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Limb Salvage In Severe Diabetic Foot Infection

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ABSTRACT

Background: **The purpose of our study was to determine the efficacy of a management algorithm that includes negative pressure wound therapy (NPWT) in diabetic feet with limb-threatening infection.** ***Materials and Methods:*** **Forty-five septic diabetic feet were treated with NPWT between 2006 and 2008. After emergent abscess evacuation, early vascular intervention was performed if necessary. Debridement, with or without partial foot amputation, was followed by NPWT. Wound progress was measured using a digital scanner. A limb was considered salvaged if complete healing was achieved without any or with minor amputation through or below the ankle. The mean followup after complete wound healing was 17 (range, 6 to 35) months.** ***Results:*** **Thirty-two cases (71%) were infected with two or more organisms. Negative pressure wound therapy was applied for 26.2 ± 14.3 days. The median time to achieve more than 75% wound area granulation was 23 (range, 4 to 55) days and 104 (range, 38 to 255) days to complete wound healing. Successful limb salvage was achieved in 44 cases (98%); 14 (31%) without any amputation and 30 (67%) with partial foot amputations. Total number of operations per limb was 2.4 ± 1.3. One case of repeated infection and necrosis was managed with a transtibial amputation. There were no complications associated with NPWT.** ***Conclusion:*** **This study provides the outcome of a management algorithm which includes NPWT in salvaging severely infected diabetic feet. With emergent evacuation of abscess, early vascular intervention and appropriate debridement, NPWT can be a useful adjunct to the management of limb-threatening diabetic foot infections.**

Level of Evidence: IV, Retrospective Case Series

Key Words: Diabetic Foot; Infection; Amputation; Limb Salvage; Negative Pressure Wound Therapy

INTRODUCTION

Diabetic feet, especially when accompanied by neuropathy or ischemia, are at risk for severe or extensive infection. A septic foot, defined by the presence of purulent discharge or abscess in the deep soft tissue or bone,[21] is often limb-threatening and can lead to major amputation.

Salvaging a limb is critical because reduced activity after major amputation can cause a variety of morbidities and increased risk of mortality.[17,20] Through various multidisciplinary programs, a substantial decrease in the incidence of major amputations in diabetic patients has been achieved.[10,11] However, when accompanied by severe or limb-threatening infections, the rate is reported as high as 51%.[5,21–22]

Negative pressure wound therapy (NPWT) has proven its effectiveness in various diabetic foot problems through several randomized controlled studies.[1,4,7] Compared to standard moist gauze dressings, NPWT showed a higher proportion and rate of wound healing in diabetic ulcers,[4] cavitatious wounds,[7] and after partial foot amputation.[1]

Although whether NPWT actually reduces bacterial load is debatable,[15–16,23] its clinical effectiveness in many infected wounds has been demonstrated.[3,18] However, in diabetic patients, higher infection rates have been reported in an NPWT group and therefore using NPWT on clean wounds and monitoring them carefully for infection has been recommended.[1] Most of the studies regarding the effects of NPWT on diabetic feet have not addressed the preoperative infectious status and few studies have been performed regarding the use of NPWT in severely infected diabetic feet. Therefore, we utilized an algorithm in which NPWT is a part and evaluated its efficacy in severe diabetic foot infections.

MATERIALS AND METHODS

Between January 2006 and September 2008, 43 consecutive diabetic patients (45 feet) who presented with severe

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foot infection with deep abscess were selected for application of a treatment algorithm including NPWT. Those with only a mild to moderate degree of infection according to the Infectious Diseases Society of America's diabetic foot infection classification system[13] were not included in this study. All wounds were classified according to the University of Texas diabetic wound classification system.[12] Only wounds penetrating to tendon or capsule (grade II), or to bone or joint (grade III) were included in the study. Five patients had god circulation (stage B), while 40 had clinical signs of ischemia (stage D). Ischemic patients with absence of one or more foot pulses of the involved foot or ankle-brachial index (ABI) less than 0.8 were included, but those who presented with dry gangrene involving most of the foot requiring primary transtibial amputation were excluded from this study. Mean age was 59.9 years and the mean followup duration after complete wound healing was 17 (range, 6 to 35) months.

Management protocol

Our treatment algorithm is shown in Figure 1. Initial evacuation of abscess and debridement of definitely necrotic tissue was done immediately. Debrided deep soft tissue or abscess samples were obtained during this process for bacteriological analysis. Broad-spectrum antibiotic coverage consisting of a third generation cephalosporin, aminoglycoside, and metronidazole was simultaneously initiated. This empirical regimen was adjusted when the specific culture and sensitivity information became available. Wounds were left open and saline-wet gauze dressings were changed every 12 hours until definitive surgery was performed.

After the emergent procedures, we assessed arterial status and performed interventional angioplasty if necessary. Diagnosis of lower-extremity ischemia was made by a combination of clinical signs and noninvasive vascular studies. Clinical signs were based on the absence of one or more foot pulses of the involved foot and noninvasive criteria included an ABI of less than 0.8. For the ischemic limbs with successfully identified target lesions amenable to treatment in the CT angiogram, percutaneous transluminal angioplasty (PTA) was performed within 1 or 2 days. All ischemic limbs received antithrombotics: intravenous prostaglandin E1 during admission and oral prostacylin after discharge.

Presence of sensory neuropathy was determined by absent protective threshold using a 5.07 (10 g) Semmes-Weinstein monofilament. The initial blood exam encompassed a complete blood count with a differential count, erythrocyte sedimentation rate, C-reactive protein, and routine chemistry including plasma glucose level and HbA1c. Simple radiographs were routinely performed and in cases where osteomyelitis was suspected, Technetium-99 whole body bone scans or magnetic resonance imaging scans were performed.

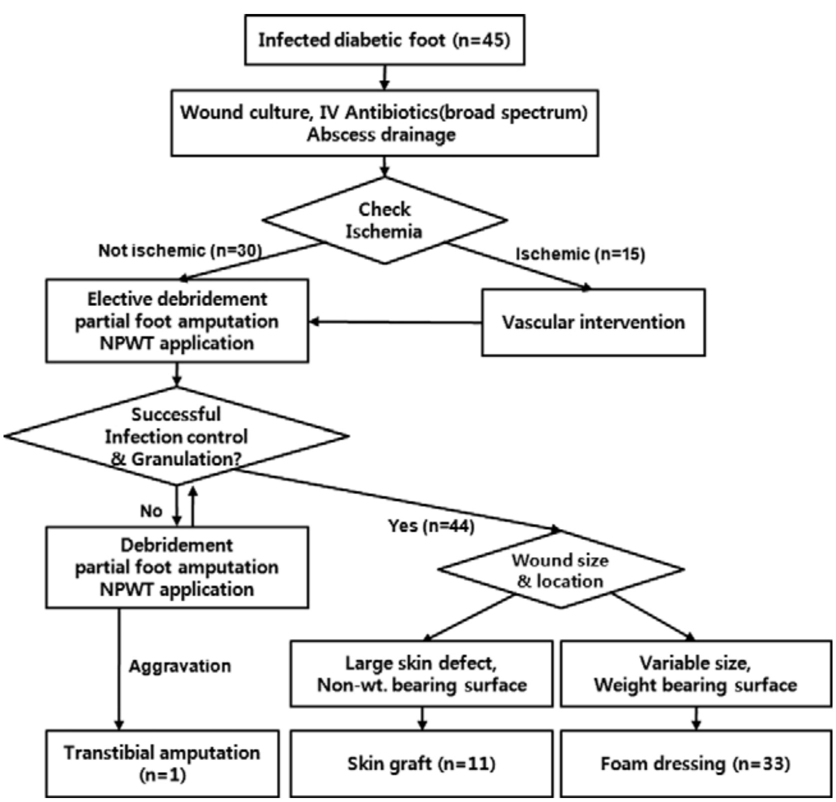

Fig. 1: Management algorithm and flow chart of patients.

After any required revascularization, elective debridement was conducted. All gangrenous and necrotic tissues were removed, while viable structures were preserved. Partial foot amputation was conducted if necessary. After debridement, wounds were left open and NPWT was instituted in the operating room. Negative pressure was delivered through the VAC therapy system (KCI USA, San Antonio, TX). Continuous suction mode of 125 mmHg was applied and the wounds were evaluated carefully for any residual necrotic tissue with frequent dressing change and subsequent debridement for the first 2 or 3 days. Once the infection was controlled and the wounds became stable, the suction mode was changed to intermittent cycle of 5 minutes on and 2 minutes off and the dressings were changed every 24 to 48 hours. Intermittent cycle maintains increased blood flow and has been shown to enhance cell proliferation and granulation.[15] If infection or wound necrosis worsened, further debridement and additional minor amputation was performed and NPWT was reapplied. If the limb failed to improve despite repeated surgical interventions and NPWT and if the patient's general condition was poor, it was amputated transtibially.

Negative pressure wound therapy was removed when the wound developed a sufficient amount (75% to 100% of wound area) of healthy and well-vascularized granulation tissue. Then, depending upon the location and size of the wound, either split-thickness skin graft (STSG) was conducted or hydrocellular foam dressing (Allevyn®, Smith & Nephew, Hull, UK) was applied. Healing by secondary intention was induced using foam dressings and epidermal growth factor (EGF®, Daewoong Pharm., Korea) for wounds on weightbearing surfaces, while large skin defects on nonweightbearing surfaces were suitable for STSG. A case is shown in Figure 2.

Wound progress was measured using a digital scanner (Visitrak®, Smith & Nephew, Hull, UK). The percentage of the wound area that was filled with granulation tissue was measured. Time to achieve more than 75% wound area coverage with granulation tissue and days until complete wound closure were analyzed. Complete wound closure was defined as 100% re-epithelisation without drainage or as successful coverage with STSG.

Any further operations performed after removal of the NPWT were analyzed and the final status of the limb was assessed. A limb was considered salvaged if complete healing was achieved without any or with minor amputation through or below the ankle.[11] Treatment was successful when a plantigrade foot was achieved or when the patient could walk independently by bearing weight on their heel.

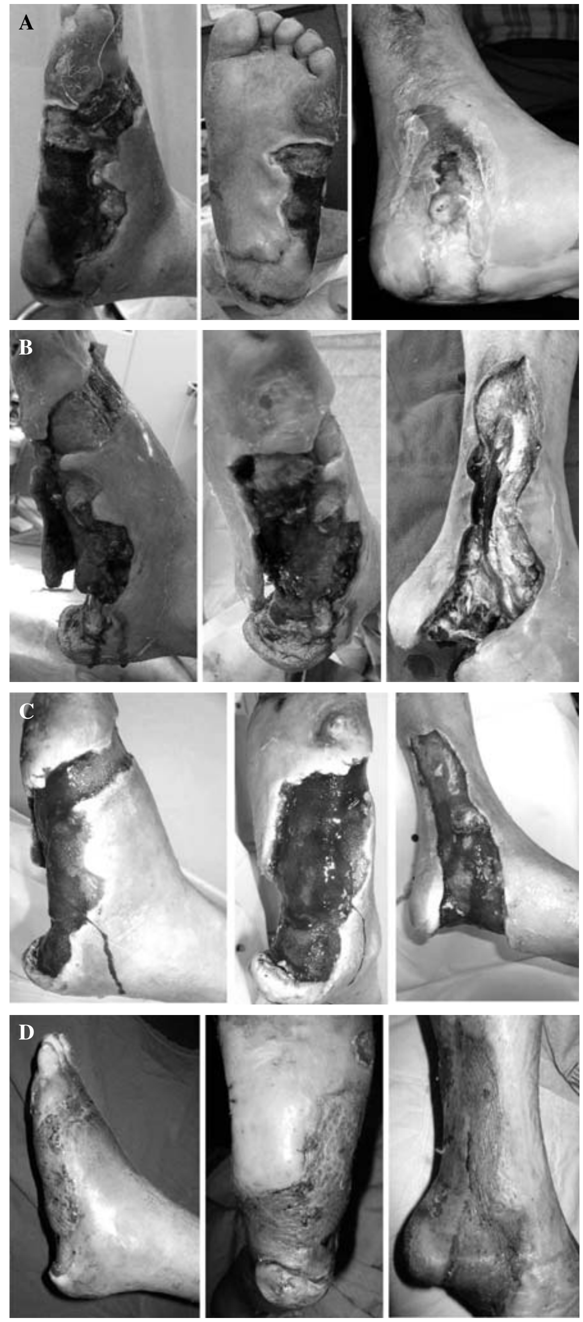

Fig. 2: A case showing successful limb salvage. A 34-year-old male patient presented with severe diabetic foot infection with foul odor (A). Negative pressure was applied after thorough debridement (B) and the defect was filled with well vascularized granulation tissue after 25 days (C). Skin grafting was performed to cover the large defect and complete wound healing was achieved (D).

Statistical analysis

Statistical evaluation was performed with SPSS software (version 12.0; SPSS, Chicago, IL). The median time to achieve more than 75% wound area granulation and complete wound healing was calculated. Pearson correlation test was used to determine the relationship between continuous variables of laboratory results and the rate of wound healing. Student t-test was used to compare rates of granulation and healing in different body mass index (BMI) groups.

Table 1: Demographics of the Study Population

Age (years)	59.9 ± 12.0
Sex (male:female)	35:10 (78:22%)
Body-mass index (kg/m^2)	22.9 ± 3.2
Glycosylated hemoglobin (HbA_1C)	8.8 ± 2.1
Type 2 diabetes (%)	42 (93.3%)
Duration of diabetes (years)	16.3 ± 8.4
Insulin use (%)	28 (62.2%)
Wound duration (weeks)	15.7 ± 29.4
Deficient pedal pulse (%)	15 (33.3%)
Loss of protective sensation (%)	42 (93.3%)

RESULTS

Demographics of the study population are summarized in Table 1. Thirty-nine patients (87%) had poorly controlled blood glucose levels (i.e., HbA1c $>$ 7.0%). The level of HbA1c did not correlate with the median time for obtaining more than 75% of granulation tissue ($r = 0.02$, $p = 0.91$) or time for complete wound healing ($r = 0.2$, $p = 0.91$). Twelve patients (27%) were overweight with BMI more than 25 kg/m^2, but their rate of granulation and wound healing did not differ from the others ($p = 0.71$ and 0.88, respectively). For 15 patients (33%) with deficient pedal pulse, diagnosis of peripheral arterial occlusive disorder was confirmed after CT angiogram. Percutaneous transluminal angioplasty was successful in 13 patients and failed in two. Two limbs with failed PTA survived with the use of intravenous prostaglandin E1 and each ended up with a ray amputations. Deep wound cultures were performed in all cases and Staphylococcus aureus was the most common pathogen (Table 2). Thirty-two patients (71%) were infected with two or more organisms, and 14 of them (31%) were infected with three or more pathogens. Two patients had negative culture results due to previous antibiotic treatments from other hospitals.

Thirty-four cases (76%) had wounds penetrating to bone or joint with infection and ischemia (grade III, stage D according to the University of Texas diabetic wound classification system), six (13%) had wounds penetrating to tendon or capsule with infection and ischemia (grade II, stage D), four (9%) had wounds penetrating to bone or joint with infection (grade III, stage B), and one (2%) had a wound penetrating to tendon or capsule with infection (grade II, stage B).

The mean duration of NPWT was 26.2 ± 14.3 days. The median time to obtain more than 75% wound area granulation was 23 (range, 4 to 55) days, and 104 (range, 38 to 255) days to complete wound healing. After removal of the NPWT, 11 patients (24%) received STSG and the other 34 patients (76%) were treated with foam dressings. The time interval

Table 2: Infectious Organisms

Mixed infection	
Infected with two or more organisms	32 (71.1%)
(three or more organisms)	14 (31.1%)
Cultured organisms	
Staphylococcus aureus (including 8 MRSA*)	17 (37.8%)
Streptococcus	9 (20.0%)
Staphylococcus epidermidis (including 4 MRCNS†)	7 (15.6%)
Peptostreptococcus sp.	7 (15.6%)
Enterococcus faecium (including 1 VRE‡)	7 (15.6%)
Pseudomonas	7 (15.6%)
Enterobacter sp.	6 (13.3%)
Escherichia coli (including 1 ESBL§ producing)	6 (13.3%)
Bacteroides fragillis	6 (13.3%)
Proteus vulgaris/mirabillis	6 (13.3%)
Morganella morganii	4 (8.9%)
Serratia marcescens	4 (8.9%)
Diphtheroids	4 (8.9%)
Others (*Acinetobacter, Citrobacter,* etc.)	6 (13.3%)

*, MRSA: Methicillin-resistant *Staphylococcusaureus*, †, MRCNS: Methicillin Resistant Coagulase-Negative *Staphylococci*, ‡, VRE: Vancomycin Resistant *Enterococcus*, §, ESBL: Extended Spectrum Beta Lactamase.

Table 3: Final Outcome of the Treatment

Final status of the limb	***n* = 45 (%)**
Success	44 (97.8)
No amputation (debridement)	14 (31.1)
Resection arthroplasty (metatarsophalangeal joint)	1 (2.2)
Ray amputation	19 (42.2)
One ray	9 (20)
One ray + one metatarsophalangea joint resection arthroplasty	2 (4.4)
Two rays	5 (11.1)
Two rays + one toe amputation	2 (4.4)
Three rays	1 (2.2)
Transmetatarsal amputation	5 (11.1)
Lisfranc disarticulation	2 (4.4)
Chopart disarticulation	1 (2.2)
Syme amputation	2 (4.4)
Failure	1 (2.2%)
Transtibial amputation	1 (2.2)

between removal of the NPWT and complete wound healing was 82.1 ± 42.7 days.

Successful limb salvage was achieved in 44 cases (98%). Complete wound healing was achieved in all patients and none were left with chronic unhealed wounds. The final status of the salvaged limbs is listed in Table 3. Forty-two (93%) patients were able to bear weight on their hindfoot and two patients who received Syme amputation were able to walk independently with bearing weight on the heel pad over the tibial stump.

Thirty-nine cases (87%) were salvaged with debridement or forefoot amputations, and six cases (13%) had amputations at midfoot or higher level. All six of these cases occurred in grade III, stage D category (Table 4). This resulted in 18% (6/34) of midfoot or higher level amputation in grade III, stage D wounds.

With NPWT removed, 19 (43%) did not require further operations, and nine (21%) healed after debridement or stump revisions. Sixteen (36%) had further partial foot amputation and reapplication of NPWT. The total number of operations per limb, including operations performed before NPWT, was 2.4 ± 1.3.

Table 4: Wound Distribution According to the University of Texas Diabetic Wound Classification System

		Grade			
		0	**I**	**II**	**III**
Stage	A	0	0	0	0
	B	0	0	1 (2.2%)	4 (8.9%)
	C	0	0	0	0
	D	0	0	6 (13.3%)	34 (75.6%)

One patient underwent a transtibial amputation. The patient had type 2 diabetes mellitus for 12 years and was on hemodialysis due to end-stage renal disease. Pedal pulses were weakly palpable and the protective sensation was lost. A grade III, stage D wound was on the medial aspect of the first ray and was infected with Methicillin-resistant Staphylococcus aureus. After the initial first ray amputation, aspiration pneumonia, urinary tract infection, VRE sepsis, and uremic encephalopathy occurred and the patient had been bedridden for seven months. Despite stump revision and reapplication of NPWT, the infection persisted with mixed pathogens (Pseudomonas aeruginosa, Acinetobacter baumanii, Enterococcus faecium, Citrobacter freundii) and necrosis extended proximally to the midfoot with additional gangrenous change on the ipsilateral heel. Considering the patient's poor general condition, transtibial amputation was performed.

There were no complications associated with NPWT. Some complained of intermittent pain during the application of negative pressure, but were managed with reduced pressures. After complete wound healing, three patients developed new wounds at different sites on the same limb. One was managed with NPWT, while the other two required minor amputations.

DISCUSSION

The results of this study indicate that a management algorithm in which early vascular intervention and NPWT forms a part is beneficial in treating severe diabetic foot infections. Not having a control group to compare the results is a limitation of this study. However, indirect comparison with the literature shows that our salvage rate (98%) is higher than previously reported results with conventional moist gauze dressings.[8,21–22]

The rate of granulation tissue formation was fast with the median time to obtain more than 75% wound area covered with granulated tissue being 23 (range, 4 to 55) days. This result is encouraging when compared to a similar study by Armstrong et al.[1] because all our cases were severely infected ones. Although direct comparisons between the two studies are difficult to make, they applied NPWT to wounds after partial foot amputation, and reported a median of 42 days for patients receiving NPWT and 84 days for control patients to achieve more than 75% wound area filled with granulation tissue. Interestingly, subsequent debridement during dressing change was performed in only 21% of patients in their study. We believe that the efforts to create a healthy bleeding surface through routine debridement during each dressing change in our protocol played an important role in faster granulation. Also, efforts to address the ischemic problem as early as possible, and adequate use of antithrombotics, together with changing the suction mode from continuous to intermittent once the infection is controlled, could all have contributed to faster granulation.

We utilized the University of Texas diabetic wound classification system because it includes depth, infection, and ischemia assessments. The severity and risk of amputation escalates as depth and stage increases. Armstrong et al.[2] reported that amputation at the midfoot or higher was performed in 100% of grade II, stage D and grade III, stage D cases. They did not describe their wound management method in their paper. Most of the wounds (74%) in our study were grade III, stage D and with use of NPWT, the rate of amputations at the midfoot or higher level was much lower (18%) in our series.

Additional surgical interventions including stump revisions or further partial amputations were still necessary during or after the NPWT in more than half of the cases. This rate might seem high and could have been reduced if one level higher or safer level of amputation was chosen in the index operation. However, the objective of lower extremity amputation surgery is to create a viable, functional residual limb to maximize patient mobility and independence,[6] and therefore, every attempt should be made to preserve as much foot function as possible. We left all viable bony structures in the primary operation. This may require subsequent surgeries, but we believe that NPWT helped to reduce the amount of secondary bony resections by providing good surrounding granulated tissue.

Using simple dressings while evaluating the wound for any residual necrotic tissue and delaying application of the NPWT for one or two days after the debridement could also be a good method of treatment and maybe more economic. The NPWT may not show any gross change in the first 24 to 48 hours, however, we believe that applying negative pressure immediately following debridement provides a good environment for subsequent granulation by reducing the interstitial edema and rapidly removing the harmful bacterial enzymes.

The benefit of saving a limb against the loss from repeated surgeries and long duration of treatment is debatable. Primary amputation can be the best option for patients who were bedridden or nonambulatory because the benefits yielded by preserving the leg are not compelling.[19] However, for those who were ambulatory before, we believe that the treatment is successful when the patient is able to return to independent ambulation with heel weight bearing.

The relatively short followup duration is another limitation as recurrent wound problems that lead to reamputations gradually increase over the 3-, 5-, and 10-year periods.[9,14] We had three patients who experienced newly developed wounds on the ipsilateral feet after a certain period of complete wound healing. Compared to the rate of wound development in a diabetic patient, this recurrence rate is reasonable. All three cases were managed with minor procedures and the limbs were kept in salvaged status. Currently, there is lack of long-term followup data in the literature regarding limb-salvage using NPWT in septic diabetic feet. Therefore, caution should be exercised when applying our results and future study with longer followup is needed.

CONCLUSION

This study provides the outcome of a management algorithm which includes NPWT in salvaging severely infected diabetic feet. With emergent evacuation of abscess, early vascular intervention and appropriate debridement, NPWT can be a useful adjunct to the management of limb-threatening diabetic foot infections.

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