

WOUND CARE



Adjuvant Use of Acoustic Pressure Wound Therapy for Treatment of Chronic Wounds

A Retrospective Analysis

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PURPOSE: Small studies have indicated that the addition of acoustic pressure wound therapy (APWT) to conventional wound care may hasten healing of chronic wounds. We evaluated our early clinical experience using APWT as an adjunct to conventional wound care.

DESIGN: The study was a retrospective chart review of consecutive patients receiving APWT in addition to conventional wound care in a hospital-based, primarily outpatient setting.

METHODS: Medical records of all patients treated with APWT between August 2006 and October 2007 were reviewed. Analysis included the 41 patients with 52 wounds who received APWT at least 2 times per week during the study period. Statistical comparisons were made for wound dimensions, tissue characteristics, and pain at start versus end of APWT.

RESULTS: Thirty-eight percent of wounds (N = 20) healed completely with a mean 6.8 weeks of APWT. Median wound area and volume decreased significantly (88% [$P < .0001$] and 100% [$P < .0001$], respectively) from start to end of APWT. The proportion of wounds with greater than 75% granulation tissue increased from 26% (n = 12) to 80% (n = 41) ($P < .0001$), and normal periwound skin increased from 25% (n = 13) to 54% (n = 28) ($P = .0001$). Presence of greater than 50% fibrin slough decreased from 50% (n = 24) to 9% (n = 4) of wounds ($P = .006$).

CONCLUSIONS: This early experience supplementing conventional wound care with APWT suggests it may promote healing in chronic wounds, where the ordered cellular and molecular processes leading to healing have stalled.

Introduction

As a considerable source of morbidity, disability, and an increased mortality, chronic wounds have a substantial impact on both patient quality of life and healthcare costs.¹ By some estimates, the annual incidence of chronic wounds in the United States is between 5 million and 7 million, with annual costs for care of these wounds exceeding \$20 billion.¹ Furthermore, the potential for complications, such as infection, depression, limb amputation, and mor-

tality, gives way to a host of additional costs both financial and psychosocial.^{2,3}

The ability to successfully treat chronic wounds in an outpatient setting has implications for quality of life and cost. Due to increased costs commonly associated with inpatient care and the risk of hospital-acquired infection,^{4,5} wound care modalities that are safe and effective for use in the outpatient setting are quite valuable, particularly given the long healing times typical of chronic wounds. Eligibility for outpatient care of a chronic wound is also largely dependent on patient factors (ie, comorbid conditions and transportation issues that may preclude outpatient care) and wound characteristics (ie, wound type and/or size and location). In addition, outpatient care requires that the patient be able to perform the required self-care or has assistance available through family, friends, or home care. In some cases, reliable transportation to and from a clinic for regular visits is also needed.

A noncontact, nonthermal form of therapeutic ultrasound that operates at low intensity (maximum 1.7 W/cm²) and low frequency (40 kHz) was introduced in 2001 and is FDA-approved to promote wound healing in chronic wounds. The clinician should be aware that this therapy differs significantly from traditional diathermy ultrasound applications (eg, fetal monitoring and musculoskeletal therapy), which utilizes high frequencies (1-3 MHz). This acoustic pressure wound therapy (APWT)

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is FDA-indicated to promote wound healing through cleansing and maintenance debridement by removing yellow slough, fibrin, tissue exudates, and bacteria. APWT is easily administered at a wound care facility, generally 3 times per week for approximately 3 to 5 minutes at each visit; it is intended as a supplement to standard moist dressings, other modalities for wound bed preparation, specific care based on wound etiology, and nutritional supplementation as needed.

Clinicians have reported using APWT to painlessly debride wounds of slough and eschar and to promote development of healthy granulation tissue.⁶⁻⁸ In randomized clinical trials, APWT has been associated with improvements in the proportion of wounds healed when compared to conventional wound care for recalcitrant diabetic foot ulcers⁹ and lower-extremity wounds complicated by chronic critical limb ischemia.¹⁰ Results of an *in vitro* experiment suggest that APWT may not only remove bacteria along with slough and eschar but also destroy the cell walls of several bacterial organisms that commonly infect chronic wounds.¹¹ The study reported here is a retrospective evaluation of our early experience using APWT in a hospital-based wound clinic that treats primarily chronic wounds in a patient population that is approximately 75% outpatient. In our practice, APWT is primarily used as a means to augment and possibly accelerate the wound-healing cascade via germ load reduction and promotion of new granulation tissue. It is our practice to start with sharp debridement and moist wound-healing principles for a patient's first wound, provided the wound is not particularly severe or complicated by comorbid conditions associated with impaired wound healing. For more severe or medically complex cases, or in the case of a subsequent wound in a patient previously treated with conventional wound care, we administer advanced wound-healing modalities, including APWT, negative pressure wound therapy, external pneumatic compression, nonthermal infrared, pulsed lavage with suction, and total contact casing.

■ Methods

Study Population

This study was a retrospective chart review of consecutive patients who presented to our center for outpatient wound care between August 2006 and October 2007 and were treated with APWT as an adjunct to conventional wound care.

Patients were considered for this analysis if they had been treated with APWT during the study period and met the study eligibility criteria. Eligible patients were 18 years and older with a nonhealing wound of any etiology who had received APWT to the wound a minimum of 2 times per week during the study period. Nonhealing wounds were those that had failed to progress with at least 15% closure in the prior 2 weeks of therapy. Ineligible patients were those who received APWT less than 2 times per week

or had a life expectancy less than 6 months. Patients who were ineligible for APWT included those with a known contraindication to this therapy: those with an electronic implant/prosthesis near the treatment site (eg, near or over the heart or thoracic area in a patient with a cardiac pacemaker), pregnant patients whose treatment site was on the lower back or over the pregnant uterus, and patients whose wound was complicated by malignancy. In general, contraindications for use of any ultrasonic device would also include use on epiphyseal plates of children.

The study protocol was approved by the Institutional Review Board (IRB) for Park Nicollet Institute. Charts were included and reviewed only for patients who gave general consent in their electronic medical record according to IRB policy and approval.

Data Collection

Patient records were reviewed to collect data on medical history, physical examinations (height, weight, vital signs), history and etiology of the treated wound, wound dimensions, tissue and exudate characteristics, wound care modalities administered, dressings applied, and patient-reported pain scores using the visual analog scale (VAS) (0 = no pain, 10 = extreme pain). For APWT, treatment time (minutes per session), frequency (number of times per week), and duration of treatment (number of weeks) were recorded, as well as total number of treatments.

Study Treatments

Conventional wound care consisted of dressings that promote moist wound healing, modalities for wound bed preparation, that is, removal of necrotic tissue and reduction of bacterial loads to below critical colonization, nutritional education and supplementation, and interventions specific to wound etiology (ie, offloading for pressure ulcers and diabetic foot ulcers).

The APWT device (MIST Therapy System, Celleration, Inc, Eden Prairie, Minnesota) delivers low-frequency (40 kHz) ultrasound energy to the wound bed via a fine, sterile, saline mist. There is no direct contact between the device and the wound tissue. The biophysical effects of low-frequency ultrasound on cellular processes related to wound healing have been described previously.¹² Per the manufacturer's treatment algorithm, treatment times range from 3 to 20 minutes for wound areas ranging from less than 10 to 180 cm². APWT was administered 2 to 3 times per week until wound size was reduced to a maximum of 1 cm². Dressings that maintained moist wound healing and minimal wound bed disruption were continued until complete epithelialization.

Study Assessments

The primary effectiveness endpoint was the percentage change in wound area from the start of APWT to the end of APWT. Wound area was measured as either the greatest length times the greatest width that is perpendicular to the

length or using a head-to-toe anatomical orientation measuring the length from 12:00 to 6:00 and the perpendicular width from 3:00 to 9:00, unless otherwise noted for obvious obliques. Percentage change in wound area from the beginning to the end of APWT was calculated as $[(\text{beginning area} - \text{ending area})/(\text{beginning area})] \times 100$. The primary safety endpoint was the proportion of patients experiencing treatment-related adverse events during the study period. Secondary endpoints included changes in pain ratings and wound tissue characteristics and exudation from beginning to end of APWT.

Statistical Analysis

For this retrospective chart review, consecutive patients treated with APWT in addition to conventional wound care during a prespecified study period were reviewed against the inclusion criteria to determine eligibility. Formal power calculations to determine sample size were not performed. Descriptive statistics were performed to describe patient and wound characteristics at the start and the end of APWT treatment. Paired comparisons between baseline and end of treatment were made using the Wilcoxon Signed Rank test for continuous variables and McNemar's test for categorical variables. Statistical analyses were performed using SAS Version 9.1.3 (SAS Institute Inc, Cary, North Carolina).

Results

Patient and Treatment Characteristics

Between August 2006 and October 2007, 41 patients were treated with APWT as an adjunct to conventional wound care at least 2 times per week. APWT was administered a mean 2.5 times per week (range: 2.0-3.0 times) for a mean 3.7 minutes per session (range: 2.0-6.7 minutes). During the course of this study, patients received APWT for a mean 7.6 weeks (range: 2-18 weeks), with no treatment-related adverse events.

As shown in Table 1, most patients were women and Caucasian. Mean age was 65 years. Most patients had comorbid cardiovascular, vascular, or musculoskeletal disorders. Disorders of the integumentary, gastrointestinal, pulmonary, and neuropsychologic systems were also common.

Wound Characteristics

Eight of the 41 patients in this study had multiple wounds, resulting in a total of 52 wounds treated with APWT. Wound characteristics are shown in Table 2. Prior to initiating APWT, wounds had been present for a median 8 weeks. A substantial difference between mean and median values for baseline wound dimensions was observed. Along with the wide range of wound dimensions, this disparity between mean and median reflects a wound population skewed by a few very large wounds. The smaller 50% of the wounds had baseline area between 0 and 3.29 cm²,

TABLE 1.

Patient Characteristics at the Start of APWT

Characteristics	Patients (N = 41), % (n/N)
Women	59 (24/41)
Mean age (y; range)	65 (25-90)
Race	
Caucasian	93 (38/41)
Asian	5 (2/41)
Black/African American	2 (1/41)
Smoking (current)	10 (4/40)
Cardiovascular/vascular disorder	82 (32/39)
Hematologic disorder	11 (4/36)
Neuro/psychological disorder	31 (12/39)
Pulmonary disease	32 (12/38)
Diabetes	27 (11/41)
Gastrointestinal disorder	39 (15/38)
Musculoskeletal disorder	64 (25/39)
Integumentary disorder	46 (18/39)
Genitourinary	28 (11/39)
Cancer	28 (10/36)

and the upper 50% of wounds had baseline area between 3.29 and 195 cm². The top 5 wounds had baseline areas of 195, 104, 85, 59, and 45 cm², respectively.

As shown in Table 2, most of the wounds in this study were located on the lower extremities. From an etiologic perspective, nonhealing surgical wounds and pressure ulcers comprised nearly half of the wound population.

Wound Healing

During the study period, 38% (N = 20) of wounds healed completely, with a mean time to healing of 6.8 weeks (range: 3.0 to 16.0 weeks). As shown in Figure 1, median wound area and volume decreased significantly during the APWT treatment period. The percent area reduction (median: 88%, mean: 60%, $P < .0001$) was statistically significant and reflects clinically significant improvements in wound area during APWT treatment. Similarly, the percent volume reduction (median: 100%, mean: 60%, $P < .0001$) was statistically and clinically significant. In order to assess the potential impact of individual patient factors on healing outcomes, we performed an analysis of the first wound in each patient (n = 41). Median percent reductions in wound area (86%, $P < .0001$) and volume (100%, $P < .0001$) were not substantially altered from the original analysis of all 52 wounds.

As shown in Table 3, improvements in wound tissue and exudates during APWT treatment are consistent with a healing response. The proportion of wounds with greater than 75% healthy granulation tissue increased significantly from 26% to 80% ($P < .0001$) after a mean

TABLE 2.

Wound Characteristics at the Start of APWT

Characteristics	Wounds (N = 52)
Mean/median chronicity in wk (SD) (range)	10.9 (8.0) (11.7) (1.0-72.0)
Mean/median wound area—cm ² (SD) (range)	17.3/3.3 (33.3) (0-195.0)
Mean/median wound volume—cm ³ (SD) (range)	17.2/1.5 (42.2) (0-220.7) (N = 48)
Location—% (n)	
Leg	40 (21)
Heel	8 (4)
Foot ^a	8 (4)
Sacrum	4 (2)
Buttock	12 (6)
Other ^b	29 (15)
Etiology—% (n)	
Pressure	21 (11)
Venous insufficiency	15 (8)
Arterial insufficiency	12 (6)
Surgery	27 (14)
Trauma	15 (8)
Other ^c	10 (5)

^aIncludes diabetic foot ulcer (1); foot (2); great toe (1).

^bOther locations: abdomen (4); ankle (4); back (4); panus (1); sternum (1); ischium (1).

^cOther etiologies: cellulitis (1); diabetic foot ulcer (1); diabetic leg ulcer (1); livedoid vasculopathy (2).

7.6 weeks of APWT treatment. Although eschar was present in only 3 wounds, it was eliminated by study end ($P = .39$). Fibrin slough, which was present in 83% of wounds, decreased significantly by study end ($P = .006$).

The 50% of wounds with greater than 50% fibrin slough at the start of APWT was reduced to 9% by study end. The amount of exudate was also significantly reduced ($P = .006$), such that the proportion of wounds with no exudate increased from 6% to 33%. Changes in type of exudate (ie, less purulent and/or serosanguineous drainage and more serous drainage) did not reach statistical significance, although it should be noted that paired data were available for only 9 patients. The proportion of wounds with normal periwound skin increased significantly from 25% before APWT to 54% at study end ($P = .0001$), with marked reductions observed for erythematous and edematous skin (Table 3). Undermining, tunneling, and odor (present in 12%-17% of wounds) were reduced at study end, although only the decrease in tunneling reached statistical significance ($P = .03$). Results from analysis of tissue characteristics and exudates in only the first wound for each patient ($N = 41$; not shown) did not differ substantially from the analysis of all wounds.

In post hoc analysis of wound infection ($n = 50$), the proportion of wounds with clinical signs of infection (ie, erythema beyond the border of the wound, glossy and slick appearance of the wound bed, increased pain, odor with dressing removal, and moderate to heavy exudates) decreased from 30% ($n = 15$) to 10% ($n = 5$) ($P = .01$). It is important to note that this study was not designed to evaluate infection and that wounds were not consistently cultured to identify bacterial organisms. Nonetheless, clinical evidence of infection decreased significantly after initiating APWT treatment.

Wound Pain

Paired data on patient-reported pain scores at start and end of APWT were available for 34 wounds (65%) and 26 patients (63%). In this paired analysis, pain scores decreased

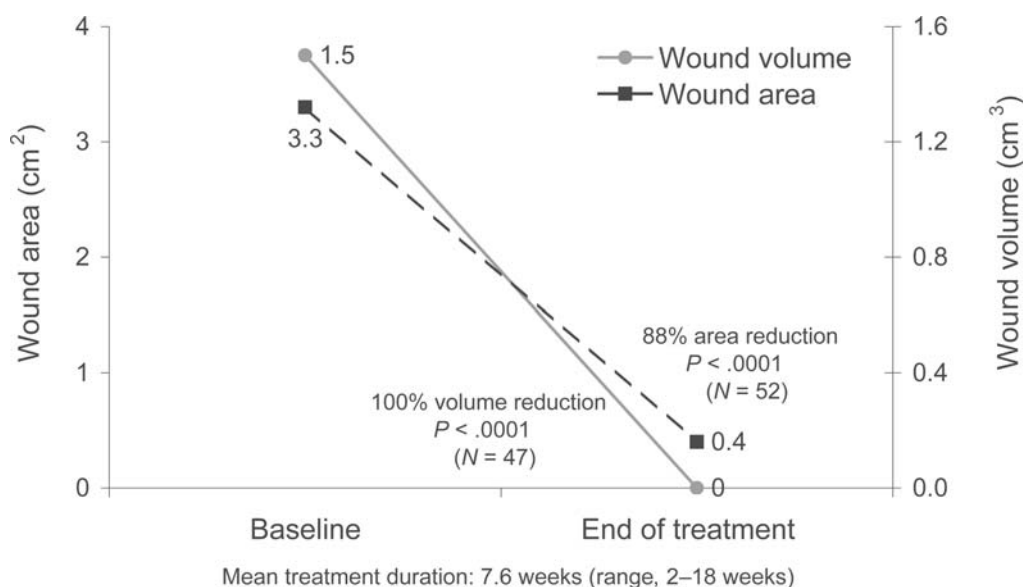


FIGURE 1. Median reduction in wound area and volume from start to end of APWT.

TABLE 3.

Tissue Characteristics and Drainage at Start and End of APWT

Characteristic	Baseline, % (n)	End of Treatment, % (n)	P ^a
Amount of healthy granulation tissue, N	46	51	<.0001 ^b
Complete closure	0	39 (20) ^c	
76%-99%	26 (12)	41 (21)	
51%-75%	17 (8)	8 (4)	
26%-50%	17 (8)	8 (4)	
1%-25%	22 (10)	4 (2)	
None	17 (8)	0	
Amount of eschar, N	46	44	.39
None	93 (43)	100 (44)	
<50%	0	0	
≥50%	7 (3)	0	
Amount of fibrin slough, N	48	45	.006
None	17 (8)	31 (14)	
<50%	33 (16)	60 (27)	
≥50%	50 (24)	9 (4)	
Amount of exudate, N	51	43	.006
None	6 (3)	33 (14)	
Scant	53 (27)	44 (19)	
Moderate	27 (14)	23 (10)	
Maximum	14 (7)	0	
Type of exudate, N	18	17	.26 ^d
Sanguineous	0	0	
Serous	22 (4)	47 (8)	
Serosanguineous	50 (9)	41 (7)	
Purulent	28 (5)	12 (2)	
Peri wound skin, N	52	52	
Normal	25 (13)	54 (28)	.0001 ^e
Irritation	4 (2)	6 (3)	
Erythematous	65 (34)	15 (8)	
Edematous	56 (29)	17 (9)	
Callus	2 (1)	4 (2)	
Other	33 (17) ^f	21 (11) ^g	
Undermining	17 (9/52)	8 (4/50)	.096
Tunneling	12 (6/52)	2 (1/49)	.03
Odor	14 (7/51)	4 (2/52)	.06
Maceration, N	50	49	
None	94 (47)	96 (47)	.26
Minimal	2 (1)	2 (1)	
Moderate	4 (2)	2 (1)	
Maximum	0	0	

^aMcNemar's Test.

^bComparison of greater than 75% granulation tissue at start versus end of treatment.

^cComplete closure based on "amount of granulation" data as reported for 51 patients. Overall closure rate based on "area equal to 0 cm²" is 38% (20/52).

^dPaired data for comparison of start versus end of treatment available for only 9 patients.

^eComparison of percent normal peri wound skin at start versus end of treatment.

^fOther = cool (2); dry skin (3); ecchymosis (1); hair loss (2); hemosiderin deposits (2); hyperpigmented (2); indurated (6); mottled (2); scaly (5); weepy (1). Note: categories of peri wound skin were not mutually exclusive.

^gOther = hemosiderin deposits (1); indurated (3); dry skin (1); epiboly (1); pigmented (1); scaly (3); scar (1).

by a mean 2.9 points per wound ($P < .0001$) on the 10-point VAS. Similarly, analysis of pain scores for only the first wound per patient yielded a mean pain score reduction of 3.1 points.

Discussion

In this retrospective chart review, nearly 40% of chronic, nonhealing wounds healed completely during the

designated study period with the addition of a mean 6.8 weeks of APWT to conventional wound care. Clinically and statistically significant reductions in median wound area and volume (88% and 100%, respectively) were accompanied by clinically and statistically significant increases in healthy granulation tissue and normal periwound skin as well as decreases in fibrin slough and exudate.

The stated indication for APWT—to promote wound healing through cleansing and maintenance debridement by removing fibrin, yellow slough, tissue exudates, and bacteria—suggests multifaceted effects on the wound-healing process. In keeping with the general maintenance debridement indication, we administered APWT as an adjunct to conventional wound care (ie, moist healing, wound bed preparation, and type-specific care) until the wound was near closure (approximately 1 cm²), after which we continued appropriate dressings and type-specific wound care until complete closure was achieved.

Regarding the removal of bacteria, an *in vitro* experiment by Kavros and Schenck¹¹ suggests that APWT may do more than remove bacteria from the wound bed. In that preliminary investigation, an apparent bactericidal effect was observed when APWT was applied to *Staphylococcus aureus*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant *Enterococcus*. Scanning and transmission electron micrographs showed destruction of cell walls in the organisms exposed to APWT compared with intact cell walls of the organisms exposed to a saline-drip control. In the current study, we observed a statistically significant reduction in clinical signs of infection from 30% of wounds before APWT to 10% of wounds after APWT ($P = .01$). With the caveats that this was a post hoc analysis in a study where wounds were not consistently cultured to identify bacterial organisms and concomitant treatment of infection was likely occurring, we propose that this decrease in clinical signs of infection may reflect a clinical manifestation of the bactericidal effect of APWT observed *in vitro*.

It is generally accepted that APWT does not cause pain. This feature makes it a unique debridement option as compared to sharp and mechanical debridement techniques, which frequently cause pain. In this study, APWT was associated with a reduction of nearly 3 points on the 10-point VAS. Our finding of pain reduction is consistent with the observations of Gehling and Samies,¹³ who reported a statistically significant 80% reduction (8.07 to 1.67, $P = .0007$, 95% confidence interval 5-7.56) in patient-reported VAS pain scores after 2 to 4 weeks of APWT in a retrospective analysis of 15 consecutive patients with lower-extremity wounds. Such reductions in patient-reported pain are clearly relevant to patient quality of life and may even have implications for reducing the need for narcotic pain medication. In the Gehling and Samies¹³ study, 5 patients discontinued narcotic pain medications within 2 weeks of starting APWT.

Our findings must be considered in light of inherent limitations in the study design. First, the retrospective de-

sign and lack of a control group do not allow for direct comparison of outcomes between APWT and other advanced wound-healing modalities or in a similar patient cohort without the use of APWT. Furthermore, the possibility that these wounds could have healed in a similar time frame without the addition of APWT cannot be excluded. Second, as is often the case in single-center wound care studies, the study population is small and yet relatively diverse in wound etiology, leaving the question of which wound types may benefit most from APWT unanswered. The results of this study do support other studies suggesting that APWT may contribute to healing of complex wounds. Previous studies have suggested that APWT may actually accelerate the healing process as compared to conventional wound care; Ennis and colleagues reported healing of 41% of recalcitrant diabetic foot ulcers in 12 weeks (compared with only 13% of controls) in a randomized, sham-controlled study of 55 patients⁹ and 69% of lower-extremity wounds in a mean 7 weeks in a series of 23 patients.¹⁴ The volume reduction in the current study is also relatively consistent with that reported by Kavros and Schenck¹¹ in a series of 51 lower-extremity ulcers of varied etiology (95% with APWT vs 37% with conventional wound care, $P < .0001$). In a randomized study of 70 lower-extremity ulcers complicated by chronic critical limb ischemia, the proportion of wounds with greater than 50% healing (as measured by wound volume) at 12 weeks was significantly greater with APWT added to conventional wound care than without (63% vs 29%, $P < .001$).¹⁰ This study does not permit us to draw such conclusions, since there was no control group; further study involving randomization and a control group is clearly indicated.

■ Summary

These early experiences using APWT as an adjuvant therapy to conventional wound care suggest that APWT may jump-start the healing of chronic wounds where the ordered cellular and molecular processes leading to healing have stalled. Given the billions of dollars spent annually for chronic wound care, including inpatient care and treatment of hospital-acquired infection, healing nearly 40% of these wounds in a mean 6.8 weeks of outpatient treatment represents a clinical success in chronic wound care. Larger, randomized studies are needed to directly compare the outcomes after APWT with those of other wound-healing modalities and further investigate which wound types might benefit most from this novel ultrasound therapy.

KEY POINTS

- ✓ Nearly 40% of chronic, nonhealing wounds healed completely during the study period with the addition of a mean 6.8 weeks of APWT to conventional wound care.

- ✓ Clinically and statistically significant reductions were observed in median wound area (88%) and volume (100%).
- ✓ Clinically and statistically significant increases were observed in healthy granulation tissue and normal periwound skin as well as decreases in fibrin slough and exudate.
- ✓ APWT was not associated with the treatment-related pain often reported with sharp and mechanical debridement. This study and one other suggest APWT may even alleviate wound pain.
- ✓ Further studies involving a control group and randomization are needed in order to clearly delineate the impact and role of APWT in chronic wound management.

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