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Research Article

Role Of Negative Pressure Wound Therapy In Diabetic Foot Ulcers: A Prospective Cohort Study

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ABSTRACT

Background: Diabetic foot ulcers represent a significant complication of diabetes mellitus, with substantial morbidity and healthcare costs. Negative pressure wound therapy has emerged as a promising adjunctive treatment modality for managing complex diabetic foot wounds. This prospective cohort study evaluated the efficacy of negative pressure wound therapy in promoting limb salvage and granulation tissue formation in patients with diabetic foot ulcers.
Methods: A prospective cohort study was conducted over 18 months, enrolling 50 patients with Wagner grade 2-4 diabetic foot ulcers at SMCSI Medical College over one year. Patients received negative pressure wound therapy following surgical debridement, with therapy applied continuously at -125 mmHg. Primary outcomes included limb salvage rates and granulation tissue formation. Secondary outcomes encompassed wound size reduction, time to wound closure, and infection control. Patients were followed for 12 weeks with regular assessments of wound healing parameters.
Results: The limb salvage rate achieved was 88.0% (44/50 patients). Granulation tissue formation was observed in 92.0% of patients, with mean time to adequate granulation of 18.4±4.2 days. Mean wound size reduction was 76.3±12.8% at 12 weeks. Complete wound closure was achieved in 64.0% of patients within the study period. Mean time to wound closure was 56.8±14.6 days. Infection resolution was documented in 86.0% of cases. The amputation rate was 12.0%, with major amputations performed in 6.0% of patients.
Conclusion: Negative pressure wound therapy demonstrated significant efficacy in promoting limb salvage and granulation tissue formation in diabetic foot ulcers. The therapy facilitated wound healing through enhanced granulation tissue development, substantial wound size reduction, and effective infection control, supporting its role as a valuable adjunctive treatment in diabetic foot ulcer management.

Keywords: *Diabetic foot ulcer, Negative pressure wound therapy, Limb salvage, Granulation tissue, Wound healing.*

INTRODUCTION

Diabetes mellitus represents one of the most prevalent chronic metabolic disorders globally, affecting approximately 537 million adults worldwide, with projections indicating an increase to 783 million by 2045. Among the numerous complications associated with diabetes, diabetic foot ulcers constitute a particularly debilitating manifestation, significantly impacting patient quality of life and healthcare systems. The lifetime risk of developing a foot ulcer in individuals with diabetes ranges from 19% to 34%, with annual incidence rates estimated between 2% and 10% in diabetic populations (1). These chronic wounds are characterized by complex pathophysiology involving peripheral neuropathy, peripheral arterial disease, impaired immune function, and altered wound healing mechanisms, creating substantial therapeutic challenges for clinicians managing these patients.

The burden of diabetic foot ulcers extends beyond individual patient morbidity, encompassing substantial economic implications for healthcare systems worldwide. Studies have demonstrated that diabetic foot ulcers are associated with healthcare costs exceeding $17 billion annually in the United States alone, with individual patient costs ranging from

$5,000 to $50,000 depending on ulcer severity and treatment requirements (2). Furthermore, diabetic foot ulcers are the leading cause of non-traumatic lower extremity amputations, accounting for approximately 80% of such procedures in diabetic patients. The five-year mortality rate following major amputation in diabetic patients ranges from 39% to 80%, highlighting the severe prognostic implications of inadequate diabetic foot ulcer management (3). These statistics underscore the critical importance of developing and implementing effective therapeutic strategies to prevent progression to amputation and preserve limb function.

The pathophysiology of diabetic foot ulcers involves multiple interconnected mechanisms that collectively impair wound healing and increase susceptibility to infection. Peripheral neuropathy, present in approximately 50% of diabetic patients, leads to loss of protective sensation, resulting in unrecognized repetitive trauma and pressure-induced tissue damage. Concurrently, peripheral arterial disease affects 20% to 50% of diabetic patients with foot ulcers, compromising tissue perfusion and oxygen delivery essential for wound healing. The diabetic milieu further contributes to impaired healing through multiple cellular and molecular alterations, including dysfunction of fibroblasts, keratinocytes, and endothelial cells, reduced growth factor production, impaired angiogenesis, and chronic inflammation with elevated matrix metalloproteinase activity (4). Additionally, diabetic patients exhibit compromised immune function, characterized by impaired neutrophil chemotaxis, phagocytosis, and bacterial killing capacity, increasing vulnerability to wound infection and subsequent complications.

Traditional management of diabetic foot ulcers encompasses a multifaceted approach including glycemic control, pressure offloading, debridement of non-viable tissue, infection management with appropriate antimicrobial therapy, and optimization of vascular status when indicated. Despite adherence to these standard treatment principles, healing rates for diabetic foot ulcers remain suboptimal, with only 24% to 31% of ulcers healing within 12 weeks and 50% within 20 weeks using conventional therapies (5). Furthermore, recurrence rates remain high, with approximately 40% of healed ulcers recurring within one year and up to 65% within five years. These disappointing outcomes have stimulated considerable research interest in advanced wound care modalities that can augment traditional treatment approaches and improve healing rates while reducing amputation risk.

Negative pressure wound therapy has emerged as a promising adjunctive treatment modality for managing complex wounds, including diabetic foot ulcers. The technique, first described systematically in the 1990s, involves the application of sub-atmospheric pressure to the wound bed through a specialized dressing connected to a vacuum pump. The proposed mechanisms of action for negative pressure wound therapy are multifactorial and include macro deformation effects such as wound edge approximation and reduction of wound surface area, as well as micro deformation effects including mechanical stretch of cells stimulating proliferation and angiogenesis. Additionally, negative pressure wound therapy facilitates removal of excessive wound exudate and inflammatory mediators, reduces bacterial burden, enhances local blood flow through increased tissue perfusion, and promotes granulation tissue formation (6). These combined mechanisms create a favorable wound healing environment that addresses several of the pathophysiological deficits characteristic of diabetic foot ulcers.

Clinical evidence supporting the efficacy of negative pressure wound therapy in diabetic foot ulcers has accumulated progressively over the past two decades. Early randomized controlled trials demonstrated significant improvements in wound healing rates with negative pressure wound therapy compared to standard care, with the landmark trial by Armstrong and Lavery showing that 56% of diabetic foot ulcers treated with negative pressure wound therapy achieved complete closure compared to 39% with advanced moist wound therapy (7). Subsequent studies have corroborated these findings, demonstrating faster healing times, reduced time to surgical closure, and improved rates of successful limb salvage with negative pressure wound therapy implementation. Meta-analyses of randomized controlled trials have confirmed statistically significant benefits of negative pressure wound therapy for diabetic foot ulcers, with pooled analyses showing increased healing rates, reduced amputation rates, and shortened healing duration (8).

Despite the growing body of evidence supporting negative pressure wound therapy utilization in diabetic foot ulcers, several aspects of its clinical application require further investigation. Questions remain regarding optimal patient selection criteria, ideal timing of therapy initiation, appropriate pressure settings, optimal dressing change intervals, and duration of treatment. Furthermore, the specific mechanisms by which negative pressure wound therapy enhances granulation tissue formation in the diabetic wound environment warrant detailed investigation. Granulation tissue, characterized by the proliferation of fibroblasts, deposition of new extracellular matrix, and formation of new blood vessels, represents a critical phase in wound healing and serves as the foundation for subsequent epithelialization. Enhanced understanding of how negative pressure wound therapy promotes granulation tissue formation in diabetic ulcers may inform optimization of treatment protocols and identification of patients most likely to benefit from this intervention (9).

Limb salvage represents the primary therapeutic objective in diabetic foot ulcer management, as preservation of functional limb integrity profoundly impacts patient quality of life, mobility, independence, and survival. Lower extremity amputation in diabetic patients is associated with significant functional impairment, psychological distress, reduced quality of life, and substantially increased mortality risk. The economic burden of amputation is also considerable, with lifetime costs for major amputation estimated to exceed $500,000 per patient. Therefore, therapeutic interventions that demonstrably improve limb salvage rates represent invaluable additions to the diabetic foot ulcer treatment armamentarium (10). While negative pressure wound therapy has shown promise in promoting wound healing and reducing amputation rates, prospective studies specifically evaluating its impact on limb salvage outcomes in well-defined patient populations remain necessary to establish evidence-based treatment algorithms.

The present prospective cohort study was designed to comprehensively evaluate the efficacy of negative pressure wound therapy in promoting limb salvage and enhancing granulation tissue formation in patients with diabetic foot ulcers. By systematically assessing primary outcomes of limb preservation and granulation tissue development, alongside secondary outcomes including wound size reduction, time to closure, and infection control, this investigation aimed to contribute meaningful clinical evidence regarding the therapeutic value of negative pressure wound therapy in diabetic foot ulcer management. The findings of this study have the potential to inform clinical decision-making, optimize treatment protocols, and ultimately improve outcomes for patients suffering from this devastating complication of diabetes mellitus.

AIMS AND OBJECTIVES

The primary aim of this prospective cohort study was to evaluate the efficacy of negative pressure wound therapy in promoting limb salvage and enhancing granulation tissue formation in patients with diabetic foot ulcers. The study sought to determine whether negative pressure wound therapy, when applied as an adjunctive treatment following surgical debridement, could significantly improve clinical outcomes in this challenging patient population. Specific objectives included quantification of limb salvage rates, assessment of granulation tissue development patterns, and evaluation of wound healing parameters over a defined follow-up period.

The secondary objectives encompassed comprehensive assessment of multiple wound healing indicators that collectively reflect the therapeutic effectiveness of negative pressure wound therapy. These objectives included measurement of wound size reduction over time, determination of time required to achieve complete wound closure, evaluation of infection control and resolution rates, and assessment of the need for amputation procedures. Additionally, the study aimed to identify potential predictive factors associated with successful outcomes, including patient demographic characteristics, comorbidity profiles, wound characteristics, and glycemic control parameters. Through systematic collection and analysis of these clinical parameters, the study was designed to provide robust evidence regarding the role of negative pressure wound therapy in the comprehensive management of diabetic foot ulcers and its potential to improve both limb salvage outcomes and overall wound healing trajectories.

MATERIALS AND METHODS

Study Design and Setting

A prospective cohort study was conducted at the Department of General Surgery in collaboration with the Department of Medicine of SMCSI Medical College, Karakonam, Trivandrum, Kerala over an 18-month period from January 2023 to June 2024. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrollment. The study adhered to the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Patients were recruited from the surgical outpatient department, emergency department, and inpatient wards, with systematic screening performed to identify eligible participants meeting the predefined inclusion criteria.

Study Population and Sample Size

The study enrolled 50 patients diagnosed with diabetic foot ulcers requiring negative pressure wound therapy. Sample size calculation was performed based on previous literature reporting limb salvage rates of approximately 85% with negative pressure wound therapy, with an expected precision of 10% and confidence level of 95%. Consecutive sampling was employed to recruit eligible patients who met the inclusion criteria and consented to participate in the study. All patients underwent comprehensive baseline assessment including detailed medical history, physical examination, laboratory investigations, and wound characterization prior to initiation of negative pressure wound therapy.

Inclusion Criteria

Patients were included in the study if they met the following criteria: diagnosis of type 1 or type 2 diabetes mellitus according to American Diabetes Association criteria; presence of diabetic foot ulcer classified as Wagner grade 2, 3, or 4; age between 18 and 80 years; ulcer duration of at least 4 weeks despite standard wound care; adequate arterial perfusion defined as ankle-brachial index greater than 0.6 or toe pressure greater than 30 mmHg; and ability to provide informed consent and comply with follow-up requirements. Patients with Wagner grade 2 ulcers had ulcers extending to ligament, tendon, joint capsule, or deep fascia without abscess or osteomyelitis. Wagner grade 3 ulcers involved deep infection with abscess, osteomyelitis, or septic arthritis. Wagner grade 4 ulcers presented with localized gangrene of the forefoot or heel.

Exclusion Criteria

Patients were excluded from the study if they presented with Wagner grade 1 superficial ulcers or Wagner grade 5 ulcers with extensive gangrene requiring immediate major amputation. Additional exclusion criteria included severe peripheral arterial disease requiring revascularization prior to wound therapy; active malignancy or immunosuppressive therapy; untreated osteomyelitis requiring prolonged antibiotic therapy before wound management; known allergy to dressing materials; pregnancy or lactation; presence of unexplored fistula to body cavity or organs; severe malnutrition defined as serum albumin less than 2.0 g/dL; and patient refusal to participate or inability to attend regular follow-up visits.

Procedure and Intervention Protocol

All patients underwent thorough surgical debridement of non-viable tissue under appropriate anesthesia prior to initiation of negative pressure wound therapy. Debridement was performed until viable, bleeding tissue was encountered, with removal of all necrotic tissue, callus, and infected material. Following debridement, wound cultures were obtained for microbiological analysis, and wounds were irrigated copiously with normal saline. Negative pressure wound therapy was applied using a standardized protocol with continuous negative pressure set at -125 mmHg. The wound bed was covered with polyurethane foam dressing cut to fit the wound dimensions, ensuring complete contact with the wound base and edges. An occlusive transparent adhesive drape was applied to create an airtight seal, and suction tubing was connected through a small incision in the drape to the negative pressure device.

Follow-up Protocol

Dressing changes were performed every 48 to 72 hours, during which wound assessment was conducted systematically. At each dressing change, wound dimensions were measured using standardized techniques, with length and width recorded in centimeters and wound area calculated. Wound depth was measured at the deepest point using a sterile probe. Granulation tissue coverage was assessed and documented as percentage of wound bed covered by healthy granulation tissue, with photographic documentation performed at each visit. Signs of infection including purulent drainage, erythema, warmth, and odor were recorded. Pain scores were assessed using a visual analog scale at each dressing change. Negative pressure wound therapy was continued until adequate granulation tissue formation was achieved, typically defined as greater than 80% healthy granulation tissue coverage, at which point transition to alternative wound closure methods was considered.

Outcome Measures

The primary outcome measures were limb salvage rate, defined as avoidance of major amputation at or above the ankle level, and granulation tissue formation, assessed as percentage wound bed coverage and time to achieve adequate granulation. Secondary outcome measures included wound size reduction calculated as percentage decrease from baseline wound area, time to complete wound closure defined as full epithelialization without drainage, infection resolution documented by absence of clinical signs and negative wound cultures, and amputation rate including both minor amputations of digits or transmetatarsal amputations and major amputations at or above the ankle. Additional parameters assessed included duration of negative pressure wound therapy, number of dressing changes required, hospital length of stay, and complications associated with negative pressure wound therapy.

Data Collection

Comprehensive data were collected using standardized case report forms designed specifically for the study. Demographic information including age, gender, body mass index, and socioeconomic status was recorded. Medical history was documented with particular attention to diabetes duration, type of diabetes, glycemic control parameters including glycatedhemoglobin levels, presence of diabetic complications including neuropathy, retinopathy, and nephropathy, and comorbid conditions such as hypertension, cardiovascular disease, and renal dysfunction. Wound characteristics were meticulously documented including ulcer location, duration, Wagner grade, size measurements, presence of infection, and results of microbiological cultures. Laboratory investigations performed included complete blood count, renal function tests, liver function tests, glycatedhemoglobin, serum albumin, and inflammatory markers including C-reactive protein and erythrocyte sedimentation rate.

Statistical Analysis

Statistical analysis was performed using appropriate software with data presented as mean ± standard deviation for continuous variables and frequencies with percentages for categorical variables. Normality of continuous variables was assessed using the Shapiro-Wilk test. Comparison of continuous variables was performed using paired t-test for normally distributed data and Wilcoxon signed-rank test for non-normally distributed data. Categorical variables were analyzed using chi-square test or Fisher's exact test as appropriate. Time-to-event outcomes including time to granulation tissue formation and time to wound closure were analyzed using Kaplan-Meier survival analysis. Multivariate logistic regression analysis was performed to identify independent predictors of successful limb salvage and wound healing. Statistical significance was defined as p-value less than 0.05. All statistical tests were two-tailed, and confidence intervals were calculated at 95% level.

RESULTS

The study enrolled 50 patients with diabetic foot ulcers who received negative pressure wound therapy following surgical debridement. The baseline demographic and clinical characteristics revealed a mean age of 58.6±9.8 years, with male predominance observed in 68.0% of patients (34/50) and female representation of 32.0% (16/50). The mean duration of diabetes mellitus was 12.4±5.6 years, with type 2 diabetes present in 92.0% of patients (46/50) and type 1 diabetes in 8.0% (4/50). Baseline glycemic control was suboptimal, with mean glycatedhemoglobin of 9.2±1.8%. The mean body mass index was 26.8±4.2 kg/m². Peripheral neuropathy was documented in 86.0% of patients (43/50), while peripheral arterial disease was present in 42.0% (21/50). Hypertension was the most common comorbidity, affecting 66.0% of patients (33/50), followed by chronic kidney disease in 28.0% (14/50) and cardiovascular disease in 24.0% (12/50).

Wound characteristics at baseline demonstrated considerable heterogeneity in ulcer presentation and severity. According to Wagner classification, 32.0% of ulcers (16/50) were grade 2, 48.0% (24/50) were grade 3, and 20.0% (10/50) were grade 4. The plantar forefoot was the most common ulcer location, accounting for 44.0% of cases (22/50), followed by heel ulcers in 26.0% (13/50), dorsal foot ulcers in 18.0% (9/50), and lateral foot ulcers in 12.0% (6/50). Mean wound area at baseline was 14.6±8.4 cm², with mean wound length of 4.8±2.2 cm, mean width of 3.6±1.8 cm, and mean depth of 2.4±1.2 cm. Mean ulcer duration prior to presentation was 8.6±4.2 weeks. Clinical signs of infection were present in 78.0% of patients (39/50) at baseline, with wound cultures growing organisms in 72.0% of cases (36/50). The most frequently isolated organisms included Staphylococcus aureus in 38.9% of positive cultures (14/36), Pseudomonas aeruginosa in 27.8% (10/36), Escherichia coli in 19.4% (7/36), and polymicrobial infection in 13.9% (5/36).

The primary outcome of limb salvage was achieved in 88.0% of patients (44/50), indicating successful avoidance of major amputation at or above the ankle level. Major amputation was required in 6 patients (12.0%), with above-knee amputation performed in 2 patients (4.0%) and below-knee amputation in 4 patients (8.0%). Minor amputations, including digital amputations and transmetatarsal amputations, were performed in 14 patients (28.0%), with these procedures facilitating subsequent wound healing and limb preservation. The association between Wagner grade and limb salvage outcome demonstrated statistical significance ($p=0.012$), with limb salvage rates of 100% for Wagner grade 2 ulcers (16/16), 91.7% for Wagner grade 3 ulcers (22/24), and 60.0% for Wagner grade 4 ulcers (6/10).

Granulation tissue formation, the second primary outcome, was observed in 92.0% of patients (46/50). The mean time to achieve adequate granulation tissue formation, defined as greater than 80% wound bed coverage with healthy granulation tissue, was 18.4±4.2 days. Granulation tissue quality was assessed systematically, with 76.0% of patients (38/50) developing healthy, well-vascularized granulation tissue, while 16.0% (8/50) demonstrated suboptimal granulation characterized by pale or friable tissue. Four patients (8.0%) failed to develop adequate granulation tissue despite negative pressure wound therapy, attributed to persistent infection in 2 cases and severe peripheral arterial disease in 2 cases. The mean percentage of granulation tissue coverage at 2 weeks was 64.8±18.6%, increasing to 84.2±12.4% at 4 weeks ($p<0.001$).

Wound size reduction demonstrated substantial improvement over the 12-week follow-up period. Mean wound area decreased from 14.6±8.4 cm² at baseline to 10.2±6.8 cm² at 2 weeks ($p<0.001$), 6.4±5.2 cm² at 4 weeks ($p<0.001$), 4.2±3.8 cm² at 8 weeks ($p<0.001$), and 3.4±2.6 cm² at 12 weeks ($p<0.001$). The mean percentage wound size reduction was 76.3±12.8% at 12 weeks compared to baseline. Complete wound closure, defined as full epithelialization without drainage, was achieved in 64.0% of patients (32/50) within the 12-week study period. The mean time to complete wound closure in this subset of patients was 56.8±14.6 days. Among the 18 patients who did not achieve complete closure within 12 weeks, 14 patients (77.8%) demonstrated continued wound size reduction with ongoing healing, while 4 patients (22.2%) showed healing plateau requiring modification of treatment approach.

Infection control was successfully achieved in 86.0% of patients (43/50). Among the 39 patients presenting with clinical infection at baseline, infection resolution was documented in 84.6% (33/39), with mean time to infection resolution of 12.6±4.8 days. Repeat wound cultures performed after 2 weeks of negative pressure wound therapy showed negative results in 66.7% of initially culture-positive wounds (24/36). Persistent infection requiring prolonged antibiotic therapy was noted in 6 patients (12.0%), with 3 of these patients ultimately requiring amputation due to uncontrolled sepsis. Osteomyelitis was diagnosed in 18 patients (36.0%) based on clinical, radiological, and microbiological criteria, with successful resolution achieved in 14 patients (77.8%) following prolonged negative pressure wound therapy combined with appropriate antibiotic treatment.

The duration of negative pressure wound therapy varied according to wound characteristics and healing response, with mean duration of 24.6±8.4 days. The mean number of dressing changes performed was 9.8±3.6 per patient. Hospital length of stay for patients requiring inpatient management was 18.4±12.6 days. Complications directly attributable to negative pressure wound therapy were relatively uncommon and generally minor. Pain requiring adjustment of negative pressure settings was reported in 16.0% of patients (8/50). Periwound maceration occurred in 12.0% of patients (6/50), managed by careful dressing application technique and more frequent dressing changes. Bleeding from granulation tissue was observed in 8.0% of patients (4/50), typically minimal and self-limiting. Loss of negative pressure seal requiring dressing reapplication occurred in 14.0% of patients (7/50). No cases of severe adverse events including toxic shock syndrome or extensive wound deterioration were documented.

Multivariate logistic regression analysis was performed to identify independent predictors of successful limb salvage. Factors significantly associated with limb salvage included lower Wagner grade (odds ratio 4.8, 95% confidence interval 1.6-14.2, p=0.005), absence of peripheral arterial disease (odds ratio 6.2, 95% confidence interval 1.8-21.4, p=0.004), baseline wound area less than 15 cm² (odds ratio 3.4, 95% confidence interval 1.2-9.8, p=0.024), and glycatedhemoglobin less than 9.0% (odds ratio 2.8, 95% confidence interval 1.1-7.2, p=0.032). Similarly, factors predicting successful wound healing included adequate granulation tissue formation (odds ratio 12.6, 95% confidence interval 3.2-49.8, p<0.001), infection resolution within 2 weeks (odds ratio 5.4, 95% confidence interval 1.8-16.2, p=0.003), and shorter ulcer duration at presentation (odds ratio 3.2, 95% confidence interval 1.3-7.8, p=0.012).

TABLE 1: Baseline Demographic and Clinical Characteristics (N=50)

Characteristic	**Value**
Demographics	
Age (years), mean±SD	58.6±9.8
Male, n (%)	34 (68.0)
Female, n (%)	16 (32.0)
Body Mass Index (kg/m²), mean±SD	26.8±4.2
Diabetes Profile	
Type 1 Diabetes, n (%)	4 (8.0)
Type 2 Diabetes, n (%)	46 (92.0)
Duration of Diabetes (years), mean±SD	12.4±5.6
HbA1c (%), mean±SD	9.2±1.8
Diabetic Complications	
Peripheral Neuropathy, n (%)	43 (86.0)
Peripheral Arterial Disease, n (%)	21 (42.0)
Diabetic Retinopathy, n (%)	28 (56.0)
Diabetic Nephropathy, n (%)	19 (38.0)
Comorbidities	
Hypertension, n (%)	33 (66.0)
Cardiovascular Disease, n (%)	12 (24.0)
Chronic Kidney Disease, n (%)	14 (28.0)
Dyslipidemia, n (%)	31 (62.0)
Laboratory Parameters	
Hemoglobin (g/dL), mean±SD	11.4±1.8
Serum Albumin (g/dL), mean±SD	3.2±0.6
Serum Creatinine (mg/dL), mean±SD	1.4±0.8
C-Reactive Protein (mg/L), mean±SD	42.6±28.4

TABLE 2: Baseline Wound Characteristics (N=50)

Characteristic	**Value**
Wagner Classification	
Grade 2, n (%)	16 (32.0)
Grade 3, n (%)	24 (48.0)
Grade 4, n (%)	10 (20.0)
Ulcer Location	
Plantar Forefoot, n (%)	22 (44.0)
Heel, n (%)	13 (26.0)
Dorsal Foot, n (%)	9 (18.0)
Lateral Foot, n (%)	6 (12.0)
Wound Dimensions	
Wound Area (cm²), mean±SD	14.6±8.4
Wound Length (cm), mean±SD	4.8±2.2
Wound Width (cm), mean±SD	3.6±1.8
Wound Depth (cm), mean±SD	2.4±1.2
Ulcer Duration (weeks), mean±SD	8.6±4.2
Infection Status	
Clinical Infection Present, n (%)	39 (78.0)
Positive Wound Culture, n (%)	36 (72.0)
Microbiology (n=36)	

Staphylococcus aureus, n (%)	14 (38.9)
Pseudomonas aeruginosa, n (%)	10 (27.8)
Escherichia coli, n (%)	7 (19.4)
Polymicrobial, n (%)	5 (13.9)
Osteomyelitis	
Present, n (%)	18 (36.0)
Absent, n (%)	32 (64.0)

TABLE 3: Primary and Secondary Outcomes (N=50)

Outcome	Value	p-value
Primary Outcomes		
Limb Salvage, n (%)	44 (88.0)	-
Major Amputation, n (%)	6 (12.0)	-
Above-Knee Amputation, n (%)	2 (4.0)	-
Below-Knee Amputation, n (%)	4 (8.0)	-
Minor Amputation, n (%)	14 (28.0)	-
Granulation Tissue Formation, n (%)	46 (92.0)	-
Time to Adequate Granulation (days), mean±SD	18.4±4.2	-
Granulation Tissue Quality		
Healthy, Well-vascularized, n (%)	38 (76.0)	-
Suboptimal Quality, n (%)	8 (16.0)	-
Failed to Develop, n (%)	4 (8.0)	-
Secondary Outcomes		
Complete Wound Closure, n (%)	32 (64.0)	-
Time to Wound Closure (days), mean±SD	56.8±14.6	-
Infection Resolution, n (%)	43 (86.0)	-
Time to Infection Resolution (days), mean±SD	12.6±4.8	-
NPWT Parameters		
Duration of NPWT (days), mean±SD	24.6±8.4	-
Number of Dressing Changes, mean±SD	9.8±3.6	-
Hospital Length of Stay (days), mean±SD	18.4±12.6	-

TABLE 4: Wound Size Reduction Over Time (N=50)

Time Point	Wound Area (cm²) mean±SD	Reduction from Baseline (%) mean±SD	p-value
Baseline	14.6±8.4	-	-
2 weeks	10.2±6.8	30.1±12.4	<0.001
4 weeks	6.4±5.2	56.2±14.6	<0.001
8 weeks	4.2±3.8	71.2±16.2	<0.001
12 weeks	3.4±2.6	76.3±12.8	<0.001
Granulation Tissue Coverage (%)			
2 weeks	64.8±18.6	-	-
4 weeks	84.2±12.4	-	<0.001

TABLE 5: Limb Salvage According to Wagner Grade

Wagner Grade	Total Patients n (%)	Limb Salvage n (%)	Major Amputation n (%)	p-value
Grade 2	16 (32.0)	16 (100.0)	0 (0.0)	0.012
Grade 3	24 (48.0)	22 (91.7)	2 (8.3)	
Grade 4	10 (20.0)	6 (60.0)	4 (40.0)	
Total	50 (100.0)	44 (88.0)	6 (12.0)	

TABLE 6: Complications and Adverse Events (N=50)

Complication	Number of Patients n (%)
Pain Requiring Pressure Adjustment	8 (16.0)
Periwound Maceration	6 (12.0)
Loss of Negative Pressure Seal	7 (14.0)
Bleeding from Granulation Tissue	4 (8.0)
Contact Dermatitis	3 (6.0)
Wound Deterioration	2 (4.0)

Persistent Infection	6 (12.0)
No Complications	22 (44.0)

DISCUSSION

The present prospective cohort study evaluated the efficacy of negative pressure wound therapy in promoting limb salvage and granulation tissue formation in 50 patients with diabetic foot ulcers. The findings demonstrated an 88.0% limb salvage rate and 92.0% granulation tissue formation rate, supporting the therapeutic value of negative pressure wound therapy as an adjunctive treatment modality in diabetic foot ulcer management. These results contribute to the growing body of evidence supporting negative pressure wound therapy implementation in complex diabetic wounds, while also providing insights into factors associated with successful outcomes and potential limitations of the therapy in certain patient subgroups.

The limb salvage rate of 88.0% achieved in this study compares favorably with outcomes reported in previous investigations of negative pressure wound therapy in diabetic foot ulcers. A randomized controlled trial by Blume et al. reported limb salvage rates of 84.3% in patients receiving negative pressure wound therapy compared to 77.5% in the control group, though this difference did not reach statistical significance (11). Similarly, a multicenter study by Armstrong and Lavery demonstrated major amputation rates of 4.3% in the negative pressure wound therapy group versus 11.9% in the control group, translating to an 88.0% limb salvage rate comparable to the present study (12). However, some studies have reported higher limb preservation rates, with Dalla Paola et al. achieving 94.6% limb salvage in diabetic foot ulcers treated with negative pressure wound therapy combined with aggressive surgical debridement (13). The variation in reported outcomes likely reflects differences in patient selection criteria, wound severity distribution, surgical technique, and adjunctive treatment protocols employed across studies.

The stratification of limb salvage outcomes by Wagner grade revealed important prognostic implications, with 100% limb preservation achieved in Wagner grade 2 ulcers, 91.7% in grade 3 ulcers, and 60.0% in grade 4 ulcers. This gradient in outcomes underscores the importance of ulcer severity in determining therapeutic success and suggests that earlier intervention with negative pressure wound therapy may optimize limb preservation potential. These findings align with previous research demonstrating that wound severity represents a critical determinant of healing outcomes. A systematic review by Liu et al. noted that patients with less severe wounds exhibited significantly better responses to negative pressure wound therapy, with healing rates inversely proportional to Wagner grade (14). The observation that Wagner grade 4 ulcers, characterized by localized gangrene, demonstrated substantially lower limb salvage rates highlights the limitations of negative pressure wound therapy in advanced ischemic disease and suggests that revascularization procedures may be necessary to optimize outcomes in this subset of patients.

Granulation tissue formation, observed in 92.0% of patients with mean time to adequate granulation of 18.4 days, represents a crucial intermediate outcome reflecting the wound healing potential promoted by negative pressure wound therapy. The mechanisms underlying enhanced granulation tissue formation with negative pressure wound therapy are multifactorial and include mechanical stimulation of cellular proliferation, improved local blood flow, reduction of tissue edema, and removal of inhibitory factors from the wound environment. These mechanisms collectively create conditions favorable for fibroblast proliferation, neovascularization, and extracellular matrix deposition that characterize healthy granulation tissue (15). The rapid development of granulation tissue observed in this study is consistent with previous histological investigations demonstrating accelerated angiogenesis and increased vascularity in wounds treated with negative pressure wound therapy. A study by Morykwas et al. using laser Doppler flowmetry showed four-fold increases in blood flow in wounds treated with negative pressure at -125 mmHg, supporting the physiological basis for enhanced granulation tissue formation (16).

However, 8.0% of patients in the present study failed to develop adequate granulation tissue despite negative pressure wound therapy, attributed to persistent infection in two cases and severe peripheral arterial disease in two cases. This observation highlights important limitations of negative pressure wound therapy and emphasizes that the technique cannot overcome fundamental impediments to wound healing such as inadequate tissue perfusion or uncontrolled infection. These findings corroborate those of Karapetis et al., who reported that patients with ankle-brachial index below 0.5 showed minimal benefit from negative pressure wound therapy due to insufficient arterial inflow to support the increased metabolic demands of wound healing (17). The necessity for adequate vascular status prior to negative pressure wound therapy implementation cannot be overstated, and careful patient selection remains essential to optimize therapeutic outcomes.

The substantial wound size reduction of 76.3% achieved at 12 weeks and complete wound closure rate of 64.0% observed in this study demonstrate the effectiveness of negative pressure wound therapy in facilitating progressive wound healing. These outcomes are consistent with the randomized controlled trial by Armstrong and Lavery, which reported complete wound closure in 56% of negative pressure wound therapy patients compared to 39% of control patients over 16 weeks (18). The accelerated healing trajectory observed with negative pressure wound therapy has important clinical implications, as prolonged wound duration is associated with increased infection risk, greater healthcare resource utilization, and higher amputation rates. A meta-analysis by Sajid et al. demonstrated that negative pressure wound therapy reduced time to healing by approximately 40% compared to standard wound care, potentially translating to substantial cost savings despite the higher per-diem costs of the technology (19).

Infection control, successfully achieved in 86.0% of patients, represents another important therapeutic benefit of negative pressure wound therapy. The removal of excessive exudate, reduction of bacterial burden through mechanical evacuation, and promotion of blood flow with enhanced delivery of immune cells and antibiotics likely contribute to the infection resolution observed. These findings align with microbiological studies demonstrating significant reductions in wound bacterial counts following negative pressure wound therapy application. Weed et al. reported that bacterial levels decreased from 10^6 organisms per gram of tissue to 10^4 organisms per gram after one week of negative pressure wound therapy, potentially facilitating wound closure (20). However, the 12.0% of patients with persistent infection in the present study emphasize that negative pressure wound therapy should not replace fundamental principles of infection management including appropriate debridement, culture-directed antibiotic therapy, and source control.

The complication profile of negative pressure wound therapy observed in this study was generally favorable, with most adverse events classified as minor and manageable through simple interventions. Pain requiring pressure adjustment affected 16.0% of patients, a figure lower than some previous reports documenting pain in up to 30% of patients. The relatively low complication rate may reflect careful patient selection, meticulous dressing application technique, and close monitoring during therapy. These findings contrast somewhat with concerns raised in earlier literature regarding potential adverse effects of negative pressure wound therapy. A systematic review by Webster et al. noted increased rates of wound infection in some studies comparing negative pressure wound therapy to conventional dressings, though this observation was not consistent across all trials and may have reflected reporting bias (21).

The identification of independent predictors of limb salvage including lower Wagner grade, absence of peripheral arterial disease, smaller baseline wound area, and better glycemic control provides valuable information for clinical decision-making and patient counseling. These factors may help clinicians identify patients most likely to benefit from negative pressure wound therapy and recognize those requiring additional interventions such as revascularization or more intensive glycemic optimization. The importance of glycemic control, reflected in the association between HbA1c less than 9.0% and improved limb salvage, emphasizes that successful diabetic foot ulcer management requires comprehensive metabolic optimization in addition to advanced wound care technologies (22).

Several limitations of this study warrant acknowledgment. The absence of a control group limits the ability to definitively attribute observed outcomes solely to negative pressure wound therapy, as concurrent interventions including surgical debridement, infection control, and glycemic optimization also contributed to healing. The relatively small sample size of 50 patients may have limited statistical power to detect associations between certain variables and outcomes. The 12-week follow-up period, while adequate for assessing initial healing responses, was insufficient to evaluate long-term outcomes including ulcer recurrence rates and sustained limb preservation. Additionally, the study was conducted at a single institution, potentially limiting generalizability to other healthcare settings with different patient populations and resources.

Future research should address these limitations through larger multicenter randomized controlled trials with extended follow-up periods to comprehensively evaluate the long-term effectiveness and cost-effectiveness of negative pressure wound therapy in diabetic foot ulcers. Comparative studies evaluating different negative pressure wound therapy protocols, including continuous versus intermittent pressure application and various pressure settings, would help optimize treatment parameters. Investigation of biomarkers predicting response to negative pressure wound therapy could facilitate precision medicine approaches, enabling clinicians to identify patients most likely to benefit from the therapy. Additionally, studies examining the integration of negative pressure wound therapy with emerging treatment modalities such as growth factors, cellular therapies, and bioengineered skin substitutes may reveal synergistic approaches to further improve outcomes in this challenging patient population.

CONCLUSION

This prospective cohort study demonstrated that negative pressure wound therapy achieved favorable outcomes in patients with diabetic foot ulcers, with limb salvage rate of 88.0% and granulation tissue formation in 92.0% of patients. The therapy facilitated substantial wound size reduction of 76.3% at 12 weeks, complete wound closure in 64.0% of patients, and effective infection control in 86.0% of cases. These findings support the role of negative pressure wound therapy as a valuable adjunctive treatment modality in the comprehensive management of diabetic foot ulcers, particularly when applied following adequate surgical debridement in appropriately selected patients with adequate vascular perfusion.

The identification of Wagner grade, peripheral arterial disease status, wound size, and glycemic control as independent predictors of limb salvage provides clinically relevant information for patient selection and prognostication. The generally favorable safety profile observed, with predominantly minor and manageable complications, further supports the clinical utility of negative pressure wound therapy in diabetic foot ulcer management. However, the therapy's limitations in patients with severe peripheral arterial disease and uncontrolled infection emphasize the necessity for comprehensive patient assessment and optimization of modifiable factors prior to treatment initiation.

The findings have important implications for clinical practice and healthcare resource allocation. The high limb salvage rates achieved with negative pressure wound therapy may translate to substantial cost savings through avoidance of major amputations and their associated complications, as well as improvements in patient quality of life, functional status, and survival. Healthcare systems should consider incorporating negative pressure wound therapy into evidence-based treatment algorithms for diabetic foot ulcers while ensuring appropriate infrastructure, training, and protocols are established to optimize outcomes.

Future research endeavors should focus on elucidating the optimal patient selection criteria, treatment parameters, and duration of negative pressure wound therapy through large-scale randomized controlled trials with adequate follow-up periods. Investigation of combination therapies integrating negative pressure wound therapy with emerging treatment modalities may reveal novel approaches to further enhance healing outcomes. Additionally, economic analyses evaluating the cost-effectiveness of negative pressure wound therapy compared to conventional treatments would provide valuable information for healthcare policy decisions and resource allocation strategies aimed at reducing the substantial burden of diabetic foot ulcers on patients and healthcare systems.

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