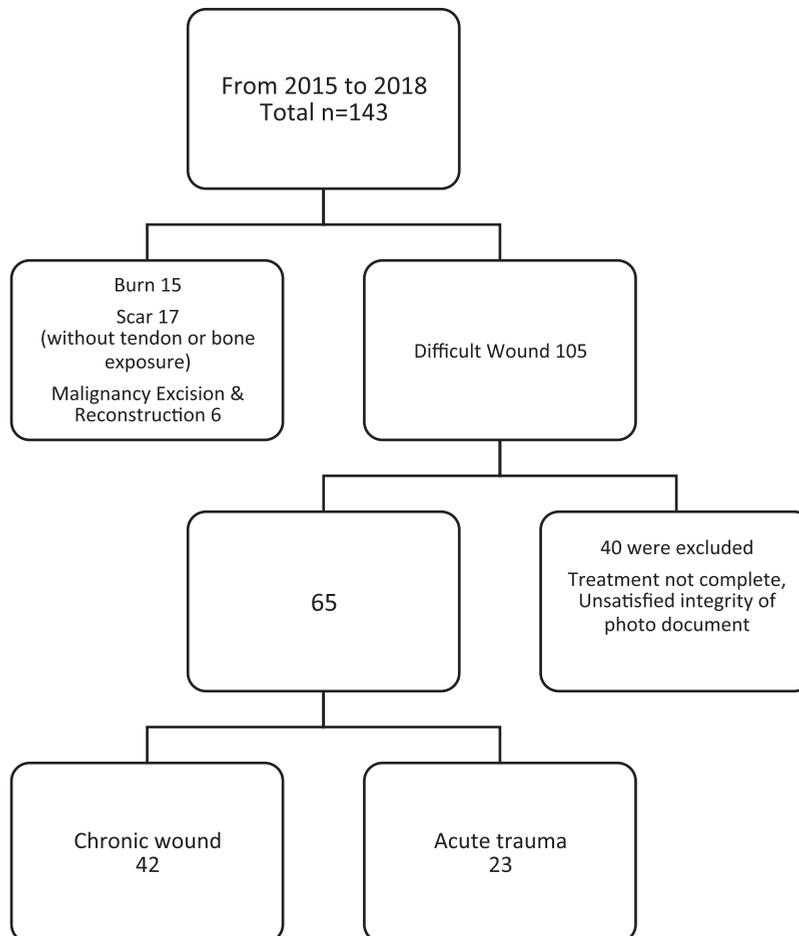
Corp., Tokyo, Japan), a product commonly used in Japan and in our hospital.

The purpose of this article is to report our experiences with NPWT combined with artificial dermis (Terudermis) in the treatment of acute or chronic wounds with exposed tendinous and bony structures, and retrospectively to analyze the clinical efficacy of this method as an alternative to flap surgery for reconstructing such complex soft-tissue wounds.

## 2. Materials and methods

From 2015 to 2018, we used artificial dermis 182 times in 143 patients at the Division of Plastic and Reconstructive Surgery, Department of Surgery, Tri-Service General Hospital. We retrospectively reviewed the photographs of the surgeries and the medical records of 65 patients including 20 females and 45 males ranging in age from 3 to 86 years, who had 67 tendon- or bone-exposing wounds that were treated with Terudermis artificial dermis (Fig. 1). A successful clinical outcome was defined as good acceptance 14 days after skin grafting.

All tendon- or bone-exposing wounds were debrided several times until no nonviable tissue remained. The time to granulation (TG) was defined as the interval between the last active



**Figure 1.** From 2015 to 2018, total 143 patients, with 182 times artificial dermis were used at Division of Plastic and Reconstructive Surgery, Department of Surgery, Tri-Service General Hospital. We retrospectively reviewed the patient's operation pictures, and medical records, 65 patients including 20 females and 45 males, age ranged from 3 to 86 years, with 67 tendon or bone exposure wounds which treated with Terudermis artificial dermis were included in the study.

debridement and the application of artificial dermis. Survival time of Terudermis (TST) was defined as the time from Terudermis application to the time of skin graft or the next application of artificial dermis. For cases who required repeated artificial dermis application, the TST was counted together for each application of artificial dermis. Placement of artificial dermis (slit-fenestrated or manually fenestrated Terudermis) occurred after adequate wound-bed preparation and meticulous hemostasis. Staples were used for fixation, and NPWT (vacuum-assisted closure [VAC] KCI Inc., San Antonio, TX) was applied over the silicone layer, at a pressure between 75 and 125 mmHg depending on clinical considerations and the patient's tolerance: pressure was decreased in patients with low tolerance of pain. The NPWT system was changed twice a week for disinfection and wound-bed observation. As soon as the implanted artificial dermis had changed to a fresh-pink or red color indicating the formation of a neodermis, the outer silicone layer was removed, and STSGs of varying thickness (8/1000–10/1000 inches) were applied.

Patient data pertaining to sex, age, area of exposed bone and tendon (AEBT), TG, TST, and medical comorbidities, including diabetes mellitus (DM), peripheral arterial occlusive disease (PAOD), end-stage renal disease (ESRD), hypertension (HTN), coronary artery disease (CAD), cerebral vascular accident (CVA), dyslipidemia, congestive heart failure (CHF), valvular heart disease (VHD), and chronic kidney disease (CKD) were analyzed. Data were analyzed using IBM SPSS 20.0 software (IBM Corp., Armonk, IL). Continuous variables were expressed as means and standard deviations, whereas frequencies and percentages were calculated for category variables. Outcome comparisons (success versus fail) were assessed using the Mann–Whitney test and  $\chi^2$  test.

This study was performed according to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by our Institutional Review Board (Ethics Committee No. 2–106-05-040). The patients provided informed consent for the publication of this report.

### 3. Results

#### 3.1. Study characteristics and outcome

A total of 67 wounds were included in the analysis of this study, with 70.1% being male ( $n_T=47$ ) and 29.9% female ( $n_T=20$ ) (Table 1). Patients were categorized according to comparison groups of chronic wound ( $n_T=44$ ) and acute wound ( $n_T=23$ ). The age of the study cohort range from 3–88 years, with mean age was  $53.46 \pm 20.8$  years, with much elderly in chronic wound group than in acute wound group ( $60.25 \pm 16.25$  vs  $40.48 \pm 22.66$ ,  $P < .01$ ). The overall AEBT was  $15.71 \pm 16.91$  cm<sup>2</sup>; TG was  $8.19 \pm 7.38$  days; and TST was  $13.64 \pm 7.20$  days. There was no significance statistically difference between chronic and acute group in these 3 parameters. About the outcome, the overall success rate was 88.1% (59/67): 88.6% (39/44) in the chronic wounds group and 87% (20/23) in the acute-trauma group separately; there was no significant statistical difference between 2 groups. The prevalence of comorbidities was also analyzed. DM occurred more commonly at a rate of 81.8% in the chronic group, in comparison with 21.7% in the acute group, with a significant difference ( $P < .001$ ). Also, PAOD was more common with 31.8% in chronic group, compare with 4.3% in acute group, with a significant difference ( $P < .05$ ). The other comorbidities were having no statistical difference between 2 groups.

**Table 1**

**Study Characteristics of separately group and outcome.**

	Chronic ( $n_T=44$ ) n (%) / Mean $\pm$ SD	Acute ( $n_T=23$ ) n (%) / Mean $\pm$ SD	Overall ( $n_T=67$ ) n (%) / Mean $\pm$ SD
sex			
Male	30 (68.2)	17 (73.9)	47 (70.1)
Female	14 (31.8)	6 (26.1)	20 (29.9)
Age*	$60.25 \pm 16.25$	$40.48 \pm 22.66$	$53.46 \pm 20.80$
AEBT	$16.02 \pm 17.30$	$15.11 \pm 16.49$	$15.71 \pm 16.91$
TG	$9.20 \pm 7.74$	$6.26 \pm 6.36$	$8.19 \pm 7.38$
TST	$13.52 \pm 7.31$	$13.87 \pm 7.16$	$13.64 \pm 7.20$
Outcome	39 (88.6)	20 (87.0)	59 (88.1)
Comorbidity			
DM**	36 (81.8)	5 (21.7)	41 (61.2)
HTN	17 (38.6)	5 (21.7)	22 (32.8)
PAOD***	14 (31.8)	1 (4.3)	15 (22.4)
CAD	10 (22.7)	1 (4.3)	11 (16.4)
ESRD	5 (11.4)	1 (4.3)	6 (9.0)
Dyslipidemia	6 (13.6)	0	6 (9)
Old CVA	5 (11.4)	0	5 (7.5)
CHF	3 (6.8)	0	3 (4.5)
VHD	3 (6.8)	0	3 (4.5)
CKD	3 (6.8)	0	3 (4.5)
ESRD+CKD	8 (18.2)	1 (4.3)	9 (13.4)

AEBT=area of exposed bone and tendon, CAD=coronary artery disease, CHF=congestive heart failure, CKD=chronic kidney disease, CVA=cerebral vascular accident, DM=diabetes mellitus, ESRD=end-stage renal disease, HTN=hypertension, n=numbers of patients,  $n_T$ =numbers of wounds, PAOD=peripheral arterial occlusive disease, TG=time of granulation, TST=times for survival of terudermis, VHD=valvular heart disease.

\*  $P < .01$ .

\*\*  $P < .001$ .

\*\*\*  $P < .05$ .

#### 3.2. Comparison of outcome in overall result

When cases were divided into success and failure group (Table 2), there was no statistically difference in sex and age of these 2 groups. The AEBT was  $15.31 \pm 15.71$  cm<sup>2</sup> in success versus  $18.66 \pm 25.26$  cm<sup>2</sup> in failure group; TG was  $7.98 \pm 7.54$  days in success versus  $9.75 \pm 6.23$  days in failure group; and TST was  $13.24 \pm 7.14$  days in success versus  $16.63 \pm 7.43$  days in failure group. All of 3 parameters have no significant statistically difference amongst success and failure group. When regarding the comorbidity prevalence, there were no significant differences between success and failure cases, except PAOD, which is higher in the failure group (75% vs 15.3%,  $P < .001$ ).

#### 3.3. Comparison of outcome in chronic and acute wound group separately

There was no statistical difference in sex and age between success and failure cases in these 2 groups (Table 3). In chronic-wound group, the largest successfully reconstructed AEBT was 80 cm<sup>2</sup>, and mean successful reconstructed AEBT was  $17.17 \pm 18.06$  cm<sup>2</sup>, but the parameters of AEBT, TG, and TST have no statistically significant difference among success and failure cases. The comorbidity prevalence of PAOD is higher in the failure group (100% vs 23.1%,  $P < .001$ ). Of 5 patients with failed treatments of chronic wounds, 2 underwent below-knee amputation, one a local flap, one a toe amputation, and one underwent free-flap coverage. In the acute-trauma group, the largest successfully reconstructed AEBT was 31.5 cm<sup>2</sup>; there were significant statistical difference of AEBT ( $11.68 \pm 8.97$  cm<sup>2</sup> vs  $38.00 \pm$

**Table 2**  
Compares of outcome in overall result.

	Success (n <sub>T</sub> =59)	Fail (n <sub>T</sub> =8)	P
	n (%) / Mean ± SD	n (%) / Mean ± SD	
Sex*			1.000
Male	41 (69.6)	6 (75.0)	
Female	18 (30.4)	2 (25.0)	
Age†	52.29 ± 21.10	62.13 ± 17.14	.134
AEBT†	15.31 ± 15.71	18.66 ± 25.26	.854
TG†	7.98 ± 7.54	9.75 ± 6.23	.354
TST†	13.24 ± 7.14	16.63 ± 7.43	.135
Comorbidity			
DM	34 (57.6)	7 (87.5)	.215
HTN	20 (33.9)	2 (25.0)	.919
PAOD	9 (15.3)	6 (75.0)	.001
CAD	9 (15.3)	2 (25.0)	.850
ESRD	5 (8.5)	1 (12.5)	1.000
Dyslipidemia	6 (10.2)	0	.775
Old CVA	5 (8.5)	0	.889
CHF	3 (5.1)	0	1.000
VHD	3 (5.1)	0	1.000
CKD	2 (3.4)	1 (12.5)	.796
ESRD + CKD	7 (11.9)	2 (25.0)	.638

AEBT=area of exposed bone and tendon, CAD=coronary artery disease, CHF=congestive heart failure, CKD=chronic kidney disease, CVA=cerebral vascular accident, DM=diabetes mellitus, ESRD=end-stage renal disease, HTN=hypertension, n=numbers of patients, n<sub>T</sub>=numbers of wounds, PAOD=peripheral arterial occlusive disease, TG=time of granulation, TST=times for survival of terudermis, VHD=valvular heart disease.

\*  $\chi^2$  Test.

† Mann-Whitney test.

36.39 cm<sup>2</sup>, P=.046) and TST (12.45 ± 6.44 days vs 23.33 ± 4.04 days, P=.018) between success and failure cases. The TG (5.30 ± 6.11 days vs 12.67 ± 4.51 days, P=.060) was no statistically difference. Also, there were no significant differences of

comorbidity prevalence between success and failure cases. One of the 3 failed trauma cases underwent wound closure with a pedicled muscle flap combined with STSG, and the other 2 cases underwent free anterolateral thigh flap coverage. All of the patients were followed up for 3 to 24 months. During and at the end of follow-up, the skin grafts had good color and a soft texture.

**3.4. Case reports**

**3.4.1. Case 01.** A 65-year-old man with underlying diabetes mellitus and PAOD developed necrotizing fasciitis of his left lower leg (Fig. 2A). He had received a series of debridements resulting in a large area of soft-tissue defect and was transferred to our hospital for further treatment. Subsequent wound cultures revealed *Peptostreptococcus magnus* and *Acinetobacter baumannii* infection. After serial debridement surgeries and 1 percutaneous transluminal angioplasty of the leg, the wound area was approximately 20 × 7 cm with a relatively clean wound base and an area of exposure of the extensor tendon of approximately 20 × 4 cm (Fig. 2B). NPWT was applied over the clean wound base, and Terudermis (slit-drainage type) was applied 3 days later; the grafted area was 10 × 10 cm (Fig. 2C). A second Terudermis application was performed 26 days later because granulation tissue had not grown over the exposed tendon (Fig. 2D, E). An autologous STSG (0.010 inches thick and mesh 1:1.5) was grafted onto the whole well-granulated wound base (Fig. 2F, G). The NPWT was continued for 4 days for STSG fixation, and the skin engrafted well and healed within the following 10 days (Fig. 2H).

**3.4.2. Case 02.** A 45-year-old man with diabetes mellitus developed a chronic ulcer over his right plantar region that was complicated by methicillin-resistant *Staphylococcus aureus*

**Table 3**  
Compares of outcome in chronic and acute wound group separately.

	Chronic			Acute		
	Success (n <sub>T</sub> =39)	Fail (n <sub>T</sub> =5)	P	Success (n <sub>T</sub> =20)	Fail (n <sub>T</sub> =3)	P
	n (%) / Mean ± SD	n (%) / Mean ± SD		n (%) / Mean ± SD	n (%) / Mean ± SD	
Sex*			1.000			.690
Male	27 (69.2)	3 (60.0)		14 (70.0)	3 (100.0)	
Female	12 (30.8)	2 (40.0)		6 (30.0)	0	
Age†	59.21 ± 16.71	68.40 ± 9.63	.230	38.80 ± 22.60	51.67 ± 24.09	.230
AEBT†	17.17 ± 18.06	7.05 ± 2.43	.347	11.68 ± 8.97	38.00 ± 36.39	.046
TG†	9.36 ± 7.91	8.00 ± 6.89	.471	5.30 ± 6.11	12.67 ± 4.51	.060
TST†	13.64 ± 7.53	12.60 ± 5.86	.943	12.45 ± 6.44	23.33 ± 4.04	.018
Comorbidity						
DM	31 (79.5)	5 (100)	.614	3 (15.0)	2 (66.7)	.203
HTN	16 (41.0)	1 (20.0)	.674	4 (20.0)	1 (33.3)	1.000
PAOD	9 (23.1)	5 (100)	.001	0	1 (33.3)	.262
CAD	9 (23.1)	1 (20.0)	1.000	0	1 (33.3)	.262
ESRD	5 (12.8)	0	.919	0	1 (33.3)	.262
Dyslipidemia	6 (15.4)	0	.801	0	0	—
Old CVA	5 (12.8)	0	.919	0	0	—
CHF	3 (7.7)	0	1.000	0	0	—
VHD	3 (7.7)	0	1.000	0	0	—
CKD	2 (5.1)	1 (20.0)	.764	0	0	—
ESRD + CKD	7 (17.9)	1 (20.0)	1.000	0	1 (33.3)	.262

AEBT=area of exposed bone and tendon, CAD=coronary artery disease, CHF=congestive heart failure, CKD=chronic kidney disease, CVA=cerebral vascular accident, DM=diabetes mellitus, ESRD=end-stage renal disease, HTN=hypertension, n=numbers of patients, n<sub>T</sub>=numbers of wounds, PAOD=peripheral arterial occlusive disease, TG=time of granulation, TST=times for survival of terudermis, VHD=valvular heart disease.

\*  $\chi^2$  Test.

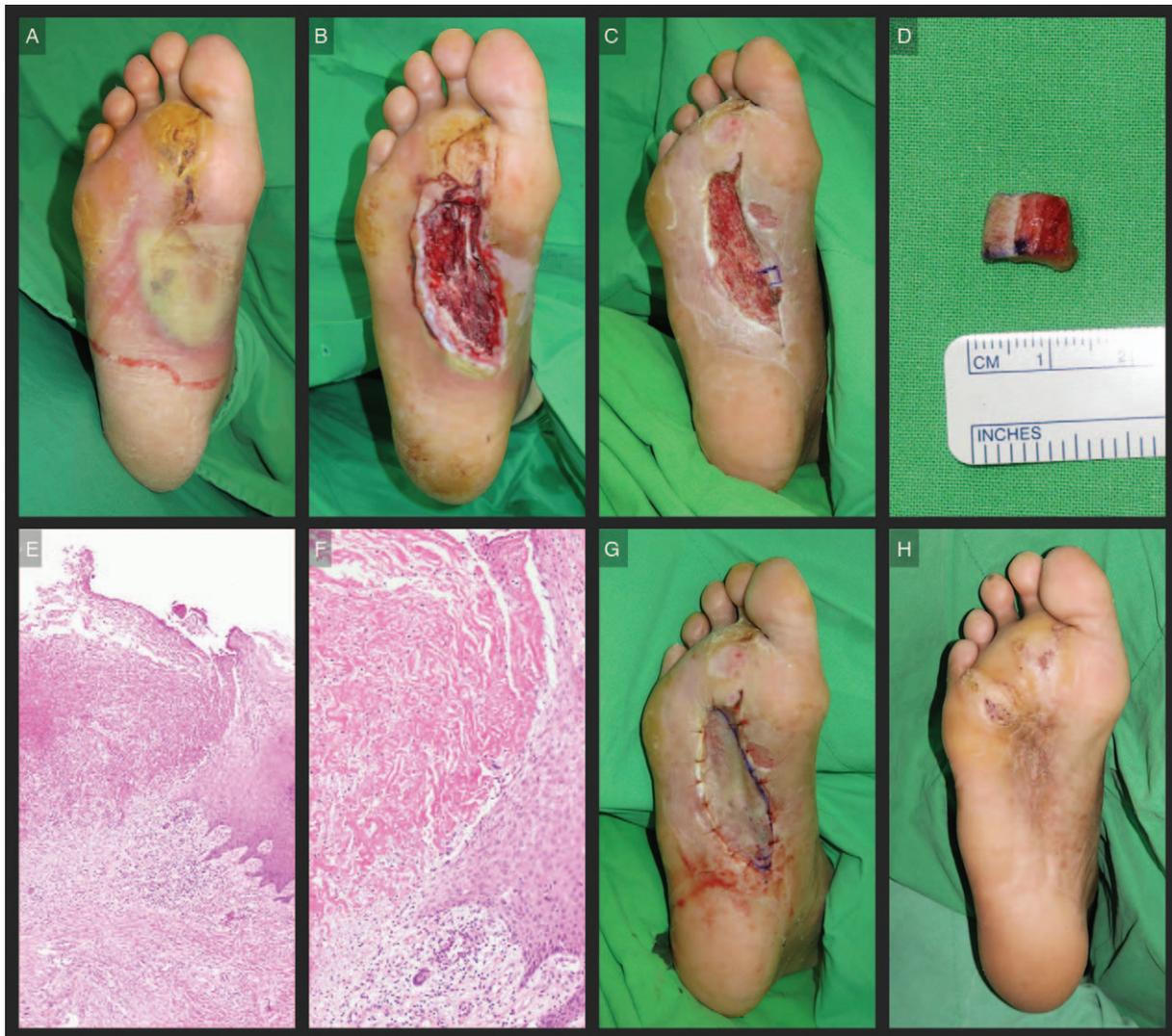
† Mann-Whitney test.



**Figure 2.** (Case 01) A 65-year-old male with diabetes foot complicated with necrotizing fasciitis of left lower leg. *Peptostreptococcus magnus* and *Acinetobacter baumannii* infection were identified by culture result. (A) After series of debridement, resultant a large area of soft tissue defect sized about  $20 \times 7$  cm, and extensor tendon exposure area about  $20 \times 4$  cm. (B) NPWT was applied over the clean wound base. (C) A slit drainage type Terudermis was applied over the healthy wound base, grafted area was  $10 \times 10$  cm. (D) Granulation grow into the artificial dermis could be visible during scheduled VAC system change. (E) Second time Terudermis application was 26 days after 1<sup>st</sup> Terudermis application. (F) Fresh granulation tissue grow over the exposed tendon was noted after 21 days of 2<sup>nd</sup> Terudermis application. (G) Split thickness skin graft, with 0.010 inches thick, mesh 1:1.5, was engrafted on well granulated whole wound base. The NPWT was continued use for STSG fixation for 4 days, and the autologous skin graft was taking well. (H) The autologous skin graft was healed within following 10 days. NPWT = negative-pressure wound therapy, VAC = vacuum-assisted closure.

infection and regional necrotizing fasciitis (Fig. 3A). After serial debridement and NPWT application until the wound was clean with early granulation, the wound base measured approximately  $9 \times 3$  cm (Fig. 3B). Terudermis (slit-drainage type) was applied over the area of the wound base because of an exposed flexor

tendon measuring approximately  $2 \times 1$  cm. On the 10th day after Terudermis application, an incisional biopsy covering the edge of the artificial dermis and the wound edge was performed (Fig. 3C, D). Histological examination of the artificial dermis confirmed complete neovascularization through the whole thickness of



**Figure 3.** (Case 02) A 45-year-old man with diabetes mellitus developed a chronic ulcer over his right plantar region that was complicated with regional necrotizing fasciitis (A). After serial debridement and NPWT application until the wound was clean with early granulation, the wound base measured approximately  $9 \times 3$  cm (B). Artificial dermis was applied over the area of the wound base because of an exposed flexor tendon measuring approximately  $2 \times 1$  cm. On the 10th day after artificial dermis application, an incisional biopsy covering the edge of the artificial dermis and the wound edge was performed (C, D). Histological examination of the artificial dermis confirmed complete neovascularization through the whole thickness of artificial dermis (E, F). An autologous STSG was performed on the same day (G), and the graft healed well over the following 14 days. At the 4-year postsurgical follow-up, the grafted area had healed well with no hypertrophic scarring and no skin breakdown (H). NPWT = negative-pressure wound therapy, STSG = split thickness skin graft.

artificial dermis (Fig. 3E, F). An autologous STSG (0.010 inches thick) was performed on the same day (Fig. 3G), and the graft healed well over the following 14 days. At the 4-year postsurgical follow-up, the grafted area had healed well with no hypertrophic scarring and no skin breakdown (Fig. 3H).

#### 4. Discussion

Terudermis (Terumo Corp., Tokyo, Japan) is an artificial skin composed of collagen sponge reconstituted from heat-denatured bovine dermal type 1 collagen that is cross-linked by dehydrothermal treatment, compare with Integra Dermal Regeneration Template (Integra LifeSciences Corp., Plainsboro, NJ) consists of bovine tendon type 1 collagen and shark chondroitin-6-sulphate glycosaminoglycan that is bonded to a silicone

pseudoepidermis.<sup>[10,12,17]</sup> Terudermis is dry, spongy, and white sheet, with thickness and pore size of 3 mm and approximately  $100 \mu\text{m}$ ; whereas Integra is wet, gelatinous, and translucent, with the thickness and pore size of 2 mm and 70 to  $200 \mu\text{m}$ .<sup>[17]</sup> There was no head to head study investigating the result of graft skin quality, durability, and vascularization difference between Terudermis and other dermal substitute (such as Integra) on the human. However, in wound contraction and scar formation, Terudermis showed the none-inferior result than the other dermal substitute in animal modal.<sup>[17]</sup> Previous histoengineering study showed that the optimal pore size was in the range 20 to  $125 \mu\text{m}$  for cells to penetrate into the scaffold and bind to the ligands present on the surface of the scaffold.<sup>[18,19]</sup> This may strengthen that Terudermis is a reliable dermal substitute on clinical usage. The development of dermal regeneration templates has reduced

the need for flap surgery, a more aggressive and complicated procedure. However, patients usually need a second-stage operation with skin grafting, with a 2~4 weeks' waiting period; only AlloDerm can be applied in a 1-stage operation with simultaneous STSG over the wound bed.<sup>[20,21]</sup>

NPWT had been reported could accelerated the incorporation of artificial dermis on the wound bed, also known as vacuum-assisted closure, provides a controlled continuous or intermittent subatmospheric pressure was reported could accelerated the incorporation of artificial dermis Integra,<sup>[15]</sup> AlloDerm,<sup>[20]</sup> Terudermis,<sup>[10]</sup> and Pelnac<sup>[10,16]</sup> over the wound bed. They showed that NPWT could help to increase the rate of graft acceptance in difficult wounds, but these series only have few cases with exposed tendon and bone. We used NPWT dressing on the fenestrated artificial dermis to speed the rate and success of revascularization over the tendon and bone exposed wound bed, with an overall success rate of 88.1% (59/67): 88.6% (39/44) in the chronic wounds group and 87% (20/23) in the acute-trauma group separately. Our successful rate is higher than previous literature reported by Yeong et al<sup>[6]</sup> with successful rate of 82% in overall, 63% in the chronic ulcer, 88% in the acute wounds, which did not use the NPWT simultaneously.

The other major concern regarding the use of artificial skin is the waiting period. Dermal substitutes are generally known to become vascularized within 2 to 4 weeks and eventually remodel into a dermal equivalent, after which an ultrathin autograft can be placed over the neodermis.<sup>[6,22,23]</sup> Moiemenn et al demonstrated their surgical protocol of Integra implantation, with autologous skin was grafted 4 weeks after Integra application.<sup>[24,25]</sup> Ko et al successfully placed an STSG over the exposed tibia 14 to 18 days after Terudermis placement,<sup>[26]</sup> and Zhang et al reported successful engraftment over the bone or tendon exposed wound by applying Pelnac and NPWT simultaneously, with average waiting period of 14 days.<sup>[16]</sup> In our series, autologous engraftment could be accomplished within 2 weeks (overall TST  $13.64 \pm 7.20$  days, with overall successful rate = 88.6%), less than 2 to 3 weeks recommended by the manufacturer, and was more rapid than previous reports of artificial dermis use in tendon- and bone-exposing wounds with or without NPWT.<sup>[6,7,23,27,28]</sup>

According to statistically result, in the acute-trauma group, the AEBT and TST had statistically difference between success and failure cases. In traumatous patient, most of the wound was caused by mangled injury or open fracture. The larger of the AEBT means larger area of trauma, which caused the devascularization of bone and tendon within the affected area, and we hypothesize this may prolong the time of wound bed granulation formation (TG, TST). Perhaps these parameters could be used as a cutting point to determine the trauma patient needs to undergo weather artificial dermis reconstruction or other treatment. This requires further in-depth research.

The statistical result also revealed that the prevalence of PAOD is higher in the failure cases, especially in chronic wound group. The successful reconstruction with artificial dermis accompanied with autologous skin graft demand vascularized wound bed and viable granulation tissue grew over the exposed bone and tendon. This underlying PAOD condition may cause lack of vascularized viable soft tissue over wound bed, and thereby, caused reconstruction failure. Most of the chronic wound also accompanied with infection, that need more times to prepare a healthy wound bed. Also, the patient with chronic wound also had more comorbidity, especially diabetes millets, peripheral

arterial occlusive disease, which may extended the time of wound healing or granulation formation.

To our knowledge, our study is the largest case series to combine the use of Terudermis and NPWT. Our study suggests that the use of NPWT with Terudermis decreased the engraftment period and accelerated reconstruction. These findings support the concept that a certain amount of NPWT contributes to the beneficial effects of artificial dermis and skin engraftment over complex wound beds. However, the overall financial cost of wound-care products should also be considered.

## 5. Conclusion

This large case series evaluating the use of Terudermis artificial dermis for wound treatment showed that it is not inferior to other dermal regeneration templates. The limitation is that our report is based on a retrospective cohort; many factors that influence wound healing might be a study bias, such as patient infection and nutritional status, which means that our findings are not final and further studies should be conducted. Despite this, our findings suggest that this technique may provide an alternative reconstruction option for wounds in which tendon and bone are exposed that avoids the donor-site morbidity following the free-flap transfer. In addition, the combination of artificial dermis with NPWT could accelerate artificial dermis granulation, decrease waiting periods, simplify any required secondary surgery, and produce excellent functional and aesthetic results. Therefore, artificial dermis (Terudermis) combined with NPWT followed by STSG might be a reliable and effective option for surgical reconstruction of difficult wounds and should be applied more widely in clinical situations.

## Author contributions

K.-F. H. contributed to the literature search, data collection, data interpretation and writing. Y.-L. C. contributed to data statistical analysis. H.-Y. C. and C.-Y. C. contributed to the literature search, data interpretation. T.-S. C., H.-H. L., C.-K. C. and C.-J. W. contributed to figure collection and formatting. Y.-J. P contributed to pathology exam and reporting. C.-T. L., C.-H. W., N.-T. D. and S.-G. C share their cases data and critical revision. Y.-S. T. contributed to the study conception, design, and editing. We also thank our nursing staff who provided expertise in managing patients with artificial dermis.

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