A Retrospective Analysis of Amputation Risk Due to Diabetic Foot and Angioplasty and Free Flap Transfer to Reduce Major Amputation

Masaki Fujioka

Abstract

Foot ulceration in persons with diabetes is the most frequent precursor to amputation, which impairs their activities. The aim of this chapter is to describe factors that lead to amputation of a diabetic foot, and propose a management strategy to prevent major amputation. I analyzed 233 patients who were admitted at the National Nagasaki Medical Center between 2008 and 2017 with foot ulcer and/or infection. We divided them into two groups: 152 patients with diabetes mellitus (DM) and 81 without DM. We analyzed their laboratory data, and evaluated the wound severity, complications of peripheral artery disease (PAD) and renal failure, and infection. Patients with DM ulcer were significantly more likely to receive amputation. Patients with DM were significantly more likely to develop infection, and tended to undergo emergency debridement. Among the patients with DM, the amputation group (85) showed significantly higher levels of CRP and WBC, and was more likely to develop infection, PAD, and renal failure. My results suggest that risk factors leading to leg amputation are severe infection and reduction of arterial blood flow. Early debridement to reduce infectious inflammation and angioplasty following free flap transfer are recommended to preserve legs.

Keywords: diabetic foot, diabetic gangrene, leg amputation, angioplasty, free flap transfer

1. Introduction

In the past four decades, over 42–56% of major lower extremity amputations in the United States and Western European countries have been due to diabetes mellitus (DM) [1–4]. The relative risk of major leg amputations for diabetes ranges from 5.1 to 31.5 times in comparison with that of nondiabetic populations [5, 6]. Extensive efforts have been made to improve the treatment of diabetes in regard to glycemic control and the prevention of diabetic complications, and foot ulcer treatments have improved for diabetic patients [7, 8]. Before 2004, trauma accounted for most amputations in the majority of hospitals, followed by malignancies [9]. However, the most common cause of amputation at present is diabetes mellitus [10, 11].
Amputation is the most appropriate therapy for an ischemic or infected limb, but the level at which to amputate is often difficult to determine. Patients who undergo only toe or trans-metatarsal amputation can walk on their own feet; however, those with major amputation require an artificial leg or a cane, which impairs their activities [12, 13]. The aim of this chapter is to describe factors that lead to amputation of a diabetic foot and propose a management strategy to prevent major amputation.

2. Materials and methods

A retrospective descriptive study including 152 diabetic patients among 233 patients with leg ulcers who were treated in our medical center was carried out between January 2008 and December 2017. All patients had been diagnosed with type II diabetes. Diabetic foot ulcers represent more than 65 percent of all leg ulcers.

To clarify the clinical characteristics of the diabetic foot, a comparison of foot ulcer patients with and without diabetes mellitus is conducted first, risk factors leading to amputation in cases of diabetic foot ulcer and “major” amputation in cases of diabetic foot are discussed, and a recommended strategy to avoid major leg amputation is presented.

Statistical analysis was performed using the Wilcoxon signed-rank test and chi-square test. The value of $p < 0.05$ was determined as significant.

The ethical committee of our medical center approved this study.

3. Results

3.1 Comparison of foot ulcer patients with and without diabetes mellitus

Profiles of foot ulcer patients with and without diabetes mellitus are shown in Table 1. Of the 233 patients with a foot ulcer, 63% (147) were men, and 37% (86) were women. Of course, levels of HbA1C and blood sugar in the diabetic foot group were significantly higher than those in the nondiabetic foot group, and men were more likely to develop leg ulcers in the diabetic patient group. There were no significant differences in CRP, WBC, serum albumin, or hemoglobin between the groups.

The severity of leg ulcers at discovery in patients with and without diabetes mellitus is shown in Table 2. In the groups, the ulcer stage based on the Wagner classification showed similar tendencies. About 80% of the diabetic foot group developed infection, being a significantly higher rate than in the nondiabetic foot group. There were no significant differences in CRP, WBC, serum albumin, or hemoglobin between the groups.

The frequencies of peripheral artery disease in foot ulcer patients with and without diabetes were 38.2 and 34.6%, respectively. There were no significant differences between the groups.

The frequencies of hemodialysis in patients with and without diabetes were 7.2 and 6.2%, respectively. There were no significant differences between the groups.
The frequencies of amputation in foot ulcer patients with and without diabetes were 53.9 and 34.6%, respectively. More than half of the patients with diabetes underwent amputation surgery, being a significantly higher rate than that in the nondiabetic foot group (Figure 3).

3.2 Comparison of foot ulcer patients with and without diabetes mellitus

We evaluated 85 amputated legs in 152 diabetic foot patients. Sixty-eight percent (104) of the patients were men, and 32% (48) were women. Profiles of diabetic patients with/without leg amputation are shown in Table 3.

Men were more likely to require amputation. CRP and WBC were significantly higher, and serum albumin was significantly lower in the major amputation group, suggesting that severe infection and malnutrition are risk factors for major leg amputation in diabetic foot patients.
Limb Amputation

Figure 1.
Infection of leg ulcers at discovery in patients with and without diabetes mellitus (MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-susceptible Staphylococcus aureus).

Figure 2.
The frequency of foot ulcer patients with and without diabetes, who required immediate debridement surgery.

Figure 3.
The frequency of amputation in foot ulcer patients with and without diabetes.
Sixty-nine (82%) of 85 amputees and 36 (57.6%) of 67 non-amputees with diabetes developed infection, showing a significant difference between the groups. More than half of amputated and only 17.9% of non-amputated patients with diabetes were complicated by peripheral artery disease, showing a significant difference between the groups (Figure 4). Furthermore, the frequency of hemodialysis in amputated patients (11.8%) was also significantly higher than that in non-amputated patients (1.5%) (Figure 5).

3.3 Comparison of diabetic foot ulcer patients who underwent major and minor leg amputation

Of the 85 amputees with diabetes, 44 patients underwent minor amputation, and 38 received major amputation. Seventy-one percent (58) were men and 29% (24) were women. Profiles of diabetic patients with/without leg amputation are shown in Table 4. Men were more likely to require major amputation. CRP and WBC were significantly higher, and serum albumin was significantly lower in the

|                      | Male/Female | Age         | Hb A1C (%) | Blood Sugar (mg/L) | CRP (mg/L) | WBC (× 10^9/L) | S-Albumin (g/dL) | Hemoglobin (g/dL) | P-value |
|----------------------|-------------|-------------|------------|-------------------|------------|----------------|-----------------|------------------|---------|
| Amputation-67        | 43/24       | 66.3±14.0   | 8.8±2.7    | 262.1±129.5       | 115.6±89.9| 10.9±6.1      | 3.0±0.8         | 11.0±2.6         | 0.35    |
| Amputation-67        | 61/24       | 65.0±17.1   | 8.5±2.2    | 251.2±122.6       | 202.0±93.1| 17.1±8.8      | 2.5±0.7         | 10.5±2.2         | <0.05*  |

Table 3.
Profiles of diabetic patients with and without leg amputation.

Figure 4.
The frequency of amputation in diabetic foot ulcer patients with and without peripheral artery disease.
major amputation group, suggesting that severe infection and malnutrition are risk factors for major leg amputation in diabetic foot patients.

4. Risk factors leading to leg amputation and strategy to prevent major amputation

Diabetic foot ulcers sometimes lead to minor or major amputation, with a high impact on patients’ life and its quality [14]. Our results suggest that risk factors for leg amputation in diabetic foot patients include male, complication of severe infection, complication of peripheral artery disease, complication of hemodialysis, and malnutrition.

4.1 Improvement of malnutrition

The importance of nutritional support in patients with wounds has been examined. Malnourished patients showed not only a higher frequency of
impaired wound healing but also an increased risk of postoperative cardiopulmonary and septic complications [15, 16]. Malnutrition cannot be improved in a short time after developing foot ulcers. Thus, patients requiring surgical treatment should also receive supplemental nourishment in the perioperative period [17]. Luo et al. suggested that the geriatric nutritional risk index was a reliable and effective predictive marker of patients’ amputation-free survival, and it could identify patients early with a high risk of amputation [18]. Appropriate blood sugar control and nutritional support are required for diabetic patients to prevent leg amputation. Malnutrition usually occurs in critical limb ischemia patients as well, because of a lack of appetite and sleeplessness due to chronic pain. These patients with peripheral artery disease also require pain control and nutritional support services [18].

4.2 Foot care for patients undergoing hemodialysis

The number of patients requiring hemodialysis has been growing because obesity-related renal diseases such as diabetes mellitus are increasing [19, 20]. Diabetic patients with renal failure had high risks of foot ulceration and lower limb complications [21]. Regarding cutaneous infection, Bencini et al. reported that the incidence of fungal infection in patients undergoing hemodialysis was 67% [22]. Because chronic renal failure patients exhibit impaired cellular immunity due to a decreased T-lymphocyte cell count, this could explain the increased prevalence of fungal infections [23]. Thus, difficulty healing wounds is a frequent problem in patients on hemodialysis [24]. Amputations of limbs are sometimes performed for these complex ulcers, because when patients receiving hemodialysis develop aggressive life-threatening infections such as sepsis, immediate surgical debridement is required in order to salvage the blood access line and save lives [25]. Fujioka reported that 13 of 17 wounds required immediate surgery, including amputation and debridement in patients with DM, while only 1 of 13 required immediate surgery in patients without DM [26].

Poor management of foot ulcers in patients receiving hemodialysis leads to prolonged ulceration, gangrene, amputation, depression, and death [27].

Marn et al. investigated the association between the implementation of a routine foot check program in diabetic incident hemodialysis patients and concluded that monthly foot checks are associated with a reduction of major lower limb amputations [28]. All patients on hemodialysis should be considered as being at high risk of developing foot complications and undergo foot checks frequently. If infection is suspected, antibiotics should be administered through the dialysis line immediately during dialysis.

4.3 Infection control

Diabetic foot infection is a common diabetic complication, which results in lower limb amputation if not treated properly. Patients with diabetes are likely to develop infections, because of the alteration of immune defense mechanisms such as a change in the neutrophil function, suppression of the antioxidant system, and modified humoral activity due to the hyperglycemic environment [29].

Once a diabetic foot develops infection, it progresses rapidly and requires the removal of all necrotizing tissue involving the bone, tendons, and skin (Figure 6).

If the toe infection progresses and spreads widely, the patient may have to undergo major amputation (Figures 7a and b). Thus, early and appropriate debridement to reduce infection is important.
4.3.1 Antibiotic treatment

Soft tissue infections in diabetic patients require multidisciplinary treatment including rapid surgical intervention, antibiotic treatment, and hyperbaric oxygen therapy to restrict the growth of pathogens [30–32]. Antibiotic therapy should be instituted immediately. The initial antibiotic should act on aerobic Gram-positive and Gram-negative bacteria but also on anaerobic bacteria. Systemic antibiotics have been demonstrated in many trials to be effective in treating acute diabetic foot infections. Tchero et al. performed a systematic review to assess the clinical efficacy of antibiotic regimens in the treatment of diabetic foot infections and concluded that piperacillin/tazobactam should be recommended for severe infections and the adjuvant use of topical agents with systemic antibiotics improved the outcomes compared with systemic antibiotics alone [33]. Mustățea et al. suggested that an
initial combination of third-generation cephalosporin, quinolone, and metronida-
zo. After germ identification, antibiotic therapy was administered according to the antibiogram [29]. Cellulitis, which shows inflammation and infection of the skin and subcutaneous tissue, can be treated with systemic Gram-positive bactericidal antibiotics only. However, if deep tissue infection, especially osteomyelitis, is suspected, removal of the infected bone and soft tissue, followed by 2–4 weeks of antibiotics, is required [30].

4.3.2 Surgical debridement

Regarding surgical intervention, early and appropriate debridement to reduce infection is recommended to achieve infection control (Figure 8).

If the infection invades deeper to the tendon, the lesions can often be extended and spread upward rapidly along the tendon tract, which can lead to systematic sepsis and require immediate limb amputation (Figure 9a and b). As the infection developing in the diabetic patients’ limbs progresses rapidly, physicians must decide on whether to carry out debridement before the infected lesion spreads upward.

Figure 8.
Views of debridement for necrotizing fasciitis in the diabetic patient’s right sole. All necrotizing, contaminated tissue was removed immediately.

Figure 9.
(a) A view of necrotizing fasciitis in the right big toe, which spreads upward rapidly.
(b) Intraoperative view showing the contaminated lesion extending along the extensor tendon tract.
Case presentations

Case 1. A 51-year-old man developed diabetic foot gangrene with osteomyelitis of the fifth toe, which had progressed for 2 weeks (Figure 10a). The patient underwent fourth and fifth toe amputation immediately, and cleansing to reduce infection was performed for 2 weeks (Figure 10b). As abundant granulation tissue developed on the wound surface, he underwent free skin grafting (Figure 10c). The wound had completely resurfaced by 1 month after skin grafting, and the patient could walk without a cane (Figure 10d).

4.3.3 Angioplasty for an ischemic foot

Peripheral artery disease (PAD) is observed in up to 50% of patients with a diabetic foot ulcer, and the presence of PAD is an important consideration in their management [34]. PAD affects the distal vessels and results in occlusion, which is one of the major causes of ulcer development and an increased risk of amputation. The treatment for these patients often requires challenging distal revascularization surgery or angioplasty to prevent limb amputation [35]. Revascularization is commonly performed in patients with critical limb ischemia and a diabetic foot ulcer, and the ulcer-healing rate after revascularization ranges from 46 to 91% [36]. Hinchliffe et al. reviewed the effectiveness of revascularization of the ulcerated foot in patients with diabetes and PAD 1 year after surgery and reported that limb salvage rates showed a median of 85% following open surgery, and more than 60% of ulcers had healed following revascularization. They concluded that revascularization improved rates of limb salvage compared with the results of conservatively treated patients [34].

Figure 10.
(a) Case 1. A view of diabetic foot gangrene with osteomyelitis of the fifth toe. (b) After fourth and fifth toe amputation, cleansing was performed for 2 weeks. (c) Intraoperative view showing free skin grafting on the wound. (d) A view of the foot 1 month after surgery showing favorable coverage of the wound.
Case presentations

Case 2. A 67-year-old man developed a diabetic foot ulcer of the right heel, which had progressed for 2 months (Figure 11a). His posterior tibial artery was not palpable. Enhanced computed tomography (CT) showed that circulation of his right lower leg was poor, with an ankle brachial pressure index (ABI) of only 0.53, which suggested that his leg ulcer might not heal spontaneously. We fashioned femoral-popliteal artery (FP) bypass to increase distal blood flow, and ABI improved to 0.83 (Figure 11b). As the patient’s foot received sufficient flow, he could safely undergo resurfacing surgery using a reversed sural flap successfully and could walk 3 months after surgery (Figure 11c–f).

Figure 11.
(a) Case 2. A view of a diabetic foot ulcer of the right heel. (b) Enhanced computed tomography scan image showing the poor circulation of the patient’s right lower leg due to obstruction of the right femoral artery (circles). After fashioning the femoral-popliteal artery bypass, increased distal blood flow was seen (small arrows). (c) Intraoperative view showing the debrided heel ulcer and design of the reversed sural flap. (d) Intraoperative view of heel reconstruction showing the transferred reversed sural flap. (e) A view of the reconstructed heel 3 months after surgery revealed favorable coverage of the wound. (f) The patient could walk 3 months after surgery.
**Case 3.** A 60-year-old man developed a diabetic foot ulcer and osteomyelitis of the calcaneus (Figure 12a). Following the removal of a sequester, he underwent FP bypass angioplasty, and ABI improved from 0.67 to 1.01 (Figure 12b). The bone-exposing wound was resurfaced using a free superficial circumflex iliac perforator (SCIP) flap (Figure 12c–e). One year after the surgery, good circulation had been achieved without infection or ulcer relapse (Figure 12f).

### 4.3.4 Advantages of resurfacing the amputation stump with a free flap

Standard stump plasty requires shortening of the remaining fine and vivid bone end to resurface the bone-exposing amputation stump (Figure 13a and b).

![Figure 12a](image1.png)  
**Figure 12a.** A view of a diabetic foot ulcer and osteomyelitis of the calcaneus.

![Figure 12b](image2.png)  
**Figure 12b.** Enhanced computed tomography scan image showing poor circulation of the patient’s right lower leg due to obstruction of right femoral artery (circle). After fashioning the femoral-popliteal artery bypass, increased distal blood flow was seen.

![Figure 12c](image3.png)  
**Figure 12c.** Intraoperative view showing the design of a free superficial circumflex iliac perforator flap.

![Figure 12d](image4.png)  
**Figure 12d.** Intraoperative view of the elevated SCIP flap. The arrow indicates the perforator of superficial circumflex iliac vessels.

![Figure 12e](image5.png)  
**Figure 12e.** Intraoperative view of the harvested SCIP flap.

![Figure 12f](image6.png)  
**Figure 12f.** A view of the reconstructed foot 1 year after surgery showing favorable coverage of the wound.
On the other hand, free flap transfer enables surgeons to maintain the bone length, which is a potential advantage, especially when amputation is performed at the trans-metatarsal lesion (Figure 14a–c).

This is because Chopart or transtibial amputation results in more debilitating functional outcomes than transmetatarsal amputation. Furthermore, transmetatarsal amputation preserves maximal foot length, allowing patients to achieve a better quality of life [37, 38].

Regarding the flap choice, the ideal flap is thought to be a good vascularized skin paddle with the same thickness and width as the wound and requiring a single-stage operation [39]. Perforator flaps are defined as flaps consisting of skin and/or subcutaneous fat, with a blood supply from isolated perforating vessels of a stem artery [40]. The development of perforator flaps has increased the number of potential donor sites because a flap can be supplied by any musculocutaneous perforator, and donor-site morbidity can be reduced [41, 42]. Furthermore, the advantage of this skin flap is that it is less invasive, so that the operation can be performed under local anesthesia if the wound is small.

Case presentation

Case 4. A 32-year-old man developed a diabetic foot ulcer on the step (Figure 15a). Following debridement, he underwent resurfacing surgery using a free superficial circumflex Iliac artery perforator flap (Figure 12b and c). As free SCIP flap transfer is less invasive, the operation can be performed under local anesthesia (Figure 15d). One year after the surgery, good circulation had been achieved without infection or ulcer relapse (Figure 15e).

The SCIP flap is recommended because it minimizes sacrifice at the donor site, causing no damage to the main vessels or muscles beneath the flap. The only disadvantage is that the pedicle vessel is sometimes short when a suitable recipient vessel cannot

Figure 13:
(a) A view of diabetic gangrene extending the first and second metatarsal bones. After removal of the necrotic bone, the navicular was exposed. (b) Intraoperative view of Chopart amputation followed by resurfacing with a local flap of the sole.
Figure 14.
(a) A view of a diabetic foot ulcer with osteomyelitis of the first and second metatarsal bones. (b) Intraoperative view of the harvested anterolateral thigh (ALT) flap. (c) A view of the reconstructed foot using a free ALT flap 1 year after surgery, showing favorable coverage, and the patient could walk without a cane.

Figure 15.
(a) Case 4. A view of a diabetic foot ulcer of the step. (b) Intraoperative view showing the design of a free superficial circumflex iliac perforator flap. (c) Intraoperative view showing the design of a free SCIP flap. (d) Intraoperative view showing that an SCIP flap transfer is less invasive, so the patient was awake and talking with the surgeon. (e) A view of the reconstructed foot 2 months after surgery revealed favorable wound coverage.
be found near the wound [43]. Identifying an acceptable recipient vessel around the contaminated area is not always easy. Chronic inflammation in recipient vessels caused by infection and fibrosis may be one of the factors leading to thrombosis of the anastomosed vessel [44]. So, it is important to select a flap with a long pedicle, as the suitable recipient vessel may be distant from the wound. The anterolateral thigh (ALT) flap is often chosen because it is supplied by the descending branch of the lateral femoral circumflex artery, which has an external diameter of more than 2 mm at the proximal end with a pedicle of more than 8 cm in length [45, 46]. This flap is also a perforator flap, so that a larger cutaneous or fasciocutaneous flap can be harvested from the thigh while avoiding the sacrificing of underlying muscle and large vessels [47, 48].

**Case presentation**

**Case 5.** A 66-year-old man developed a diabetic foot ulcer with osteomyelitis of the left fourth and fifth toes (**Figure 16a**). He had already undergone right below

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**Figure 16.**

(a) Case 5. A view of a diabetic foot ulcer. The fourth and fifth toes were amputated due to osteomyelitis.
(b) Intraoperative view showing the elevation of an anterolateral thigh (ALT) flap.
(c) Intraoperative view showing resurfacing of the bone-exposing wound with an ALT flap.
(d) A view of the reconstructed foot 2 months after surgery revealed that favorable resurfacing had been achieved and he could walk without a cane.
the knee amputation due to diabetic gangrene. Thus, he desired to preserve his left leg to walk. Following debridement, he underwent resurfacing surgery using a free ALT flap (Figure 16b and c). Two months after the surgery, good resurfacing had been achieved, and he could walk with an artificial right leg (Figures 16d).

5. Conclusion

I conclude that the risk factors of leg amputation due to a diabetic foot are complications of severe infection and PAD, so diabetic ulcer management should include the immediate removal of necrotic tissue and control of infection. The only way to prevent major amputation of a diabetic ischemic foot is angioplasty of the occluded lower extremity arteries, and reconstruction of the amputation stump using free flap transfers to preserve the foot length is a good option for preserving the walking function.
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