What is the Impact of Infrapopliteal Endovascular Intervention on Free Flap Survival in Diabetic Foot Reconstruction?

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Abstract

Background The combination of endovascular intervention and microvascular free flap transfer has been effectively used for the chronic ischemic wounds of lower limb. This study aimed to indicate the influence of angioplasty on the free flap survival in diabetic foot ulcer reconstruction.

Methods A retrospective research was conducted of 46 diabetic patients with chronic ulcer of the foot. All the patients underwent the free flap reconstruction because of their non-healing wound with tendon or bone exposure. Patient's demography, clinical data related to vascular status, vascular intervention, free flap transfer procedure were collected. Flap survival rate was compared between the group of severe arterial stenosis and non-severe group and between the different revascularization result groups as well.

Results The average was 56.2 ± 10.8 years with 14 men (30.4%) and 32 women (69.6%). All of 23 patients (50%) who had severe infrapopliteal arterial stenosis underwent endovascular intervention. The final result of the pedal arch was type 1 in 13/23 patients (56.5%), type 2A and 2B in 7/23 and 2/23 patients respectively and type 3 in only one patient. Total flap necrosis was in 5 cases (10.9%), marginal necrosis in 4 cases (8.7%) and wound dehiscence in 4 cases (8.7%). There was no significant difference of flap loss between the severe arterial stenosis patients and non-severe arterial stenosis patients. In severe arterial stenosis group, after endovascular intervention, patients with type 1 of pedal arch had a significantly lower rate of total flap necrosis compared to the others. There was also no association between using of revascularized recipient artery and flap survival.

Conclusions Our study revealed the crucial of quality of pedal arch on free flap survival. The PTA should aim to re-establish the complete pedal arch to increase the rate of wound healing as well as the flap success.

Background

Diabetic foot ulcer consequence of neuropathy and peripheral arterial disease (PAD) is a common complication of diabetes mellitus (DM). Although diabetic defects are mostly able to treat with conservative modalities or simple debridement and suture, a broad and deep ulcer with bone and tendon exposure is more challenging. The extensive diabetic foot ulcer with PAD often leads to major amputation that not only reduces the quality of life but also increase the mortality rate [1]. There are some studies successfully employed local flap or skin graft, however generally salvaging these ischemic limbs without a strong and reliable flap is limited [2, 3]. In 1985, Brigg et al. first combined the revascularization surgery and free tissue transfer to reconstruct the ischemic lower limb [4]. This combination led a trend in diabetic foot reconstruction in which the arterial bypass surgery played a crucial role to increase the blood supply for distal limbs as well as the free flap. Since the introduction of endovascular intervention with several advantages, this method has replaced the bypass surgery to be the primary indication in critical limb ischemia management [5]. Subsequently, numerous investigations of the combination between preoperative angioplasty and microvascular free flap surgery have been carried out. However, the

influence of percutaneous transluminal angioplasty (PTA) to the free flap success in diabetic patients has not been well established. Our purpose in the present study is to illuminate this matter.

Methods

A retrospective study was carried out on 46 diabetic patients who underwent foot defects reconstruction by the free flap in Plastic and Reconstructive Department of Ajou University Hospital from 2011 to 2019. Patients were indicated free flap because of their soft tissue defects with exposure of bones and/or tendons that could not be treated by the other simple procedures. Only patients with DM foot ulcers were included in the study. Patients with incomplete records would be also excluded. All the patients were followed up for more than 6 months.

Clinical data were collected via the patient's chart, radiographs of the lower extremity, preoperative and postoperative photographs. These data were patient's age, sex, medical histories, characteristics of the wounds, vascular status, detail of vascular intervention, characteristic of the flap, flap outcomes, complications and follow-up information.

Continuous variables were expressed as mean $\pm$ standard deviation. Chi-square test and Fisher's exact test were employed to analyze categorical variables. P-value < 0.05 was considered statistically significant. Statistical analyses were performed with IBM SPSS 20.0.

Treatment procedure

Treatment started with careful assessment of the wound as well as the status of the vessels. If there were any symptoms of infection such as redness, swelling or hot skin, debridement would be indicated. Simultaneously, patient would be further evaluated for vasculopathy and neuropathy, in case that we did not palpate or identify the distal pulsation of infragenicular arteries with handheld Doppler. Patients routinely underwent pre-operative CT angiography for evaluation of the infrapopliteal arterial condition and flap planning as well. According to the results of CT angiography, the severity of stenosis was graded as shown in Table 1. Patients who had grade 4 and 5 stenosed vessels were called the severe PAD group. All the patients of this group underwent PTA for increasing the distal perfusion for the foot via the pedal arch. Post-angioplasty pedal arch was classified as shown in Table 2. Free flap transfer surgery was performed once there was at least one patent blood flow to the foot and the recipient base was clean.

Table 1
Grading of severity of arterial stenosis [6]

Grade	Criteria
0	Normal patency
1	Mild (stenosis of less than 25% of diameter)
2	Moderate (stenosis of 25% – 50% of diameter)
3	Moderate severe (stenosis of 50% – 75% of diameter)
4	Severe (stenosis of 75% – 99% of diameter)
5	Complete occlusion

Table 2
Classification of pedal arch [7]

Types	Blood supply
Type 1	From both DPA and plantar artery
Type 2A	Only from DPA
Type 2B	Only from plantar artery
Type 3	Both DPA and plantar arteries occluded

Results

A total of 46 foot-defects in 46 diabetic patients were covered with free flaps, the patient's background data were shown in Table 3. The average age of patients was 56.2 ± 10.8 years (range from 37 to 80 years old) 14 men (30.4%) and 32 women (69.6%). Of 46 patients, eight patients (17.4%) were with end-stage renal disease (ESRD) and 17 (37%) patients were active smokers. The most common location was forefoot (n = 15) followed by heel and dorsum (n = 11 and n = 10 respectively), the remainder located in lateral malleolar (n = 6), plantar (n = 2) and ankle (n = 2) (Table 3.).

Table 3
Patient's demographic detail

Characteristic		No of patient (%)
Sex	Male	32 (69.6)
	Female	14 (30.4)
Location of defect	Forefoot	15 (32.6)
	Dorsum	10 (21.7)
	Heel	11 (23.9)
	Plantar	2 (4.3)
	Ankle	2 (4.3)
	Lateral malleolar	6 (13)
Comorbidity	ESRD	8 (17.4)
	Severe PAD	23 (50)
	Smoking	17 (36.9)
Infection		13 (28.3)

Twenty-three patients (50%) were diagnosed with severe PAD with grade 4 and 5. Single-arterial stenosis was found in 9/23 patients (39.1%), double-arterial stenosis in 7/23 patients (30.4%) and triple-arterial stenosis in 7/23 patients (30.4%). All of severe PAD patients underwent PTA a couple of days before the free flap surgery. The mean interval between PTA procedure and free flap surgery was 15.43 ± 12.28 days, range from 4 to 54 days. Angioplasty failed in two cases consisted of one anterior tibial artery (ATA) among single-arterial stenosis patients and one posterior tibial artery (PTa) among triple-arterial stenosis patients. The post-angioplasty pedal arch was type 1 in 13/23 patients (56.5%), type 2A and 2B in 7/23 and 2/23 patients respectively and type 3 in only one patient (Table 4.).

Table 4
Detail of vascular status of severe PAD group

No	Impaired vessels	Angioplasty	Interval (days)	Recipient artery	Type of pedal arch
1	ATA	ATA	4	ATA	1
2	ATA, PTa	ATA, PTa	32	PTa	1
3	ATA, PTa, PeA	ATA, PTa	24	ATA	1
4	ATA, PTa	ATA, PTa	12	PTa	1
5	PTa, PeA	PTa	26	ATA	2A
6	ATA, PTa, PeA	ATA, PeA	5	ATA	2A
7	ATA, PeA	ATA	10	ATA	1
8	ATA	ATA	7	PTa	2B
9	ATA	ATA	35	PTa	1
10	ATA, PTa, PeA	ATA, PeA	5	ATA	2A
11	ATA	ATA (fail)	8	ATA	2B
12	ATA	ATA	7	ATA	1
13	PTa	PTa	8	ATA	1
14	ATA, PTa, PeA	ATA, PeA	23	ATA	2A
15	PTa, PeA	PTa, PeA	5	ATA	2A
16	ATA	ATA	7	ATA	1
17	ATA, PTa, PeA	ATA, PTa	14	PTa	1
18	ATA	ATA	11	ATA	1
19	PTa, PeA	PeA	19	PTa	2A
20	ATA, PTa	ATA, PTa	7	ATA	1
21	ATA, PTa, PeA	ATA	16	ATA	2A
22	ATA, PTa, PeA	ATA, PTa (fail), PeA	54	ATA	3
23	ATA	ATA	16	ATA	1
ATA = Anterior tibial artery PTa = Posterior tibial artery PeA = Peroneal artery					

Two donor sites of free flap included anterolateral thigh (ALT) in 40 cases and medial sural artery perforator (MSAP) in 6 cases were used to cover the defects of foot. The flap size was ranged from 3 × 5.5 cm to 12 × 20 cm. Recipient vessels were 13 PTa, 33 ATA and its branch included dorsalis pedis artery (DPA) and first dorsal metatarsal artery. Among them, 18 recipient arteries (39.1%) were revascularized vessels. End-to-side method was done in 40 flaps (87%) and end-to-end was in six flaps (13%). 37 flaps had two veins and nine flaps had one vein only (Table 5.). Total flap necrosis was seen in five cases (10.9%). Of these patients, two new ALT flaps were successfully replaced in two patients and the other patients were treated with additional debridement, VAC, and split thickness skin graft. The other complications included marginal necrosis (4 flaps), wound dehiscence (4 flaps) treated with simple closure or skin graft without any special event. During the perioperative period, there was no in-hospital mortality, however, two patients died 5 months and 7 months post-operation because of pneumonia and urinary tract infection respectively. No further major amputation had been required for all the follow-up period.

Table 5
Flap characteristics

Characteristic		No. of patients (%)
Type of flap	ALT	40 (87)
	MSAP	6 (13)
Recipient art	ATA	33 (71.7)
	PTa	13 (28.3)
Arteriorrhaphy	E-E	6 (13)
	E-S	40 (87)
Vein	1	9 (19.6)
	2	37 (80.4)
Complication	Total flap necrosis	5 (10.9%)
	Marginal necrosis	4 (8.7%)
	Wound dehiscence	4 (8.7%)

Four of five total necrosis flaps were in patients with ESRD, analysis showed the significant association between ESRD and the flap failure ($p = 0.002$). There was no significant difference of the flap loss rate between the choices of flap, the types of arteriorrhaphy and using of revascularized recipient artery as well. The rate of total flap necrosis in patients who underwent PTA procedure because of severe PAD was not significantly higher than in patients without severe PAD. In the severe PAD group ($n = 23$), the rate of flap loss was significantly different between type 1 of pedal arch patients and the other types ($p = 0.024$).

Among these patients, total flap necrosis is only found in patients with type 2 or 3 of the pedal arch (Table 6.).

Table 6
Chi-square analysis for flap success

		Flap total necrosis	Flap success	<i>p</i>
ESRD	ESRD	4	4	0.002*
	No	1	37	
PAD	Severe PAD	4	19	0.346
	Non- severe PAD	1	22	
Recipient arteries	Revascularized	3	15	0.365
	Normal	2	26	
Post-angioplasty pedal arch (n = 23)	Type I	0	13	0.024*
	Type II and III	4	6	
* Statistically significant Non-severe PAD = Grade 0-3 Severe PAD = Grade 4 and 5				

Case Reports

Case 1

A 53-year-old man with a 17-year history of diabetes and ESRD admitted for an unhealed wound over the dorsal of right foot. The anterior tibial arterial pulse was not palpable in the physical examination. CT angiogram revealed total occlusion of the ATA at the proximal level (Fig. 1). In angiography, the status of ATA was confirmed. Immediate balloon angioplasty was performed, ATA was successfully revascularized, and complete blood flow in the pedal arch was resumed. After serial debridement, the tendon and bone were exposed. An ALT flap with one perforator was used for soft-tissue coverage, and the newly patent ATA was selected as the recipient artery and the recipient veins were concomitant veins. Arterial anastomosis and venous anastomosis were performed in end-to-side and end-to-end manner, respectively. No postoperative complications were noted, and a 4-month follow-up revealed a well-healing, well-perfused free flap. The patient was able to ambulate with no complaints.

Figure 1. (a) A chronic wound of dorsal foot. (b)(c) Anterior tibial artery was totally occluded, pre-operative angiography indicated the type 2B of the pedal arch. (d) Anterior tibial artery was successfully

revascularized, the foot was supplied by both dorsal pedis artery and plantar artery. (e) ALT free flap. (f) One day after operation. (g) 4 month post-operation.

Case 2

A 55-year-old man with a 20-year history of diabetes presented with diabetic gangrene on his 5th toe. Serial debridement and amputation were performed and free tissue transfer was considered for covering 5th metatarsal bone (Fig. 2). Preoperative angioplasty indicated the absence of blood flow from the PTa to the pedal arch because of total occlusion. He underwent balloon angioplasty of the left PTa and plantar artery. After angioplasty, complete pedal arch was seen with the supply from both DPA and the plantar artery. Eight days after revascularization, an ALT flap was harvested and anastomosed to the ATA in an end-to-side manner. No additional surgery was required, and a 4-years follow-up revealed a well-healing, well-perfused free flap without another wound.

Figure 2. (a) Soft-tissue defect with 5th metatarsal bone exposure. (b) Angiography showed total occlusion of posterior tibial artery and plantar artery. (c) Complete pedal arch (type 1) was seen post-angioplasty. (d) 13 × 9 cm ALT flap was performed. (e) 2 days post-operation. (f) 4 years follow-up.

Discussion

Recently, numerous studies have showed that extensive DM foot ulcer could be safely treated with free flap transfer [8–10]. A systematic review study based on 18 studies of free tissue transfer for ischemic lower limb wound coverage showed a high rate of free flap survival as 92% and limb salvage rate of 83.4% [11]. In 1985 Briggs et al. firstly described the concept of combining vascular bypass surgery and free tissue transfer which could effectively manage the ischemic limbs as well as covered the complex defects [4]. This method expressively increased the salvage rate of the critical ischemic diabetic limb. Subsequently, several studies on combination between vascular distal bypass surgery and free flap transfer have been performed [12–15]. Although bypass surgery was successfully used for chronic limb ischemia management earlier on, PTA has slowly superseded open surgical bypass because of its advantages included reducing complication and length of hospitalization, feasible in elder and patients with poor general condition or even in patients with severe multi-segmental occlusive disease [16–18]. In addition, with the introduction of small-scale balloon and drug-coated balloon, PTA is significantly effective with better primary patency and low rate of restenosis [19]. Our institute has recently employed PTA as the first-line treatment for infrainguinal PAD patients. In the present study, we combined PTA and free flap surgery for the ischemic chronic wounds in diabetic patients and the overall flap survival rate was 89.1% comparable to the previous studies. Although the flap survival rate and limb salvage rate were relatively high, Oh et al. reported some obstacle factors included PAD, history of previous angioplasty and using immunosuppressive agents after renal transplant [20]. Authors emphasized that PAD and having a history of angioplasty had a significantly higher risk of flap failure (17.59 times and 10.212 times respectively). Twenty-three patients in our study were grade 4 and 5 PAD patients with severe stenosis in at least one main of infrapopliteal arteries. Though four of five flaps loss were among severe PAD patients, the analysis showed no significant difference between the severe PAD patients and the other

patients. All of the severe PAD patients in this study underwent PTA before the flap transfer surgery to achieve the straight-line blood flow to the pedal arch, however, we failed to reconstruct the pedal arch in one patient classified as type 3. Despite having no impact on to amputation rate, the quality of pedal arch had affected the rate of wound healing and time to healing as well [7, 21]. In this series, we also found the crucial influence of quality of pedal arch to the free flap survival. Among 13 patients with complete final pedal arch after PTA procedure, there was no flap necrosis, while four flaps loss were found in the group of ten patients with compromised pedal arch.

Hong stated that the evaluation of recipient arteries perfusion and identification of an appropriate vessel may be the major challenge in reconstructive microsurgery [3]. Previous literatures showed that the appropriate recipient artery could be selected preoperatively via angiography or CT angiography images [6, 22, 23]. In addition, Kim et al. employed Doppler ultrasonography to check the recipient artery and demonstrated that over 40 cm/s of peak blood flow velocity (PBFV) should be achieved to assure the success in free tissue transfer [24]. Nevertheless, it was indicated that pre-operation blood flow measurement may not be similar to actual findings in surgery [3]. In our institute, we did not measure PBFV before the surgery but we preferred using CT angiography as a minimally invasive modality for vascular status assessment and flap planning as well. However, the final decision must be made based on the intraoperative condition of the arteries. The surgery would be abandoned if no sufficient vessel were found.

Based on the evidence of the safe utility of revascularized recipient artery, we also anastomosed the flaps to 18 arteries that had undergone PTA [22, 25]. Although three of 18 flaps totally necrosed, no significant correlation was found between the revascularized recipient artery and the flap loss rate.

End-to-side anastomosis was performed in 40 flaps because it was believed that preservation of major arteries had been very important in CLI patients. In addition, the flaps were also occasionally supplied by the retrograde blood flow, especially in case of intact pedal arch. Lee et al. found a significantly lower risk of wound complication of end-to-side anastomosis rather than end-to-end when they performed a study of factors affect the flap survival and complication [9]. Though heavy calcification of the arterial walls was common in PAD patients, we always tried to find the least atherosclerotic for anastomosis. The end-to-end modality would only be used if we could not find less diseased area or unsatisfied result after end-to-side anastomosis.

There was no consensus in using fasciocutaneous or muscle flap combined with skin graft. We believed that fasciocutaneous was sufficient for the diabetic foot ulcers often thin and superficial. In this study, ALT was our most common flap and MSAP flap was used as an alternative especially for the forefoot and small defects. However, because medial sural artery is considered as an important collateral around the knee, the MSAP flap should be avoided in order to prevent the further limb damage in patient with occlusion of popliteal artery [26, 27].

Conclusions

The diabetic foot ulcer always challenges surgeons because of prevalence of comorbidities, infection, neuropathy and vasculopathy. These chronic ischemic wounds are able to reconstruct with the combination of endovascular intervention and free flap. Our study found a significant association between the quality of post-angioplasty pedal arch and flap success rate. The endovascular intervention should aim to achieve the complete pedal arch not only for improvement of wound healing but also for optimal result of free flap.

Abbreviations

PAD: peripheral arterial disease; DM: diabetes mellitus; PTA: percutaneous transluminal angioplasty; ESRD: end-stage renal disease; ATA: anterior tibial artery; DPA: dorsal pedis artery; PTa: posterior tibial artery; ALT: anterolateral thigh; MSAP: medial sural artery perforator; PBFV: peak blood flow velocity.

Declarations

Ethical approval

This study was approved by the Institutional Review Board of Ajou Medical Center (AJIRB-MED-MDB-20-374).

Consent for publication

Not applicable.

Availability of data and materials

Please contact the corresponding author for data request.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

Conception and design: IJL. Data collection: DHL, DQT, WBL. Analysis and interpretation: DQT. HMH, DHL, WBL. Writing article: DQT. Critical revision of the article: HMH, IJL. Final approval of the article: all authors.

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Figures

Figure 1

(a) A chronic wound of dorsal foot. (b)(c) Anterior tibial artery was totally occluded, pre-operative angiography indicated the type 2B of the pedal arch. (d) Anterior tibial artery was successfully revascularized, the foot was supplied by both dorsal pedis artery and plantar artery. (e) ALT free flap. (f) One day after operation. (g) 4 month post-operation.

Figure 2

(a) Soft-tissue defect with 5th metatarsal bone exposure. (b) Angiography showed total occlusion of posterior tibial artery and plantar artery. (c) Complete pedal arch (type 1) was seen post-angioplasty. (d) 13x9 cm ALT flap was performed. (e) 2 days post-operation. (f) 4 years follow-up.