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Original

Bone Marrow Exposure during Minor Amputation for Diabetic Foot Gangrene: A Single-Center Retrospective Study

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Background: The incidence of diabetic gangrene is increasing because patients are living longer with diabetes.

Methods: Data from 27 Japanese adults with diabetic foot gangrene were analyzed. All affected sites, including bones, were surgically excised. Amputation was performed at the toe or metatarsal bones, and bone marrow was adequately exposed. This retrospective review investigated the results of this therapy.

Results: Healing was satisfactory for 26 of the 27 (96.3%) patients. Recurrence was noted in 4 (14.8%) of the 27 patients, the median number of operations was 1 (range, 1–3), and 1 (3.7%) patient required reconstructive surgery. White blood cell (WBC) count and C-reactive protein (CRP) level were significantly higher in recurrent cases than in non-recurrent cases (p = 0.009 and p = 0.001, respectively; Wilcoxon rank sum test). The cutoff values for WBC count and CRP level were 17,300/μL (specificity 100%; sensitivity 75%) and 10.23 mg/dL (specificity 81.8%; sensitivity 100%), respectively, using the Youden index. WBC count and CRP level also significantly positively associated with the number of operations (p = 0.018 and p = 0.018, respectively; Jonckheere-Terpstra trend test).

Conclusions: A higher WBC count and CRP level may predict recurrence and number of operations. Therapy using bone marrow exposure is simple and useful for diabetic foot gangrene. Thus, minor amputation with bone marrow exposure may be an effective treatment for diabetic foot gangrene.

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Keywords: diabetic foot gangrene, bone marrow, Japanese, osteomyelitis, wound healing

Introduction

The burden of diabetes is increasing. According to the International Diabetes Federation (IDF), the number of adults aged 20–79 years with diabetes was 151 million in 2000 and 589 million in 2024 and is expected to reach 853 million by 2050[1]. The IDF report maintained that the anticipated global increase in the number of diabetes patients is the result of a complex interplay of demographic, socioeconomic, environmental, and genetic factors[1]. As populations age, the number of persons with diabetes increases[1,2]. In Japan, the particularly high prevalence of diabetes among elderly adults is likely attributable to obesity[2].

Longer diabetes duration is associated with a higher incidence of diabetic foot ulcer and gangrene[3]. Persons with diabetes are predisposed to infections in the foot due to small injuries associated with diabetic neuropathy, circulatory disturbances, and impaired neutrophil function related to hyperglycemia[3]. Consequently, minor wounds may fail to heal adequately, leading to gradual

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progression of gangrene. Diabetic foot gangrene can lead to osteomyelitis, which arises primarily from the spread of adjacent soft tissue infections, hematogenous dissemination, and direct infection due to trauma or surgery[3]. Most cases of diabetic foot gangrene are caused by spread from nearby soft tissue infections[4]. Osteomyelitis often requires prolonged antibiotic therapy, and the recurrence rate was reported to be 20%[4]. In persons with diabetes the lifetime risk of developing foot ulcer is as high as 25%[5]. Frykberg et al.[6] reported that 7–20% of diabetic patients with foot ulcer eventually require lower limb amputation, indicating that the significant increase in the number of amputations parallels the rise in diabetes prevalence. Diabetic foot gangrene often presents with concurrent osteomyelitis, and major amputations (transtibial or transfemoral amputations) remain the treatment of last resort[7]. Treatment of diabetic foot gangrene should prioritize avoiding such amputations, to maintain patient quality of life and activities of daily living[7]. Although minor amputations (toe or transmetatarsal) have become more common recently, the risk of subsequent major amputation remains high[7].

Reports suggest that bone marrow contains multipotent stem cells capable of differentiating into nonhematopoietic cells, in addition to hematopoietic cells. These cells differentiate into osteoblasts, fibroblasts, and keratinocytes[8]. Bone marrow–derived stem cells can release multiple cytokines, including vascular endothelial growth factor, basic fibroblast growth factor, and transforming growth factor β, thereby promoting angiogenesis and collagen synthesis from fibroblasts[9]. These mechanisms suggest the potential for enhanced wound healing in areas of refractory ulcers[9]. Additionally, impaired collagen synthesis and angiogenesis can delay wound healing.

A groundbreaking study[10] described the artificial exposure of bone marrow for intractable diabetic foot ulcer with exposed bones. Subsequent application of epidermal sheets led to rapid wound healing. This mechanism was confirmed in an animal model[11], and this method was also effective for lower-extremity ulcer in rheumatoid arthritis[12].

These reports prompted us to reevaluate therapy for diabetic foot gangrene with osteomyelitis or joint destruction. Instead of major amputation, we exposed the bone marrow and utilized adjacent skin. Moreover, we anticipated secondary wound healing without reconstructive surgery.

Table 1 Demographic data

	Cases (n = 27)
Age (years), median (range)	63 (36–85)
Gender	
Male	23 (85.2%)
Female	4 (14.8%)
Race	
Japanese	27 (100%)
Height (cm), median (range)	164 (131–177.2)
Body weight (Kg), median (range)	70.6 (42–103.5)
Body mass index (Kg/m^2), median (range)	25.71 (16.9–33.4)
Diabetes	
Yes	27 (100%)
No	0 (0%)
Dialysis	
Yes	12 (44.4%)
No	15 (55.6%)
Neurological disorder	
Yes	27 (100%)
No	0 (0%)
Ankle-brachial index, median (range)	0.98 (0.51–1.69)
Duration of diabetes (years), median (range)	22 (0–40)
Duration of dialysis (months), median (range)	0 (0–140)
Laboratory data	
White blood cell count (/μL), median (range)	9,400 (3,800–27,200)
C-reactive protein (mg/dL), median (range)	2.57 (0.13–28.45)
Hemoglobin (g/dL), median (range)	10.5 (6.9–13.8)
Platelet count (×10^4/μL), median (range)	30.4 (6.9–58.8)
HbA1c (%), median (range)	7.1 (4.8–11.4)
Toe number	
1st	15 (55.6%)
2nd	4 (14.8%)
3rd	11 (40.7%)
4th	7 (25.9%)
5th	7 (25.9%)
Number of toes, median (range)	1 (1–6)
One	20 (74.1%)
Multiple	7 (25.9%)
Bilateral	1 (3.7%)

Values are number unless noted.

Materials and Methods

Patients

A hospital medical record system was used to collect data retrospectively from the Department of Dermatology of Nippon Medical School Hospital for the period April 2015 through May 2025 (**Table 1**). Data from 27 Japanese adults with diabetes and diabetic foot gangrene that met the diagnostic criteria (Wagner grade 3 to 4) of

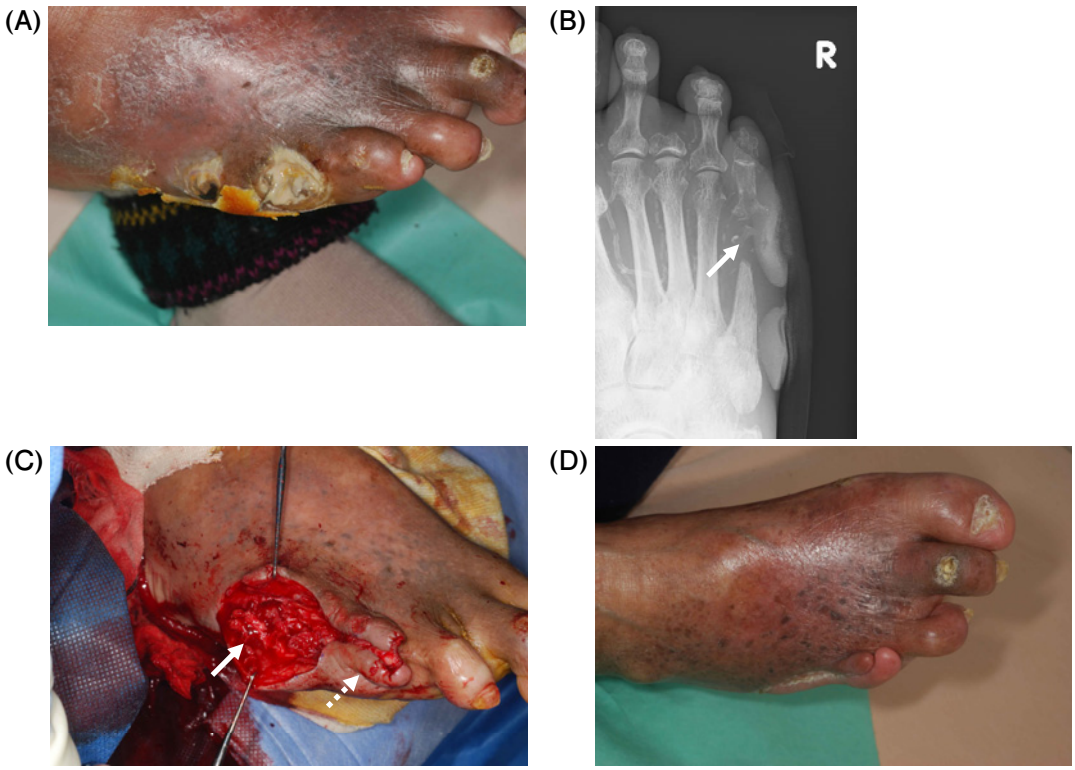

Figure 1 A representative case
(**A**) Case 17: An 84-year-old man with diabetic foot gangrene (right fifth toe) and metatarsophalangeal joint destruction.
(**B**) X-ray showing metatarsophalangeal joint destruction (arrow).
(**C**) Necrotic tissue was excised. Bone was amputated and bone marrow was adequately exposed (arrow). Surrounding viable skin and toe skin were preserved (dotted arrow).
(**D**) Wound healing was complete at 14 months after the operation.

the International Working Group on Diabetic Foot guidelines were included in the study[13]. All had peripheral neurological disorders at the affected sites and diabetic foot gangrene complicated by osteomyelitis or joint destruction. Only patients with affected bone at the metatarsals or toes were studied. **Table 1** shows the preoperative data, including age, sex, race, height (HT), body weight (BW), body mass index (BMI), dialysis status, duration of diabetes (years), duration of dialysis (months), white blood cell (WBC) count (/μL), C-reactive protein (CRP; mg/dL), hemoglobin (Hb; g/dL), platelet (PLT) count ($\times 10^4$/μL), HbA1c (%), ankle-brachial index (ABI), toe number, and number of affected toes. WBC count, CRP level, Hb, and PLT count were measured just before the first operation.

Ethical Considerations

The study was approved by the ethics committee of the Nippon Medical School (No. M-2025-281). Consent was obtained from all patients by the opt-out method.

Operations

To identify the site of osteomyelitis or joint destruction, all patients underwent preoperative evaluation by CT scanning, MRI, and radiography (**Figure 1A and 1B**). Blood glucose was stabilized during preoperative hospitalization, and antibiotics were administered as needed.

When necessary, revascularization was sometimes performed before surgery. All affected sites, including bones, were surgically excised. Amputation was performed at the toe or metatarsal bones. Toe, transmetatarsal, Lisfranc, and Chopart amputations were classified as minor, and below-knee (transtibial) and above-knee (transfemoral) amputations were classified as major. Bone marrow was adequately exposed, and satisfactory bleeding was confirmed (**Figure 1C**). Surrounding necrotic tissue was also excised; however, as much adjacent viable tissue as possible was preserved to avoid or minimize reconstructive operations (**Figure 1C**). Postoperatively, patients received appropriate antibiotics for bacteria cultured from the surgical site, including soft tissues and bone marrow samples. In a representative case, secondary wound heal-

Table 2 Prognostic data

	Cases (n = 27)
Duration of hospitalization (days), median (range)	30 (9–190)
Adverse event	0 (0%)
Revascularization	
No	20 (74.1%)
Yes	7 (25.9%)
Percutaneous transluminal angioplasty	6 (22.2%)
Femoropopliteal bypass	1 (3.7%)
Recurrence	
No	23 (85.2%)
Yes	4 (14.8%)
Number of operations	
1	19 (70.4%)
2	5 (18.5%)
3 (Median 1)	3 (11.1%)
Negative pressure wound therapy	
No	25 (92.6%)
Yes	2 (7.4%)
Reconstruction	
No	26 (96.3%)
Yes	1 (3.7%)
Amputation	
Minor	26 (96.3%)
Toe	4 (14.8%)
Metatarsal	22 (81.5%)
Lisfranc or Chopart	0 (0%)
Major	1 (3.7%)

Values are number unless noted.

ing was successful without reconstructive surgery (**Figure 1D**). Reoperations were defined as more-proximal amputation or extended soft tissue damage in patients with unsatisfactory healing. The number of operations was defined as the initial operation plus reoperations. Recurrence was defined as a wound that occurred again at the same site after wound healing. Negative pressure wound therapy (NPWT) and split thickness skin grafting were performed if needed. Reconstructive surgery was performed only if secondary wound healing could not be achieved, in which case NPWT was used. All patients were treated in the hospital. Hospitalized duration was noted. Hospitalization was required when patients could not care for wounds without assistance.

Statistical Analysis

Variables were coded and statistically analyzed using R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria), EZR version 1.68 (Jichi Medical University, Saitama, Japan), and StatView version 5.0 (SAS Institute, NC) to avoid potential software problems[14–16].

A p value of <0.05 was considered to indicate statistical significance in all tests. The Wilcoxon rank sum test with continuity correction was used to compare WBC count and CRP level between patients with and without recurrence. Correlations among the variables WBC count, CRP level, and number of operations were assessed with the Jonckheere-Terpstra trend test or Pearson product-moment correlation. Cutoff values were calculated using the Youden index. Hallux involvement and numbers of toes affected between groups with and without recurrence were compared with the Pearson χ^2 test with Yate's continuity correction.

Results

A total of 27 cases of diabetic foot gangrene were treated surgically from 2015 to 2025 (**Tables 1 and 2**).

Age, Sex, Laboratory Data, and Preoperative Information

The median age of the patients was 63 years (range, 36–85). Of the 27 patients, 23 (85.2%) were male and 4 (14.8%) were female, which is consistent with the sex ratio reported in studies from multiple countries[17]. All patients were Japanese and had type 2 diabetes. The median values for HT, BW, and BMI were 164 cm (range, 131–177.2), 70.6 kg (range, 42–103.5), and 25.71 kg/m^2 (range, 16.93–33.44), respectively. Fifteen of the 27 patients (55.6%) did not receive dialysis. The median durations of diabetes and dialysis were 27 years (range, 4–40) and 0 months (range, 0–140), respectively. The median WBC count, CRP level, Hb, PLT count, HbA1c, and ABI were 9,400/μL (range, 3,800–27,200), 2.57 mg/dL (range, 0.13–28.45), 30.4 × 10^4/μL (range, 6.9–58.8), 7.1% (range, 4.8–11.4), and 0.98 (range, 0.51–1.69), respectively. Revascularization was performed in 7/27 (25.9%) cases.

Affected Sites and Operations

The hallux was the most affected toe in 15 of the 27 patients (55.6%), and one toe was affected in 20 of the 27 patients (74.1%). Bilateral toes were affected in 1 patient (3.7%). Twenty-six of the 27 (96.3%) patients had satisfactory healing, and 25/26 (96.2%) patients did not require reconstructive surgery. No adverse events were observed. One patient (3.7%) required a major amputation without reconstruction. Neither Lisfranc nor Chopart amputation was performed. NPWT was performed for 2 of the 27 (7.4%) patients. Split thickness skin grafting was performed for 1 patient (3.7%). Recurrence and multiple operations were noted in 4/27 (14.8%) and 8/27 (29.6%) cases, respectively. The median duration of hospitaliza-

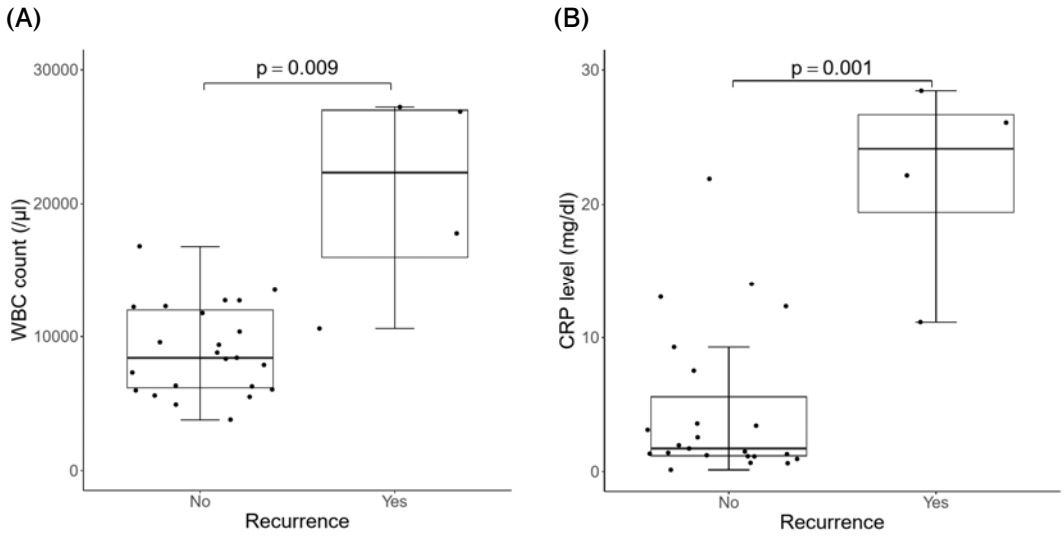

Figure 2 Correlations of recurrence status with laboratory variables
Recurrent cases had significantly higher WBC (**A**) and CRP (**B**) values ($p < 0.009$ and $p = 0.001$, respectively; Wilcoxon rank sum test). Bars show means ± standard deviation.

tion was 30 days (range, 9–190).

Factors Associated with Recurrence

In these patients with diabetic foot gangrene, WBC count was significantly higher in recurrent cases than in non-recurrent cases ($p = 0.009$; Wilcoxon rank sum test; **Figure 2A**). Similarly, CRP level was significantly higher in recurrent cases than in non-recurrent cases ($p = 0.001$; Wilcoxon rank sum test; **Figure 2B**). Interestingly, age, HT, BW, BMI, PLT count, HbA1c, ABI, revascularization, duration of dialysis, duration of diabetes, and duration of hospitalization were not significantly associated with recurrence (data not shown). Cutoff values for WBC count and CRP level were 17,300/μL (specificity 100%; sensitivity 75%) and 10.23 mg/dL (specificity 81.8%; sensitivity 100%), respectively, using the Youden index.

Factors Associated with Number of Operations

An elevated WBC count was significantly positively associated with the number of operations ($p = 0.018$, Jonckheere-Terpstra trend test; **Figure 3A**) as was a high CRP level ($p = 0.018$; Jonckheere-Terpstra trend test; **Figure 3B**). WBC count was significantly positively correlated with CRP ($r = 0.914$, $p < 0.001$; Pearson product-moment correlation; **Figure 3C**). Similarly, age, HT, BW, BMI, PLT count, HbA1c, ABI, revascularization, duration of dialysis, duration of diabetes, and duration of hospitalization were not significantly associated with the number of operations (data not shown).

The number of operations was higher in recurrent cases than in non-recurrent cases ($p = 0.012$; Pearson χ^2 test; **Table 3**). Hallux involvement and number of toes affected were not associated with recurrence. The one patient (3.7%) requiring major amputation underwent dialysis and 3 re-operations and had a WBC count of 26,900/μL and a CRP level of 28.45 mg/dL.

Discussion

In this study, diabetic foot gangrene with osteomyelitis or joint destruction could be cured without major amputation by exposing bone marrow and utilizing adjacent skin. Although some patients developed recurrence or required a reoperation, this therapeutic strategy appears to be useful for diabetic foot gangrene with osteomyelitis or joint destruction. WBC count and CRP level were significantly associated with reoperation and recurrence. Moreover, WBC count was significantly correlated with CRP. The possibility of recurrence or reoperation should be considered when WBC count or CRP level is high. It is not surprising to identify an association of increased WBC count/CRP level with recurrence/reoperation. Laboratory findings are useful in determining the severity of foot infections and thus can be used as diagnostic and prognostic indicators. Elevations in WBC count and CRP level are associated with poorer glucose metabolism and the presence of infections such as osteomyelitis, which has been shown to be a strong predictor of prognosis. Therefore, these markers may indirectly predict the need for reoperation and recurrence. However, duration of hospitalization could not be estimated in this study.

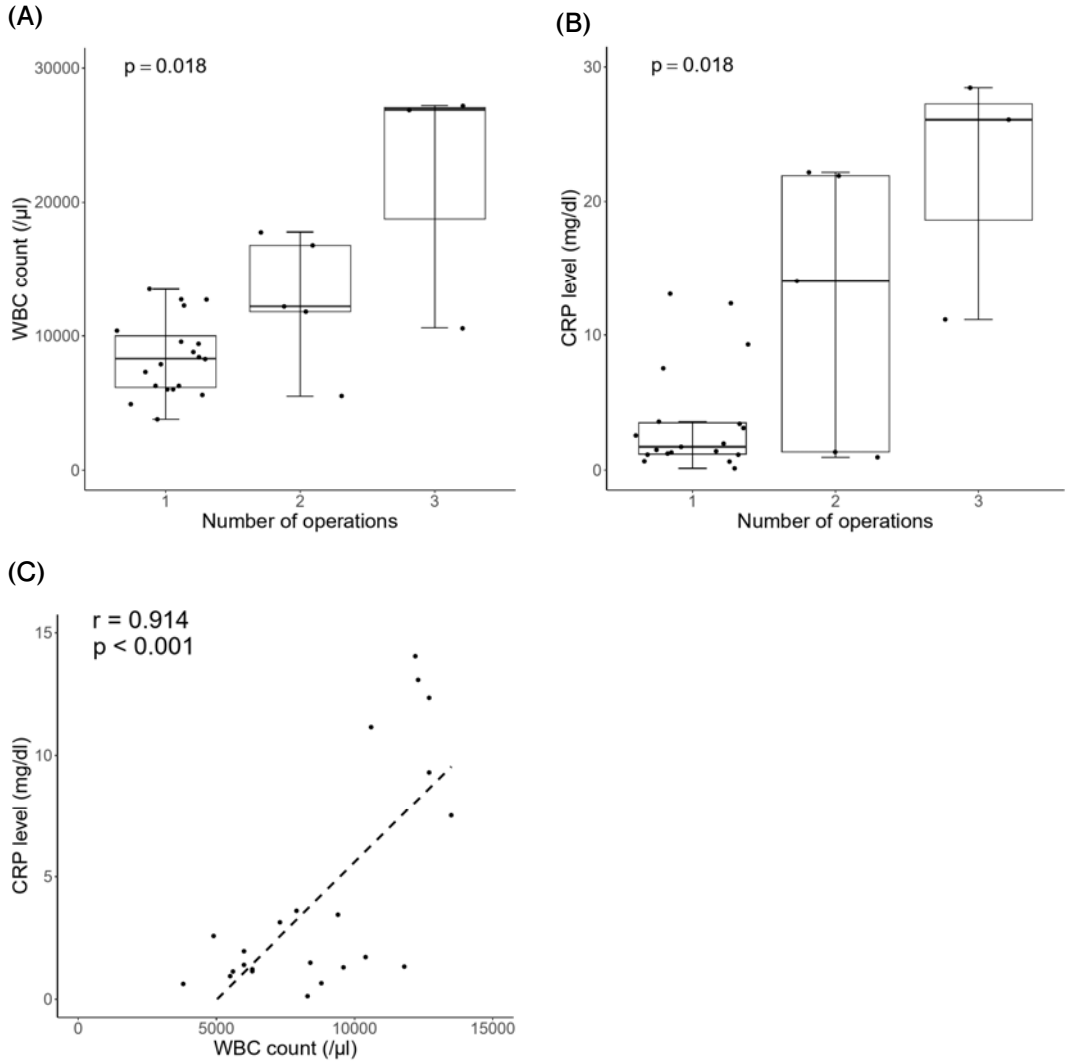

Figure 3 Correlations of number of operations with laboratory variables
WBC count (**A**) and CRP level (**B**) were significantly positively associated with the number of operations ($p = 0.018$ and $p = 0.018$, respectively; Jonckheere-Terpstra trend test). Bars show means ± standard deviation. WBC count was significantly positively correlated with CRP level (**C**) ($r = 0.914$, $p < 0.001$; Pearson product-moment correlation).

Table 3 Association of recurrence with clinical factors

Variable	Recurrence		χ^2	p-value
	No	Yes		
Number of operations				
1	19	0	7.54	0.006*
>1	4	4		
Involvement of hallux				
Yes	10	2	7.98×10^{-31}	1
No	13	2		
Number of toes				
1	17	3	9.73×10^{-32}	1
>1	6	1		

Values are number unless noted.
* $p < 0.05$

Although glycemic control and early intervention for diabetic foot conditions have decreased the need for major amputations, a substantial number of patients require minor amputation[18]. Minor amputation is associated with increased risks of recurrence and major amputation due to complications related to diabetes, increasing the likelihood of wound healing failure[7]. Therefore, we developed and investigated the usefulness of a safer surgical approach that minimizes amputation extent. Only one patient required a major amputation, probably because the infection progressed beyond visually apparent boundaries or because the infected tissue may not have been fully removed during amputation. In cases of poor infection control, wider debridement is required.

In previous reports, ABI levels were similar in patients

with failed or successful transmetatarsal amputations[19]. The timing of revascularization, ie, before or after transmetatarsal amputation, was not associated with wound healing[20]. Intriguingly, ABI and revascularization were also not associated with reoperation or recurrence in the present study. However, none of the present patients had a very low ABI level (<0.4)[5]. Such ABI cases might need to be considered separately.

For diabetic foot ulcer or gangrene, soft tissue repair is a matter of concern. If the defect is small, secondary wound healing can be expected. Simple primary suture is selected, especially for major amputations, because sufficient soft tissue can be utilized to close the wounds[6]. However, simple primary suture can be used for minor amputations only if the surrounding soft tissue permits[6]. In diabetic foot and gangrene, the amount of viable surrounding soft tissue is often insufficient. Moreover, infection or ischemic conditions might cause breakdown of the suture. Skin grafting is useful, but adequate wound bed preparation is crucial, and the presence of infectious conditions is undesirable[21]. Skin grafting relies on revascularization into the wound bed itself, and NPWT is preferred for wound bed preparation[21]. Local flaps often yield favorable functional and cosmetic results[22] because they are inheritably perfused and can cover avascular structures[23]. However, viable and sufficient soft tissue is required near the defect. Free flaps are useful because they can be used even when the defect remains infectious[24]. "Free" in this context means that the arteriovenous vascular pedicle to the flap is detached at its origin, transferred to the defect, and anastomosed to recipient vessels near the wound[25]. A viable artery that can be anastomosed is necessary. However, free flaps cannot be used in ischemic conditions.

Bone marrow contains multipotent cells related to skin wound healing, and recent reports highlight the role of multipotent cells in promoting such healing[10,26]. Our approach allows for exposure of bone marrow during amputation, which supplies essential cells for wound healing, thus enabling healing of more distal tissues. Although the risk of osteomyelitis recurrence or progression from bone marrow exposure is a concern, previous studies noted that bone marrow cells can differentiate into macrophages with phagocytic capabilities[27]. Another study reported that if the infected tissue can be adequately removed, bacteria is expelled naturally alongside granulation tissue formation[10].

In this study, minor amputations were performed and necrotic tissue was excised. As much viable surrounding soft tissue was preserved as possible, even if only thin skin remained. This operation is similar to fillet flap coverage[22]. However, because it was performed in ischemic conditions or when soft tissue was sometimes very thin, this operation substantially differs from the use of a fillet flap. When infection was controlled, the defect exhibited secondary healing and successful healing. One patient needed split thickness skin grafting, but there was no graft failure, probably because wound bed preparation was sufficient and infections were adequately controlled before skin grafting.

We should note that our study had several limitations. The numbers of patients and lesions were small, and all patients were analyzed retrospectively.

Conclusion

Fascinating reconstructions for diabetic ulcer and gangrene have recently been reported[25,28–30]. Bone marrow exposure therapy for diabetic foot gangrene is simple and can be useful. Elevated WBC count and CRP level may predict recurrence and number of operations. The strategies used in this study do not require sophisticated surgical skills or expensive devices or drugs. We thus conclude that minor amputation with bone marrow exposure therapy is potentially useful for diabetic foot gangrene. Future research should examine larger cohorts and compare this treatment with other therapies.

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References

1. International Diabetes Federation. IDF Diabetes Atlas 11th Edition [Internet]. Brussels: International Diabetes Federation; 2025. [cited 2025 Jul 6]. Available from: https://diabetesatlas.org/media/uploads/sites/3/2025/04/IDF_Atlas

_11th_Edition_2025.pdf
2. Charvat H, Goto A, Goto M, et al. Impact of population aging on trends in diabetes prevalence: a meta-regression analysis of 160,000 Japanese adults. J Diabetes Investig. 2015 Sep;6(5):533–42.
3. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012 Jun;54(12):e132–73.
4. Berendt AR, Peters EJ, Bakker K, et al. Diabetic foot osteomyelitis: a progress report on diagnosis and a systematic review of treatment. Diabetes Metab Res Rev. 2008 May-Jun;24 Suppl 1:S145–61.
5. Boulton AJ, Armstrong DG, Albert SF, et al. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. Diabetes Care. 2008 Aug;31(8):1679–85.
6. Frykberg RG, Zgonis T, Armstrong DG, et al. Diabetic foot disorders. A clinical practice guideline (2006 revision). J Foot Ankle Surg. 2006 Sep-Oct;45(5 Suppl):S1–66.
7. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. N Engl J Med. 2017 Jun 15;376 (24):2367–75.
8. Badiavas EV, Falanga V. Treatment of chronic wounds with bone marrow-derived cells. Arch Dermatol. 2003 Apr;139(4):510–6.
9. Dama G, Du J, Zhu X, Liu Y, Lin J. Bone marrow-derived mesenchymal stem cells: a promising therapeutic option for the treatment of diabetic foot ulcers. Diabetes Res Clin Pract. 2023 Jan;195:110201.
10. Yamaguchi Y, Yoshida S, Sumikawa Y, et al. Rapid healing of intractable diabetic foot ulcers with exposed bones following a novel therapy of exposing bone marrow cells and then grafting epidermal sheets. Br J Dermatol. 2004 Nov;151(5):1019–28.
11. Yamaguchi Y, Kubo T, Murakami T, et al. Bone marrow cells differentiate into wound myofibroblasts and accelerate the healing of wounds with exposed bones when combined with an occlusive dressing. Br J Dermatol. 2005 Apr;152(4):616–22.
12. Yamaguchi Y, Sumikawa Y, Yoshida S, Kubo T, Yoshikawa K, Itami S. Prevention of amputation caused by rheumatic diseases following a novel therapy of exposing bone marrow, occlusive dressing and subsequent epidermal grafting. Br J Dermatol. 2005 Apr;152(4):664–72.
13. Hinchliffe RJ, Forsythe RO, Apelqvist J, et al. Guidelines on diagnosis, prognosis, and management of peripheral artery disease in patients with foot ulcers and diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020 Mar;36 Suppl 1:e3276.
14. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant. 2013 Mar;48(3):452–8.
15. Hoashi T, Watabe H, Muller J, Yamaguchi Y, Vieira WD, Hearing VJ. MART-1 is required for the function of the melanosomal matrix protein PMEL17/GP100 and the maturation of melanosomes. J Biol Chem. 2005 Apr 8;280 (14):14006–16.
16. Miyazaki S, Hoashi T, Tone Y, et al. Narrow histopathological margins are acceptable in surgical resection of basal cell carcinoma in Japanese: a single-center retrospective study. J Nippon Med Sch. 2024;91(3):296–306.
17. Lin CW, Armstrong DG, Lin CH, et al. Nationwide trends in the epidemiology of diabetic foot complications and lower-extremity amputation over an 8-year period. BMJ Open Diabetes Res Care. 2019 Oct 11;7(1):e000795.
18. Galway U, Chahar P, Schmidt MT, et al. Perioperative challenges in management of diabetic patients undergoing non-cardiac surgery. World J Diabetes. 2021 Aug 15;12 (8):1255–66.
19. Nguyen TH, Gordon IL, Whalen D, Wilson SE. Transmetatarsal amputation: predictors of healing. Am Surg. 2006 Oct;72(10):973–7.
20. Shi E, Jex M, Patel S, Garg J. Outcomes of wound healing and limb loss after transmetatarsal amputation in the presence of peripheral vascular disease. J Foot Ankle Surg. 2019 Jan;58(1):47–51.
21. Ramanujam CL, Han D, Fowler S, Kilpadi K, Zgonis T. Impact of diabetes and comorbidities on split-thickness skin grafts for foot wounds. J Am Podiatr Med Assoc. 2013 May-Jun;103(3):223–32.
22. Kuntscher MV, Erdmann D, Homann HH, Steinau HU, Levin SL, Germann G. The concept of fillet flaps: classification, indications, and analysis of their clinical value. Plast Reconstr Surg. 2001 Sep 15;108(4):885–96.
23. Attinger CE, Ducic I, Zelen C. The use of local muscle flaps in foot and ankle reconstruction. Clin Podiatr Med Surg. 2000 Oct;17(4):681–711.
24. Chang CH, Huang CC, Hsu H, Lin CM, Huang SM. Editor's choice - Diabetic limb salvage with endovascular revascularisation and free tissue transfer: long-term follow up. Eur J Vasc Endovasc Surg. 2019 Apr;57(4):527–36.
25. Felder JM, Nageeb E, Rocha I, Qasawa R, Moltaji S, Fuse Y. The role of flaps in preventing lower extremity amputations. Semin Vasc Surg. 2025 Mar;38(1):64–73.
26. Badiavas EV, Abedi M, Butmarc J, Falanga V, Quesenberry P. Participation of bone marrow derived cells in cutaneous wound healing. J Cell Physiol. 2003 Aug;196(2): 245–50.
27. Yamaguchi Y, Yoshikawa K. Cutaneous wound healing: an update. J Dermatol. 2001 Oct;28(10):521–34.
28. Evin N. Reconstruction of wagner grade 4 diabetic foot ulcers with the superficial circumflex iliac artery perforator free flap. microsurgery. 2025 May;45(4):e70068.
29. Suh HS, Oh TS, Hong JP. Innovations in diabetic foot reconstruction using supermicrosurgery. Diabetes Metab Res Rev. 2016 Jan;32 Suppl 1:275–80.
30. Feng J, Thng CB, Wong J, et al. Outcome of rotation flap combined with incisional negative pressure wound therapy for plantar diabetic foot ulcers. Arch Plast Surg. 2025 May 15;52(3):169–77.