Evaluation of the Efficacy of Highly Hydrophilic Polyurethane Foam Dressing in Treating a Diabetic Foot Ulcer

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ABSTRACT

OBJECTIVE: To demonstrate the efficacy of a highly hydrophilic polyurethane foam dressing in the treatment of diabetic ulcers.

BACKGROUND: Diabetic foot ulcers often pose a difficult treatment problem. Polyurethane foam dressings have been used worldwide to accelerate wound healing, but only a few clinical studies demonstrate the effect of foam dressing on the healing of diabetic ulcers.

METHODS: Medical records of 1342 patients with diabetic ulcers who were admitted and treated at the authors' institution were reviewed. A total of 208 patients met the study's inclusion criteria. Of these 208 patients, 137 were treated with a highly hydrophilic polyurethane foam dressing, and 71 were treated with saline gauze (control group). Except for the application of polyurethane foam dressing, the treatment method was identical for patients in both groups. The wound healing outcomes of the 2 groups were compared.

RESULTS: Complete wound healing occurred in 87 patients (63.5%) in the polyurethane foam dressing group and in 28 patients (39.4%) in the control group within 12 weeks ($P < .05$, X^2 test). The mean percentage of wound area reduction in both groups was statistically significant ($P < .05$, Mann-Whitney U test). The mean time required for complete closure in patients who achieved complete healing within 12 weeks was 6.2 (SD, 3.4) weeks and 7.3 (SD, 2.6) weeks in the polyurethane foam dressing and control groups, respectively ($P < .05$, Mann-Whitney U test).

CONCLUSION: These results indicate that the highly hydrophilic polyurethane foam dressing may provide an effective treatment strategy for diabetic foot ulcers.

KEYWORDS: diabetic foot ulcer, highly hydrophilic polyurethane foam dressing, wound management

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INTRODUCTION

The worldwide prevalence of diabetes is estimated to be approximately 10% in the adult population.[1] Epidemiological studies suggest that 2.5% of patients with diabetes develop diabetic foot ulcers each year, and 15% develop diabetic foot ulcers during their lifetime.[1]

Selecting the appropriate dressing for the wound condition is crucial for successful wound healing in diabetic foot ulcers. An ideal wound dressing should provide effective exudate management to create a moist wound environment and protect from bacterial invasion and enable stable functional activity of cells in the wound bed.[2,3] Removal of the dressing covering the wound should be both painless and atraumatic, without shedding of particles or fibers during dressing changes. Furthermore, it should be comfortable to use, provide thermal insulation, and be cost-effective. Various dressing materials have been commercialized with the aim of supplementing the shortfalls of conventional gauze dressings. They include films, hydrocolloids, hydrogels, foams, and alginates/hydrofibers.

Among these dressing types, foam dressings are the most commonly used because they possess various important characteristics of an ideal wound dressing based on the aforementioned criteria.[4] Most of the foam dressings are made of 3-layered polyurethane foams. The outer protective layer is hydrophobic and has pores that are too small for bacteria to enter or for exudates to escape, while also allowing gases such as oxygen to be exchanged regularly. The middle absorption layer is designed to retain absorbed wound exudates. The inner contact layer is hydrophilic and has pores that have a size specifically designed to allow the passage of exudates but to prevent ingrowth of regenerated tissue. These 3 layers functionally maintain a moist environment and protect the wound from bacterial invasion without adhering to the wound, thus enabling atraumatic and less painful dressing changes.

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Currently, 2 types of foams are used for wound dressings. Early polyurethane foam dressings were made by mixing polyethylene glycol, isocyanate, catalyst, surfactant, water, and hydrophilic polyurethane in 1 step. Thereafter, a more hydrophilic polyurethane foam dressing was developed by a new process. However, there is insufficient research evidence to suggest that the polyurethane foam dressings are more effective in healing a diabetic foot ulcer than a conventional gauze dressing. A few clinical trials have been performed using early polyurethane foam dressings, but these studies did not include a large number of cases to demonstrate the definite value of the dressings.[5–7] To the authors' knowledge, no clinical study assessing the effect of highly hydrophilic foam dressings has been performed.

The purpose of this retrospective clinical study is to demonstrate the effectiveness of the highly hydrophilic polyurethane foam dressing over the conventional gauze dressing in the treatment of diabetic foot ulcers.

METHODS

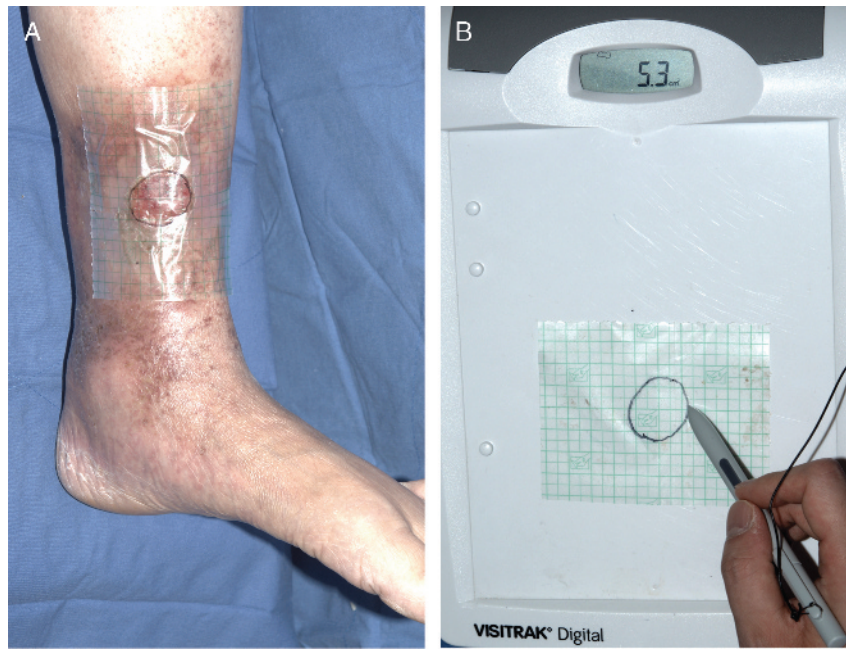
Wound Management Protocol Used in the Authors' Clinical Setting

A complete medical history was obtained at the first visit. The wound area was recorded by means of the Visitrak Digital Planimetry Wound Measurement System (Smith & Nephew, Hull, United Kingdom; Figure 1). General serologic tests including blood glucose and other inflammatory markers were performed. To evaluate the vascularity of the diabetic foot, transcutaneous partial oxygen tension ($tcpO_2$) and Doppler wave were measured. Patients with peripheral arterial disease underwent percutaneous transluminal angioplasty by an interventional cardiologist. For the management of wound bioburden, a deep tissue culture was performed. Whenever necessary, intravenously administered antibiotics were administered empirically, and they were changed according to the results of culture and sensitivity tests. Serial surgical debridement was carried out whenever necessary at the bedside or in the operating room, according to the wound condition. In patients with osteomyelitis, systemic antibiotic therapy was administered for at least 3 to 6 weeks. Osteomyelitis was diagnosed by magnetic resonance imaging and bone biopsy culture. Appropriate off-loading was provided according to the location of the ulcer.

Patients with diabetic foot ulcers who were in poor health were admitted to the hospital, as well as patients with severely infected ulcers that required surgical debridement with systemic intravenously administered antibiotic therapy, including septic diabetic foot. Other indications for admission included

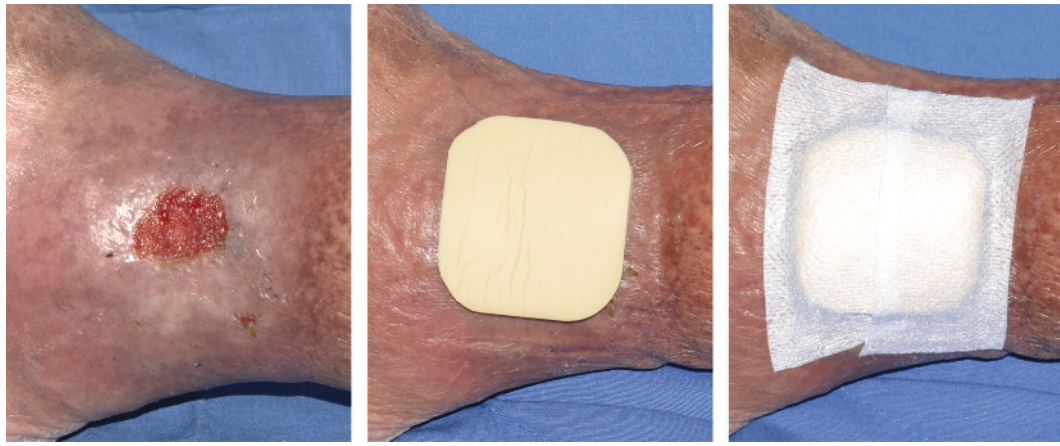
Figure 1.

MEASUREMENT OF A WOUND AREA USING THE VISITRAK DIGITAL PLANIMETRY WOUND MEASUREMENT SYSTEM



A, The edge of the wound was traced on the sterile film dressing. B, The wound outline on the film was traced on the surface of the Visitrak Digital unit. The device displayed a wound area of 5.3 cm^2.

Figure 2.
A WOUND TREATED WITH A HIGHLY HYDROPHILIC POLYURETHANE FOAM DRESSING



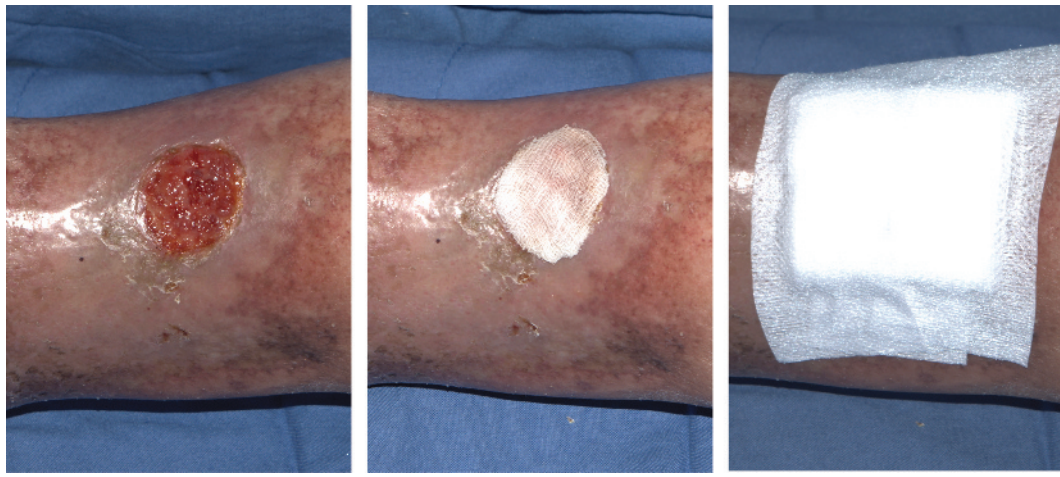
severe vasculopathy that required immediate angioplasty and clinic-based debridement that was not possible in the outpatient setting.

Patients were discharged when their general health had improved, vascularity was achieved, and severe infection had subsided. After discharge, moisture-retaining wound dressings were applied. The patients returned to the outpatient clinic 2 to 3 times per week for their wounds to be examined. The ulcer was cleaned with 3% hydrogen peroxide and saline solution to remove dirt and other debris before applying the dressing. For the moisture-retaining dressing, highly hydrophilic polyurethane foam was used (Figure 2). In cases where the patient refused treatment with the dressing products mainly because of financial reasons, a saline gauze dressing was applied (Figure 3). The wound area was recorded every week.

Materials

Medical records of 1342 patients with diabetic foot ulcers, who were admitted and treated at the Diabetic Wound Center of the authors' institution between January 2005 and December 2012,

Figure 3.
A WOUND TREATED WITH A SALINE GAUZE DRESSING



were reviewed. Of these 1342 patients, patients who had been discharged and met the following inclusion criteria were included in the study. The inclusion criteria were type 1 or 2 diabetes, a foot ulcer of more than 1.0 cm^2 but less than 10.0 cm^2, Wagner grade 1 or 2, tcpO_2 40 mm Hg or greater, wound dressing made of a highly hydrophilic polyurethane foam (Medifoam; Genewell, Seoul, Korea) or a saline gauze, and successful follow-up through the outpatient clinic until complete wound closure, or the 12th week visit if the wound was not completely healed. Patients were excluded from this study if they had a concurrent illness or a condition that might interfere with wound healing (eg, connective tissue disorders), sickle cell disease, diseases with a poor prognosis (including malignant tumors), treatment with corticosteroids or immunosuppressive agents, and severe malnutrition (serum albumin <3.0 g/dL). Cases treated with biological or biochemical therapy, including growth factors or cells, were also excluded.

Evaluation

The primary efficacy criterion was the percentage of patients who achieved complete wound closure within the 12-week study period. The secondary efficacy criteria were the mean percentage of wound area reduction at the 8th and 12th week and the mean time required for complete closure in patients who achieved complete healing within 12 weeks. Complete closure was defined as a completely epithelialized state; no discharge was present and patient was permitted to shower.

This study protocol was approved by the Institutional Review Board of the authors' institution (no. KUGH 15092-001).

Statistical Analysis

The complete wound healing ratio between the 2 groups was analyzed using x^2 test to compare the categorical proportions. The proportion of allergic dermatitis in the 2 groups was analyzed using Fisher exact test because the expected cell count was less than 5.

The mean percentage of wound area reduction and the mean time required for complete closure in the 2 groups were analyzed using the Mann-Whitney *U* test, as the data were not normally distributed. A $P < .05$ was considered statistically significant. Data were expressed as the mean (SD). The statistical analysis was performed using SPSS version 20.0 for Windows (IBM SPSS, Armonk, New York).

RESULTS

Of these 1342 patients, 208 patients with diabetic foot ulcers met the inclusion criteria. A total of 137 patients were treated with the highly hydrophilic polyurethane foam dressing, and 71 patients were treated with saline gauze.

Table 1.

PATIENT CHARACTERISTICS IN THE POLYURETHANE FOAM DRESSING GROUP AND CONTROL GROUP

		Polyurethane Foam Dressing Group (n = 137)	Control Group (n = 71)
Age, mean (SD), y		62.8 (8.2)	64.6 (9.1)
Gender, n (%)	Male	90 (66)	48 (68)
	Female	47 (34)	23 (32)
Smoking, n (%)	Nonsmoker	66 (48)	35 (49)
	Ex-smoker	45 (33)	22 (31)
	Smoker	26 (19)	14 (20)
Body mass index, mean (SD), kg/m^2		22.6 (4.1)	21.8 (3.0)
Glycated hemoglobin, mean (SD), %		7.3 (1.1)	7.4 (3.1)
Hemoglobin, mean (SD), g/dL		11.6 (1.5)	11.2 (1.8)
Albumin, mean (SD), g/dL		3.9 (0.4)	3.6 (0.3)
White blood cells, mean (SD), $\times 10^3/\mu L$		7.3 (2.1)	7.6 (2.8)

The relevant patient information at baseline in the 2 treatment groups is shown in Tables 1 to 3. There were no statistically significant differences in any clinical characteristics between the 2 groups.

After 12 weeks, complete wound healing occurred in 87 patients (63.5%) of the polyurethane foam dressing group (n = 137) and in 28 patients (39.4%) of the control group (n = 71; $P < .05$, x^2 test; Figures 4-7).

Wound infection, which required sharp or surgical debridement combined with systemic antibiotic therapy, occurred in 18 patients (13.1%) of the polyurethane foam dressing group and in 9 patients (12.7%) of the control group, respectively ($P = .925$, x^2 test; Figure 8). In addition, allergic dermatitis was reported in 8 patients (5.8%) of the polyurethane foam dressing group and in 2 patients (2.8%) of the control group, respectively ($P = .5$, Fisher exact test; Figure 9). However, none of these events were thought to be related to the study dressings, and no significant differences were noted between the 2 groups. No other adverse event was thought to be related to the study dressing in either group. The cases of infection or allergic dermatitis were evaluated as nonhealed cases and were excluded from the analysis of the mean percentage of wound area reduction.

The mean percentage of wound area reduction in the treatment group (n = 111) was 75.3% (SD, 21.6%) at the 8th week and 92.3% (SD, 10.9%) at the 12th week. The mean percentage of wound area reduction in the control group (n = 60) was 65.9% (SD, 23.4%) at the 8th week and 88.2% (SD, 10.9%) at the 12th week. The reduction rates at the 8th week and the 12th week were statistically significant ($P < .05$, Mann-Whitney *U* test).

The mean time required for complete closure in patients who achieved complete healing within 12 weeks was 6.2 (SD, 3.4)

Table 2.

CLINICAL CHARACTERISTICS OF THE ULCERS AT BASELINE

		Polyurethane Foam Dressing Group (n = 137)	Control Group (n = 71)
Ulcer size, cm^2	Mean (SD)	6.2 (2.8)	6.0 (2.7)
	Median	6.1	6.0
	Range (min–max)	1.4–9.9	1.5–9.5
Duration of the ulcer, wk	Mean (SD)	10.9 (4.5)	9.3 (3.7)
	Median	10	9
	Range (min–max)	6–15	6–16
Wagner grade, n (%)	Grade I	52 (38)	25 (35)
	Grade II	85 (62)	46 (65)
University of Texas grade, n (%)	Grade 1	52 (38)	25 (35)
	Grade 2	36 (26)	24 (34)
	Grade 3	49 (36)	22 (31)
Ulcer location	Dorsal (forefoot:midfoot:hindfoot)	70 (52:3:15)	37 (29:1:7)
	Plantar (forefoot:midfoot:hindfoot)	67 (47:2:18)	34 (25:2:7)
$TcpO_2$, mm Hg		51.2 (9.9)	53.4 (10.7)
Risk category, n (%)	Neuropathy	81 (59)	41 (58)
	Neuro-ischemia	11 (8)	6 (9)
	Foot deformity	79 (58)	37 (52)
	History of ulceration	70 (51)	34 (48)
Cause of ulcer, n (%)	Trauma	27 (20)	13 (19)
	Pressure caused by shoes	76 (55)	40 (56)
	Unknown	34 (25)	18 (25)

Abbreviation: $TcpO_2$, transcutaneous partial oxygen tension.

weeks and 7.3 (SD, 2.6) weeks in the polyurethane foam dressing (n = 87) and control (n = 28) groups, respectively ($P < .05$, Mann-Whitney *U* test).

DISCUSSION

Diabetic foot ulcers present a difficult treatment problem and respond poorly to conventional treatment. The main reason why wound healing cannot be achieved often is that the pathophysiology of this condition involves many factors. For example, fibroblasts isolated from patients with diabetes have lower migration and proliferation potential, and cause changes associated with cellular senescence in the presence of high glucose concentrations.[8] Wound fluid from diabetic ulcers also inhibits fibroblast proliferation in many cases because of excessive metalloproteinase levels and depressed levels of their natural tissue inhibitors.[9] In addition, even low concentrations of microbes in the wound bed can delay or prevent wound healing because many patients with diabetes do not have adequate defense mechanisms against bacterial invasion because of an immunocompromised status or a poor systemic profile. Therefore, selecting an appropriate dressing for a diabetic foot ulcer is crucial for wound healing.

It is difficult to select the most appropriate dressing from the wide array of wound care products available in the market today. The current concept of the "ideal wound dressing" is the one that removes excess exudate, maintains a moist environment, protects against contaminants, causes no trauma on removal, leaves no debris in the wound bed, relieves pain, provides thermal insulation, and induces no allergic reactions.[10,11] Given the biologic complexity of chronic wounds, there may be no single dressing that is perfect for all types of wounds. The ideal wound dressing should also be cost-effective.

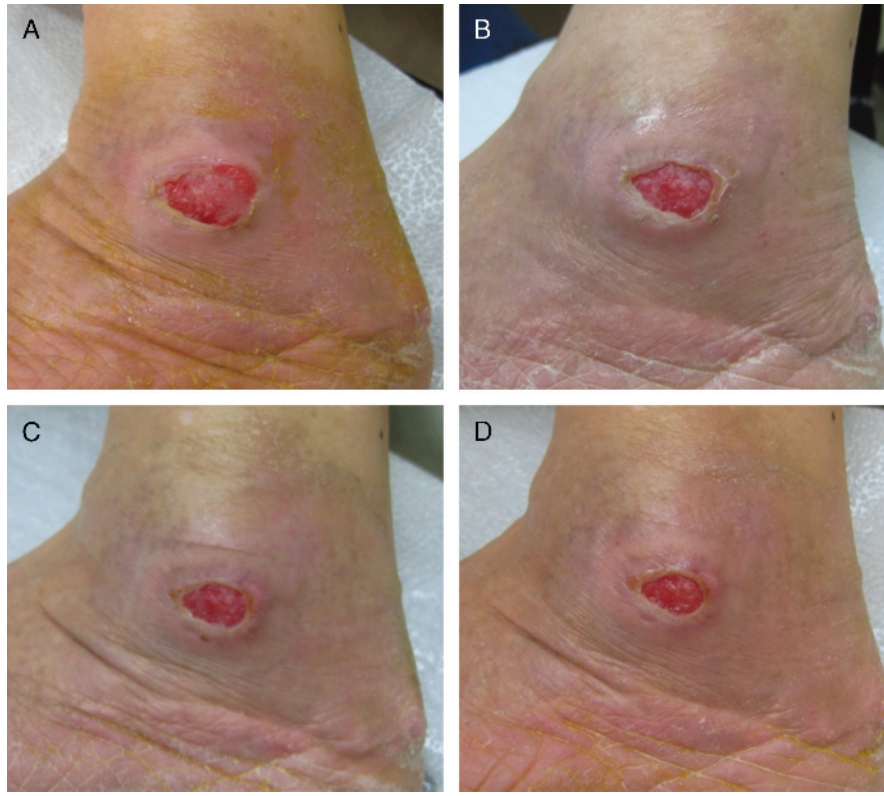
Plain gauze historically has been the most popular wound dressing. Although plain cotton gauze provides good absorption, it promotes desiccation of the wound base, which can be detrimental to healing.[12] Gauze dressings often bind to the wound surface, causing pain and trauma to the wound bed at dressing changes. In addition, because gauze dressings are susceptible to full-thickness saturation with wound fluid ("strikethrough"), they have limited ability to provide an effective barrier against

Table 3.

COMORBIDITY IN PATIENTS

	Polyurethane Foam Dressing Group (n = 137)	Control Group (n = 71)
Hypertension	112	60
Cardiac disorder	51	22
Renal disorder	38	17
Ophthalmic disorder	26	14
Tremor	9	5
Arthritis	7	3
Pruritus	5	2
Pulmonary disorder	4	3
Metabolic disorder	3	1

Figure 4.
A CONTROL GROUP WOUND ON THE LATERAL MALLEOLUS TREATED WITH SALINE GAUZE



A, Initial view. B and C, At 4 and 8 weeks after the dressing. D, At 12 weeks after the saline gauze dressing, the ulcer did not heal.

bacterial invasion.[13] Furthermore, although moisture-retentive interactive dressings are more expensive per individual dressing, they are more cost-effective over time.[14]

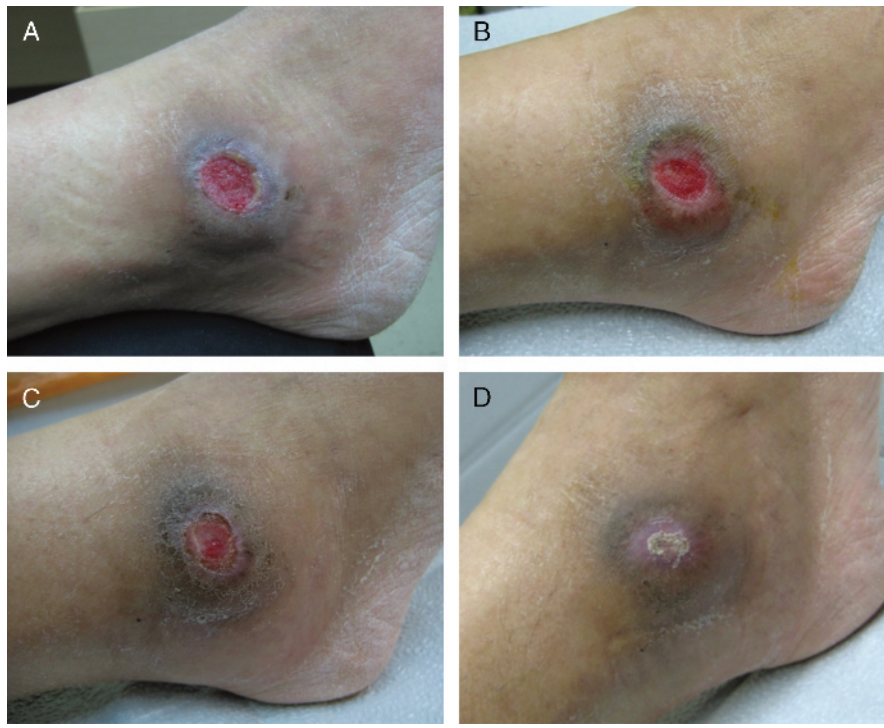
Excessive wound exudate not only hinders the healing process, but also leads to maceration of the wound margins. Wound dressings should be able to quickly and effectively draw the exudate deeply into the absorbent material and reliably hold it there. Foam is a suitable dressing material to accomplish these objectives. Many foam dressings, of varying compositions and modes of action, are primarily designed to absorb wound exudates and to provide a soft cover for the wound site. They also provide thermal insulation[15] and protect against shear,[16] and the nonadhesive wound contact layer allows for nontraumatic dressing changes. Foam dressings may occasionally be used for their cushioning effect, although they are not intended as a substitute for proper pressure-relieving devices.[17] The pores in foam dressings effectively absorb exudates, provide moist wound environment, and decrease skin maceration.

The pore size of the contact layer of foam dressings may have a significant impact on wound healing. Larger pores increase the growth of cells and tissue within the foam structure. The smaller the pore in the wound contact layer, the less likely the migration of the new healing wound tissue into the foam. It was difficult to regulate the cell size of earlier hydrophilic polyurethane foam dressings because they were made by mixing polyethylene glycol, isocyanate, catalyst, surfactant, water, and hydrophilic polyurethane in 1 step. The surface had large pores due to its open cell structure, and bacteria or regenerated tissue could invade the open cells. To prevent these invasions, a hydrophobic surface was created to allow a low absorption rate of the exudate.

The highly hydrophilic polyurethane foam dressing was developed by producing it in multiple steps. In the first step, polyurethane prepolymer was synthesized by interaction between polyether polyol and diisocyanate. Next, a foaming agent, a cross-linking agent, and additives were mixed before being injected into the mold. By modifying the type and ratio of

Figure 5.

A HIGHLY HYDROPHILIC POLYURETHANE FOAM DRESSING–TREATED WOUND WITH SIMILAR PATIENT AND WOUND CHARACTERISTICS AS THOSE OF THE WOUND IN FIGURE 4 AT BASELINE



A, Initial view. B and C, At 2 and 4 weeks after the foam dressing. D, At 6 weeks after the foam dressing, the wound was completely healed.

polyurethane prepolymer, foaming agent, and cross-linking agent, the highly hydrophilic polyurethane foam was produced with a thin, film-like epithelial layer with approximately 3–60 μm small pores and an inner layer with open cells, measuring approximately 50–500 μm. Therefore, the highly hydrophilic polyurethane foam had a smaller pore size than old foam dressings that helped to fulfill the important requirements, and this minimized the tissue ingrowth and maximized the hydrophilic property. By mixing additives such as surfactant, humectant, wound healing promoters, and antibiotics, a superior hydrophilic property could be expected.

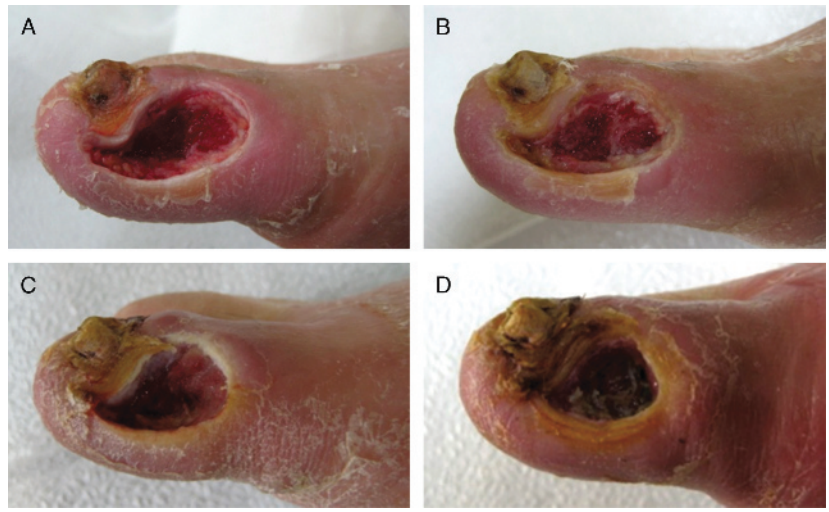
The results of the present study demonstrate that the highly hydrophilic polyurethane foam dressing was superior to the saline gauze dressing in terms of the complete wound healing rate, reduction in wound area, and time required for wound closure. No significant difference was noted in the infection rate and allergic dermatitis between the 2 groups.

It is important to emphasize that the polyurethane foam dressing should be used along with other standard principles of diabetic foot ulcer management, including debridement, infection control, pressure off-loading, and revascularization. Without adhering to these important principles, the addition of an active adjunctive modality is unlikely to result in improved healing rates. Patients with diabetic foot ulcers who do not exhibit significant signs of wound healing despite good metabolic control, acceptable vascularity (transcutaneous oxygen pressure ≥40 mm Hg), adequate pressure off-loading, and absence of infection,[18,19] may be good responders to polyurethane foam dressing. The wound bed should be healthy and clean with or without granulation tissue.

This study has some limitations that are inherent to retrospective studies. For example, patient adherence, which can affect the outcomes, was not considered. There also may be a selection bias because the authors' hospital is a tertiary referral center for the complex diabetic foot ulcer. Therefore, the results of this study might not be applicable to the general population or primary care centers. In addition, this study excluded patients who did not have an admission history because the outpatient clinic patients

Figure 6.

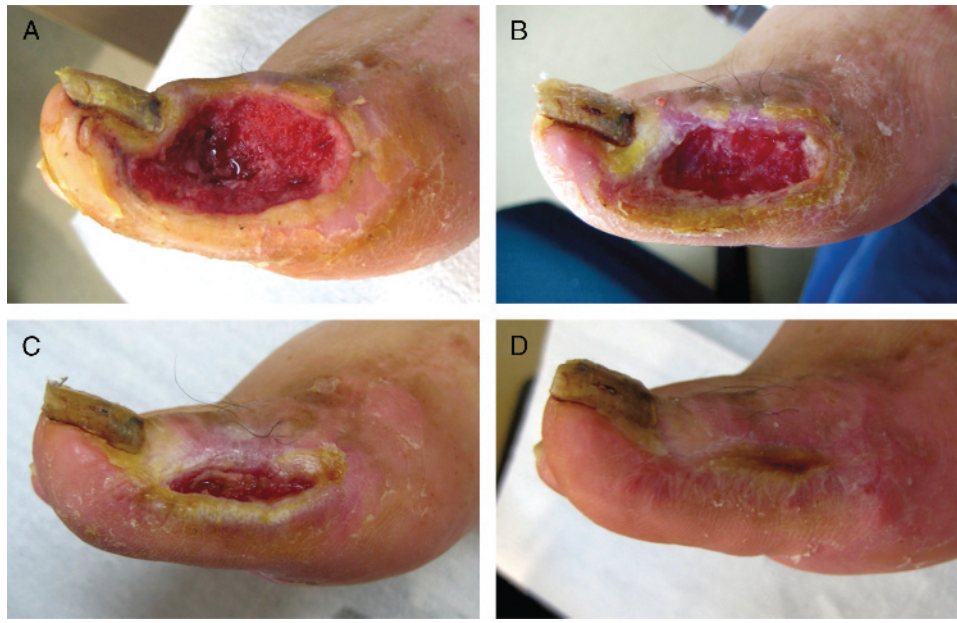
A CONTROL GROUP WOUND ON THE GREAT TOE TREATED WITH SALINE GAUZE



A, Initial view. B and C, At 4 and 8 weeks after the dressing. D, At 12 weeks after the saline gauze dressing, complete wound closure was not achieved.

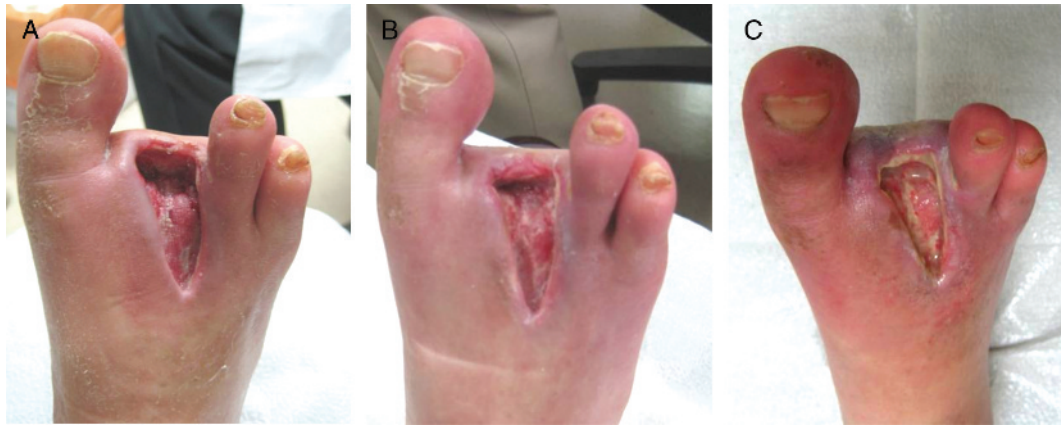
Figure 7.

A HIGHLY HYDROPHILIC POLYURETHANE FOAM DRESSING–TREATED WOUND WITH SIMILAR PATIENT AND WOUND CHARACTERISTICS AS THOSE OF THE WOUND IN FIGURE 6 AT BASELINE



A, Initial view. B and C, At 3 and 6 weeks after the foam dressing. D, At 8 weeks after the foam dressing, the wound was completely healed.

Figure 8.
A WOUND ON THE FOOT DORSUM WAS TREATED WITH A HIGHLY HYDROPHILIC POLYURETHANE FOAM DRESSING

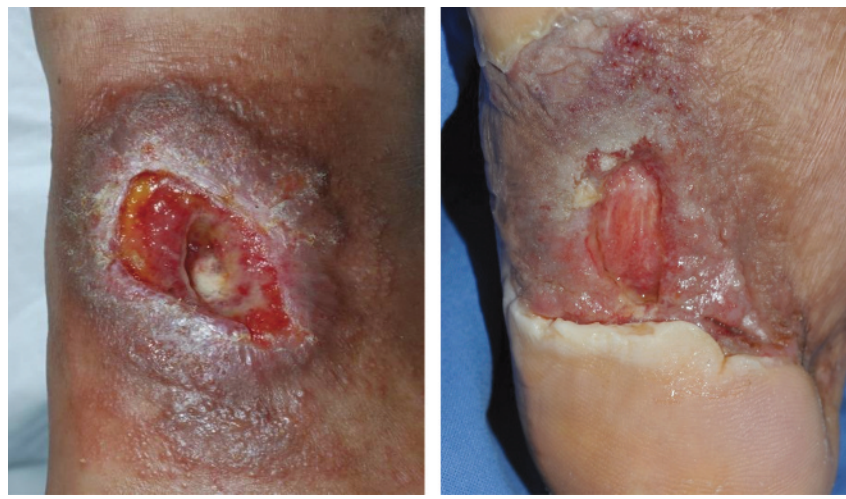


A, Initial view. B, At 2 weeks after the dressing. C, At 4 weeks after the foam dressing, wound infection developed.

did not have adequate data, and all baseline data were obtained at the time of admission.

Nevertheless, this study has some merit. In the past, there was insufficient research evidence to suggest that the polyurethane foam dressings are more effective in healing a diabetic foot ulcer, which is a well-known example of nondelayed healing wounds, than gauze dressings. Three clinical trials were performed using early polyurethane foam dressings. However, the sample sizes were not large enough to demonstrate the definite value of the dressings, and the results were inconsistent. Blackman et al[5] and Mazzone and Blackman[6] performed clinical studies comparing foam dressing and wet-to-dry saline gauze dressing with 14 and 19 patients with diabetic foot ulcers, respectively. However, there were differences in baseline characteristics between the 2 groups. A study by Roberts et al[7] comparing foam dressing and saline-soaked, low-adherent wound contact dressings in 30 patients with diabetic foot ulcers demonstrated that time to healing was not significantly different between the 2 groups.

Figure 9.
TWO REPRESENTATIVE CASES OF ALLERGIC DERMATITIS



In addition, no clinical study has reported the effect of highly hydrophilic foam dressings. To the authors' knowledge, this is the first study of the highly hydrophilic foam dressing in a large number of patients with diabetes who were treated using an identical management protocol at a single center.

CONCLUSION

The results of the study demonstrate that the highly hydrophilic polyurethane foam dressing may provide an effective treatment strategy for diabetic foot ulcers. ●

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