

Editor's Choice — Diabetic Limb Salvage With Endovascular Revascularisation and Free Tissue Transfer: Long-Term Follow up

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WHAT THIS PAPER ADDS

Care of the diabetic foot with peripheral vascular disease and soft tissue defect requires a multidisciplinary effort towards limb preservation. With changing times, lower limb revascularisation has now moved towards minimally invasive endovascular revascularisation often replacing open bypass surgery as the treatment of choice. Free tissue transfers are now performed in conjunction with angioplasty procedures instead of open bypass surgery. This long-term follow up study shows that combined endovascular revascularisation of the below knee vessels and free tissue transfer is a viable option for the salvage of diabetic ischaemic limbs.

Objective: Combining vascular bypass surgery with free flap coverage is one of the treatment methods for complex soft tissue defects in the ischaemic lower limb. Endovascular revascularisation has become the first line treatment for limb ischaemia in many centres. Surgeons now perform free tissue transfer after angioplasty. The early and long-term limb salvage rate in diabetic patients who had undergone infrapopliteal endovascular revascularisation and free flap reconstruction are assessed.

Methods: This was retrospective study of all consecutive diabetic patients who had undergone endovascular revascularisation with free flap reconstruction for lower limb salvage between 2008 and 2014. They were followed up for at least 2 years or to death (mean follow up 39 ± 17 months). Cox regression analysis was used to analyse variables influencing outcome.

Results: There were 55 patients who had undergone 60 procedures. Five patients had undergone the procedure to the contralateral leg. All tissue lesions were Wagner–Meggit classification Grades 3 or 4. Thirty-six patients had TASC C lesions and 24 patients with TASC D lesions. Combined below knee triple vessel disease was seen in 30% of the cases, 28% involved both the anterior and posterior tibial artery, 7% and 2% involved the anterior tibial or the posterior tibial and the peroneal arteries. The free flap success rate was 95%. The peri-operative mortality was 1.7%. Twenty-one cases required surgical re-intervention. Mean length of hospital admission was 32 ± 9 days. One and five year amputation free survival rates were 94% and 68%, patient survival rates were 95% and 67%, limb salvage rates were 93% and 91% and respectively.

Conclusions: The results show that excellent early and late limb salvage can be achieved with free tissue transfer based on endovascular revascularisation of infrapopliteal arteries. This can be a further treatment option in diabetic patients with complex soft tissue defects.

Keywords: Angioplasty, Diabetes mellitus, Limb, Lower extremity, Free tissue flaps

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INTRODUCTION

Diabetes mellitus is a global problem with patients all over the world facing the possibility of major limb amputation on a daily basis. Peripheral artery occlusive disease and infection are the major causes of lower limb amputation in these patients.^{1–4}

Dedicated management of ischaemia of the lower limbs with revascularisation has resulted in a decreased number of legs being amputated.^{5,6} However, in these patients there remains a constant threat of major limb amputation especially if there is extensive soft tissue loss.^{7,8} Close collaboration between the different surgical disciplines has improved the salvage rate of the critically ischaemic diabetic limb. Since the description of combining vascular bypass surgery and free flap coverage for ischaemic lesions of the lower limb in 1985 by Briggs et al.,⁹ this method has become one of the treatment options for ischaemic lower limbs with a complex soft tissue

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defect.^{9–15} But with the introduction of endovascular revascularisation for peripheral arterial occlusive disease in many centres, it has become the first line treatment for critical limb ischaemia. This technique has evolved over the past 15 years and in many centres “endovascular first” has now become the primary treatment of choice for the revascularisation of critical limb ischaemia.^{16–19} As such, the reconstructive surgeon has had to adapt and perform microvascular anastomosis to the native diseased vessels instead of the healthy bypassing vessel during free tissue transfer. This is technically more demanding. In this study the long-term outcome of diabetic patients with critical limb ischaemia, salvaged with endovascular revascularisation of the below the knee vessels and free tissue transfer were assessed, and risk factors for amputation were identified.

METHODS

Patient selection

All diabetic patients with peripheral vascular disease and soft tissue defects of the foot who had undergone endovascular revascularisation with free flap reconstruction for lower limb salvage over a six year period between 2008 and 2014 were included in this study. The patients between 2008 and 2012 had been reported in a previous study.²⁰ In this study a further two years of data were included and all the patients were now followed up for at least two years. Every patient had soft tissue loss with bone or tendon exposure. This combination of treatment had to be performed to avoid major limb amputation below the knee or higher. Informed consent was obtained from all patients prior to performing this combination of treatment. The Institution Review Board of Dalin Tzu Chi General Hospital approved this study.

Procedure

The treatment algorithm used requires initial assessment of the wound by the reconstructive surgeon and the severity was classified according to Wagner–Meggitt classification. The Wagner–Meggitt classification is based on lesion depth (Grade 1 superficial ulcers, Grade 2 deep ulcers, Grade 3 ulcer with bone involvement, Grade 4 forefoot gangrene, Grade 5 whole foot gangrene). At the same time, dry or wet gangrene was determined. If the patient presented with dry gangrene, then revascularisation takes preference over debridement as the initial form of treatment. If the patient presented with fulminant infection, debridement of the infected portion of the foot was performed first to try and achieve adequate infection control and to prevent the patient from developing sepsis. When the patient presented initially with sepsis and septic shock, debridement was always performed first.

The patient was diagnosed with peripheral vascular disease, if they had a poor healing wound with absent distal pulses and ankle brachial index (ABI) < 0.8 or flattened pulsed volume recording (PVR). Clinically, if the peripheral pulses were absent, ABI and PVR were performed. Toe

pressure and TcPO₂ were not available in the hospital. If the readings were indicative of peripheral vascular disease the vascular surgeon was consulted. The patients were diagnosed with critical limb ischaemia if the ulcers or gangrene of the foot were due to peripheral vascular disease, a monophasic waveform was seen on PVR, and vascular disease was confirmed by angiography or concomitant angioplasty. Once angiography was done, the length of stenosis or occlusion was graded according to the TASC (Trans-Atlantic InterSociety Consensus) classification.²¹

Close cooperation between the two surgeons was essential as once revascularisation was performed, angiography, concomitant angioplasty, and debridement of the wound could be performed during the same anaesthetic episode. This was undertaken in the hybrid suite. The patients were placed on aspirin, clopidogrel, and cilostazol once endovascular revascularisation was successful. After revascularisation, the distal pulses were closely monitored at eight hourly intervals with hand held Doppler. Ideally if all three infrapopliteal vessels could be revascularised, this made reconstruction much easier. But often only one or two of the vessels could be revascularised. At times the revascularised vessel was not close to the defect that required reconstruction. But if either the anterior or the posterior tibial artery was patent then a flap with a longer pedicle was chosen or the muscle flap with a long enough pedicle was harvested to reach the patent revascularised artery. Endovascular revascularisation was not undertaken when limb salvage was not considered, due to severe deep seated infection, or if the patient presented with life threatening septic shock. It was not undertaken as an initial form of treatment in the younger patients with multi-segment stenosis or long segment occlusions. Free flap reconstruction was undertaken only if the pulses were palpable or a good quality biphasic or triphasic Doppler signal was detected with hand held Doppler and if there was an extensive soft tissue defect with bone or tendon exposure. Free tissue transfer was usually undertaken one week after revascularisation. Once the wound was clean and the revascularised vessels were patent, free flap reconstruction was performed in an operating room with surgical microscope facilities. The flap of choice depends on the size of the defect and the length of pedicle that is required to reach the defect from the recipient artery. In all these patients, the free flap was anastomosed end to side to the recipient artery. If there were collaterals close to the recipient artery, these collaterals were preserved and not ligated as in patients without peripheral vascular disease or as in head and neck reconstruction. This preserves better blood supply to the surrounding tissue and prevents a steal syndrome. If the defect was not large and there was no bone or tendon exposure, then skin grafting or secondary wound healing was allowed. These patients were followed up at both the cardiovascular and the plastic surgeon's outpatient clinics. ABI and PVR were performed at the first month and then at three monthly intervals. Hand held Doppler was used if the distal pulses were not detectable by clinical palpation. Colour duplex was not routinely used in

the follow up. Repeat angiogram or angioplasty was performed if there was a deterioration of the ABI/PVR.

All the patients were followed up in the outpatient department, until December 31, 2016, or to death. If they did not return for follow up, phone contact was made to ascertain if the patient was alive and if they had undergone further major limb amputation. The patient’s peri-operative and post-operative course in the first 30 days were carefully followed up and their surgical and medical complications were noted. The demographic data that were collected included age, gender, comorbid illnesses, defect location, defect size, Wagner–Meggit classification, TASC level, type of flap, length of surgery, flap survival, and limb salvage. The long-term outcome of this study was to determine patient survival rate, lower limb salvage rate, and amputation free survival rate, as well as assessing the risk factors for amputation.

Statistical analysis

SPSS version 22 was used for statistical analysis. Kaplan–Meier analyses were used to determine the flap success rate, limb salvage rate, patient survival rate, and amputation free survival rate. Cox proportional hazards regression analysis were used to analyse variables such as age, gender, coronary artery disease, cerebrovascular accident, end stage renal disease, hypertension, Wagner–Meggit, TASC, and interval between surgery and their influence on outcome. A *p* value of < 0.05 was considered significant.

RESULTS

A total of 60 legs underwent endovascular revascularisation with free flap reconstruction for limb salvage in 55 patients. In five of the patients, they had undergone a similar procedure to the contralateral leg. There were 35 male (64%) and 20 female (36%) patients. Their average age was 66.5 years old (range 49–89 years). Patient comorbidities are presented in Table 1. All of the patients had type II diabetes mellitus. Five patients (9%) had had contralateral amputation prior to this episode. All tissue lesions were Grades 3 or 4 according to Wagner–Meggit classification. Twenty-seven (45%) of the lesions were in the forefoot, eight (13%) were of the heel area, six (10%) lesions involved only the dorsal or the plantar foot, two (3%) lesions were located over the lateral foot, and there were 17 (28%) lesions where overlapping areas of the foot were involved (Table 2). All of the patients had TASC C or D lesions of the infrapopliteal arteries. There were 36 patients (60%) with TASC C lesions and 24 patients (40%) with TASC D lesions. Combined below knee triple vessel disease involvement was seen in 18 of the cases (30%); involvement of both the anterior tibial and the posterior tibial arteries was seen in 17 cases (28%); and involvement of the anterior tibial or the posterior tibial and the peroneal arteries was seen in four (7%) and two cases (3%) respectively. Isolated lesions of the anterior tibial artery were seen in 15 cases (25%) and the posterior tibial artery in four cases (7%). Involvement of both supra- and infrapopliteal arteries was seen in 31 (52%) of the cases (Table 3). The target artery to be revascularised was

Table 1. Baseline demographics of 55 diabetic patients undergoing endovascular revascularisation and free tissue transfer for limb salvage

	n (%)
<i>Gender</i>	
Male	35 (64)
Female	20 (36)
CAD	16 (27)
CVA	10 (17)
ESRD	21 (45)
HTN	29 (48)
Contralateral amputation	5 (9)

Patients were considered to have coronary artery disease, hypertension or CVA if the cardiologist or the neurologist had made the diagnosis previously. ESRD patients were patients on haemodialysis or peritoneal dialysis. CAD = coronary artery disease; CVA = cerebrovascular accident; ESRD = end stage renal disease; HTN = hypertension.

Table 2. Location of tissue defects and Wagner classification of 55 diabetic patients undergoing endovascular revascularisation and free tissue transfer for limb salvage

	n (%)
Forefoot	27 (45)
Dorsum	3 (5)
Plantar	3 (5)
Heel	8 (13)
Lateral foot	2 (3)
Mixed	17 (28)
Wagner–Meggit 3	32 (53)
Wagner–Meggit 4	28 (47)

Wagner–Meggit classification: Grade 1 = superficial ulcers; Grade 2 = deep ulcers; Grade 3 = ulcer with bone involvement; Grade 4 = forefoot gangrene; Grade 5 = whole foot gangrene.

discussed between the cardiovascular surgeon and the reconstructive surgeon. If possible, the artery closest to the lesion should be revascularised as this made for easier reconstruction as well as providing adequate perfusion to the required ischaemic angiosome (Fig. 1A–D). Other infrapopliteal arteries were also assessed for stenotic lesions and treated if feasible to potentially improve overall vascularity. This will improve circulation to the distal foot in the event of flap failure. Stenting was performed in 13 cases (22%), all in the superficial femoral artery or the iliac arteries. No stents were placed below the knee. All patients were placed on clopidogrel, cilostazol, and aspirin once angioplasty was performed. Endovascular revascularisation and free flap reconstruction were performed in staged procedures. The mean operation time for endovascular revascularisation was 109 ± 40 min and for free flap reconstruction was 234 ± 70 min. The mean interval between endovascular revascularisation and free flap reconstruction was 9 ± 6 days. The mean length of hospital admission was 32 ± 9 days. Fifteen of the patients were bedridden and were not ambulatory. All patients who were ambulatory before reconstruction remained ambulatory after reconstruction

Table 3. Characteristics of vascular lesions in 55 diabetic patients undergoing endovascular revascularisation and free tissue transfer for limb salvage

Artery affected	n (%)
Anterior tibial artery	15 (25)
Posterior tibial artery	4 (7)
Peroneal artery	—
Anterior + posterior + peroneal artery	18 (30)
Anterior + posterior artery	17 (28)
Anterior + peroneal artery	4 (7)
Posterior + peroneal artery	2 (3)
Supra- and infrapopliteal lesions	31 (52)
TASC C	36 (60)
TASC D	24 (40)

TASC = Trans-Atlantic Society Consensus.

The most common free flap used for reconstruction was the rectus femoris muscle flap in 26 cases (43%), closely followed by the vastus lateralis muscle flap in 24 cases (40%). The anterolateral thigh musculocutaneous flap was used in nine cases (15%) with the sartorius muscle flap used in one case (2%). The average flap size was 70 cm². The most commonly used recipient artery was the dorsalis pedis

artery followed by the posterior tibial artery (Fig. 2A–C). Thirty-six flaps (60%) were anastomosed to the dorsalis pedis, 12 flaps (20%) to the posterior tibial artery, and nine flaps (15%) to the anterior tibial artery. Only four patients (7%) in this series underwent endarterectomy at the planned anastomotic site. No revascularisation and free tissue transfer were performed during the same anaesthetic episode (Table 4).

All patients had multiple comorbid illnesses. The most common were the following: 29 (48%) hypertension, 21 (45%) renal failure, 16 (27%) coronary artery disease, and 10 (17%) cerebrovascular accident. The overall flap success rate was 95%. Peri-operative three month mortality occurred in one patient (1.7%). One patient died 2 weeks after free flap surgery due to sudden cardiac arrest. Peri-operative complications (≤ 30 days) related to endovascular revascularisation and flap reconstruction were seen in 26 patients (43%). The most common surgery related complications were seven patients (12%) with wound infection requiring further debridement, five patients (8%) with haematoma, four patients (7%) with partial flap loss, three patients (5%) with total flap failure, one patient (2%) with below knee amputation, one patient (2%) with donor

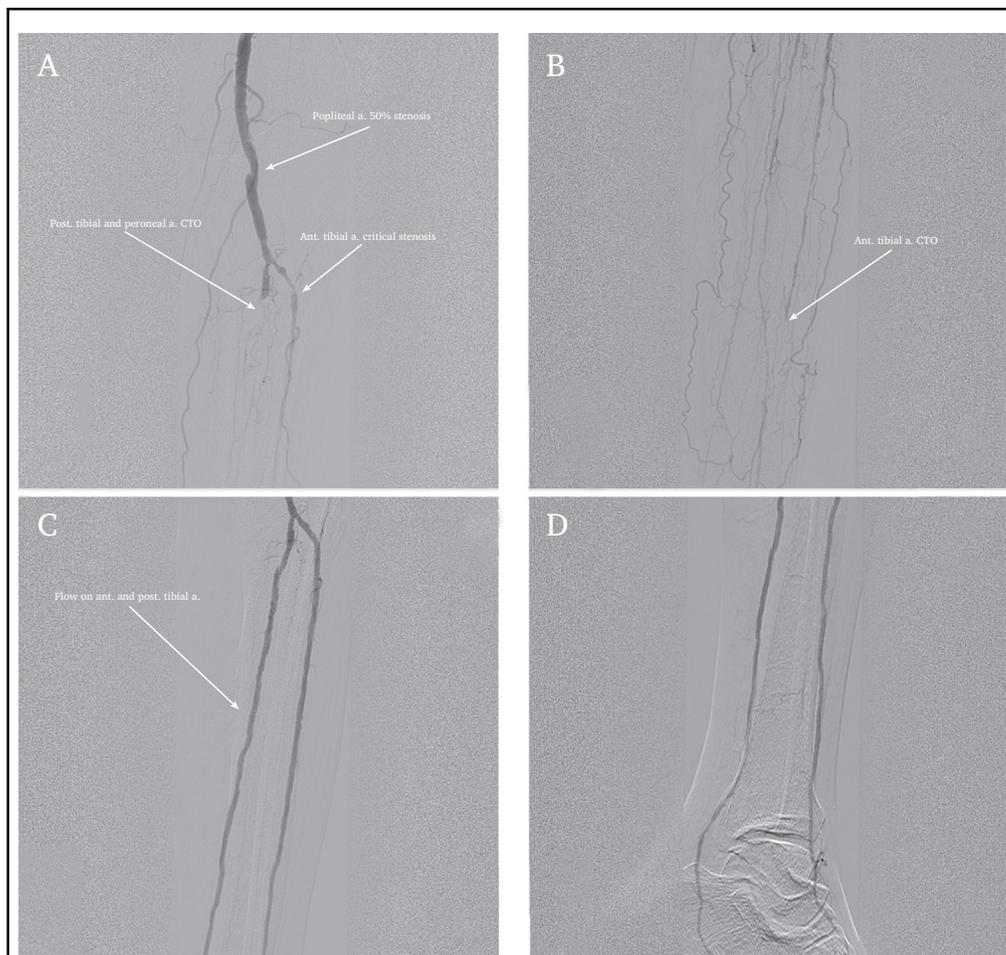


Figure 1. A–D. Angiogram shows Trans-Atlantic Society Consensus (TASC) D lesions of the infrapopliteal arteries and chronic total occlusion of the anterior tibial artery. Endovascular angioplasty was performed. Good flow was seen in the anterior tibial, posterior tibial, and pedal arteries after revascularisation. CTO = chronic total occlusion.



site haematoma. General post-operative complications were seen in five patients (8%). One patient (2%) developed aspiration pneumonia, one patient (2%) pulmonary oedema, one patient (2%) sudden death, one patient (2%) transfusion related acute lung injury, and one patient (2%) required cardiopulmonary resuscitation but made a full recovery. Diabetic foot ulcers recurred in five patients (8%) but were treated with conservative wet to dry wound care in the outpatient department. Of the three patients that encountered total flap failure, two were due to technical

difficulties encountered while anastomosing to a patent calcified recipient vessel. Regular wound care with normal saline wet dressings was performed and secondary healing took place. The third patient underwent below knee amputation due to persistent infection (Table 5). No immediate (<30 days) restenosis or re-occlusion of the feeding artery to the flaps was seen in this series. The mean follow up time was 39 ± 17 months. Twelve patients were lost to follow up at the outpatient clinic but were contacted by telephone.

Table 4. Characteristics of 60 reconstructions in 55 diabetic patients

	n (%)
<i>No. of Endovascular procedures</i>	
1	54 (90)
2	5 (8)
3	1 (2)
Stent deployed	13 (22)
<i>Type of free tissue flap</i>	
VL	24 (40)
RF	26 (43)
ALT	9 (15)
Sartorius	1 (2)
<i>Donor artery</i>	
DP	36 (60)
PT	12 (20)
AT	9 (15)
Others	3 (5)
<i>Recipient vein</i>	
Concomitant vein	36 (60)
GSV	23 (38)
Others	1 (2)

VL = vastus lateralis; RF = rectus femoris; ALT = anterolateral thigh; DP = dorsalis pedis; PT = posterior tibial; AT = anterior tibial; GSV = greater saphenous vein.

Long-term outcome

The one, two, and five year limb salvage rates were 93%, 91%, and 91% (Fig. 3). The one, two, and five year patient survival rates were 95%, 91%, and 67% respectively (Fig. 4). The one, two, and five year amputation free survival rates were 94%, 82%, and 68% (Fig. 5). The leg amputations in the four patients were due to overwhelming infection in the foot. Gender, age, Wagner–Meggit classification, site of defect, and end stage renal disease were not statistically significant in influencing the outcome of limb salvage. A longer interval between endovascular revascularisation and free tissue reconstruction as well as TASC D vascular lesions were associated with a higher risk of major limb amputation ($p = .043$ and 0.036 respectively) (Table 6).

Table 5. Medical and surgical complications

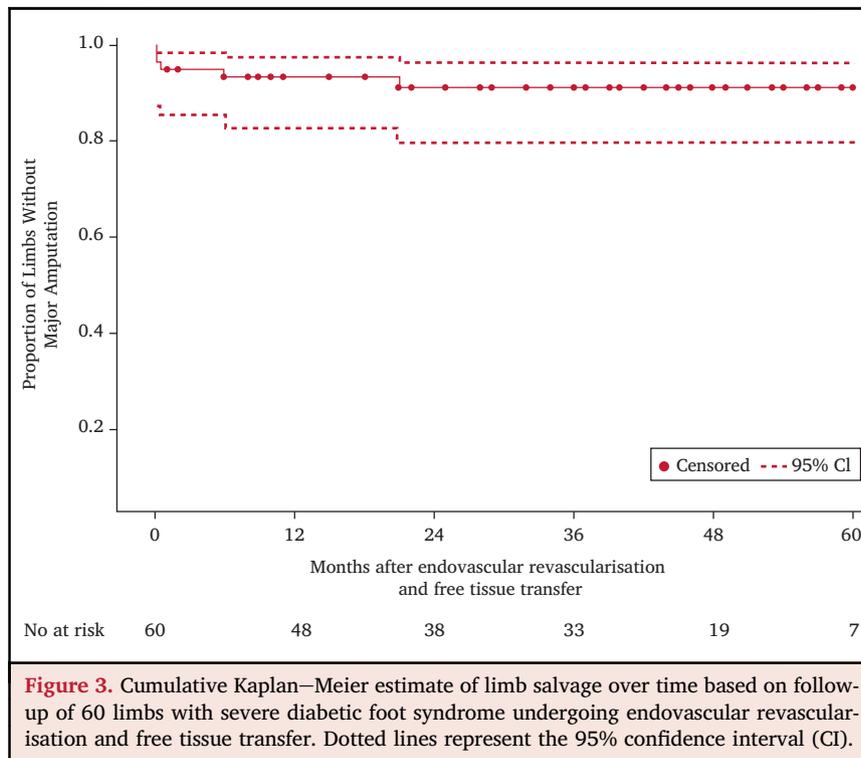
	n (%)
<i>Surgical complications</i>	
Partial flap failure	4 (7)
Total flap failure	3 (5)
Wound infection	7 (12)
Haematoma	5 (8)
Major limb amputation (BKA)	1 (2)
Donor site haematoma	1 (2)
<i>Medical complications</i>	
Pneumonia	1 (2)
Pulmonary oedema	1 (2)
Sudden death	1 (2)
TRALI	1 (2)

Peri-operative medical and surgical conditions are included if they occurred ≤ 30 days after surgery. BKA = below knee amputation; TRALI = transfusion related acute lung injury.

DISCUSSION

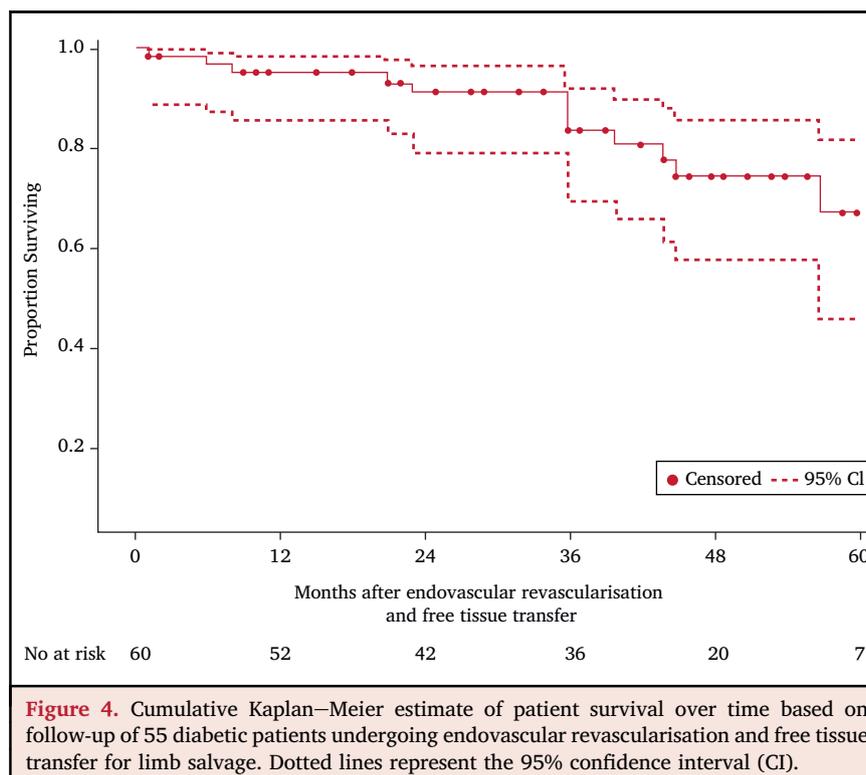
Revascularisation of the ischaemic leg prior to reconstruction is a well understood principle.²² But in the presence of an associated extensive soft tissue defect with bone or tendon exposure, coverage by free tissue transfer will be required. In 1985 Briggs et al.⁹ established the concept of combining vascular reconstruction with free flap surgery for limb salvage in the critically ischaemic limb. Since then numerous studies on vascular reconstruction and free flap transfer for critically ischaemic legs with extensive soft tissue defects have been published.^{10–14,22–24} Many limbs that would have had undergone major amputation, now have the possibility of being saved. Studies have found that after anastomosing the free flap to the bypassed vessel, they can serve as the sole outflow for the bypassed graft increasing the success rate of the bypass surgery.^{24–26} Lorensetti et al.²⁷ described how the transferred free muscle flap can function as a low resistance outflow bed, allowing the bypassed graft outflow to increase by as much as 50%. Mimoun et al.²⁸ introduced the idea that neo-vascularisation from the free muscle flap to the surrounding ischaemic tissue occurs three weeks after free flap surgery and can function as a “nutrient flap”. Randon et al.¹⁴ showed that with the establishment of these neo-vascularizations, the flap survived even when the bypassed vessel had occluded. These observations form the basis for the current consensus in the treatment of ischaemic lower limbs with extended soft tissue loss.

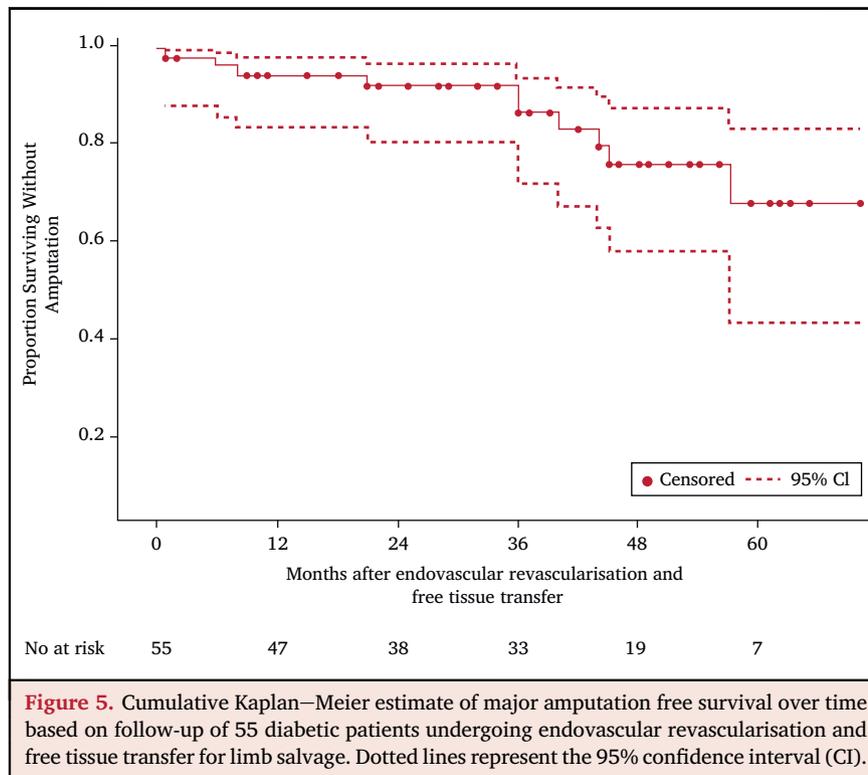
Comparison between this study and previous studies is difficult as most of the previous studies were based on open bypass revascularisation. But the studies provide a valuable baseline. The studies by Vermassen et al.¹⁰ and Randon et al.¹⁴ had a pure diabetic population. Vermassen reported a one and three year limb salvage rate of 84% and 65%. Randon found a one and three year limb salvage of 75.8% and 64.3%. The studies by Moran et al.¹¹ and by Tukiainen et al.¹³ had 25% non-diabetic patients. Moran et al. reported a five year limb salvage rate of 63% and Tukiainen found a five year limb salvage rate of 66%. These findings are similar to the current findings. The present study focused strictly on the diabetic population with endovascular revascularisation of the infrapopliteal arteries. The one and five year limb salvage rates for this study were 93% and 91%, and the one and five year patient survival rates were 95% and 67% respectively. As revascularisation of the lower limb has evolved from open bypass surgery to endovascular surgery, the reconstructive surgeons have needed to keep up with this evolution and were, in a way, forced to perform free flap reconstructive surgery after endovascular revascularisation. At present there are only a handful of studies that describe using endovascular revascularisation together with a free flap for lower limb salvage.^{20,29–34} The present study concentrated on the long-term follow up of diabetic patients who had undergone endovascular revascularisation together with a free tissue transfer for lower limb reconstruction. The study was further limited to endovascular revascularisation of the below knee arteries. All the current



patients had undergone angioplasty of the infrapopliteal arteries. The benefits of this approach were that pre-operative CT angiogram or standard angiogram was not required. This is different from Jang et al.,³⁰ and Oh et al.,³⁴ where a pre-operative CT scan was required, and DeFazio et al.,³¹ where a pre-operative angiogram was performed. The angioplasty was performed at the same time as the

angiogram in the present study. In this way, the patients were prevented from over exposure to unnecessary contrast medium. This was most beneficial to the group of patients where abnormal renal function was often found. This study demonstrated that even for patients with Wagner–Meggit stages 3 or 4 diabetic foot with infrapopliteal arterial lesions of TASC C or D, the use of





endovascular revascularisation with free flap reconstruction showed promising results and major limb amputation could be avoided in a large number of patients.

There was a 7–10 day interval between endovascular intervention and free flap reconstruction. Once the angioplastied vessels had remained patent, and no acute thrombosis or intimal dissection had occurred, free flap reconstruction was undertaken. The recipient vessel, the dorsalis pedis, the anterior tibial artery, or the posterior tibial artery were the most commonly used. As mentioned in Methods, often only one to two of the infrapopliteal vessels can be revascularised, and at times the revascularised artery is distant from the soft tissue defect. In these

scenarios a flap was chosen with a longer pedicle or a muscle flap with a longer pedicle was harvested, to allow reconstruction of the defect. This way the free tissue transfer provides further outflow to the newly revascularised vessel and provides vascularised tissue to an otherwise ischaemic area in an angiosome not supplied by the revascularised vessel. The concomitant veins were the most commonly chosen recipient veins. The greater saphenous vein was often used as the recipient vein. This would not have been possible if in situ greater saphenous vein bypass had been performed. If the recipient artery was atherosclerotic, a portion of the artery that was the least atherosclerotic was found and anastomosis was performed to the least diseased area. If this was not possible, endarterectomy was performed prior to vascular anastomosis. Free flap reconstruction was only abandoned if the vessel was so heavily calcified that endarterectomy was not possible, and when the surgical needle could not penetrate the calcified vessel wall thus making anastomosis impossible. If endovascular revascularisation had been successful in these patients, wound care with normal saline wet dressings was provided. Amputation can be prevented due to the improved circulation. In these patients bypass surgery would also be abandoned due to the poor condition of the vessels. With endovascular revascularisation these patients have the potential for limb salvage. A higher free flap failure rate, or a higher return to the operating room to salvage the compromised free flap was expected, as vascular anastomosis to the native diseased vessels was being performed, which tend to be more heavily diseased with atherosclerotic plaques and calcification than the bypassing graft, making microvascular anastomosis more

Table 6. Summary of statistical results of factors influencing limb salvage

Predictor	Limb salvage	p value
	HR (95% CI)	
Age	1.00 (0.93–1.08)	.91
Gender	0.67 (0.13–3.47)	.64
CAD	3.43 (0.46–25.50)	.23
CVA	1.07 (0.10–11.65)	.95
ESRD	0.24 (0.04–1.36)	.11
HTN	4.26 (0.63–29.01)	.14
Wagner	3.78 (0.78–18.29)	.10
TASC D	0.07 (0.005–0.84)	.036 ^a
Interval between surgery	1.09 (1.00–1.18)	.043 ^a

CAD = coronary artery disease; CI = confidence interval; CVA = cerebrovascular accident; ESRD = end stage renal failure; HR = hazard ratio; HTN = hypertension; TASC = Trans-Atlantic Society Consensus.

^a Statistically significant.

difficult. A 95% flap survival rate was achieved, with total flap failure seen in only three cases (5%). There was also a large group of patients with end stage renal failure on haemodialysis (21/55 patients, 38%). There was only one total flap failure and one partial flap failure in this group of patients. A high wound complication rate and bleeding from the recipient site were encountered. This may be due to the antiplatelet therapy that was prescribed after the endovascular procedure, which led to persistent oozing, with a higher rate of haematoma formation and therefore increased wound infection. The treatment algorithm was modified in the later cases, where these medications were stopped three days prior to reconstructive surgery, and restarted one day after free tissue transfer. Fewer haematomas and wound infections were encountered.

In this series the rectus femoris, the vastus lateralis, and the anterolateral thigh flap were the most commonly used flaps. The donor site and the recipient site could be prepared at the same time, within the same operative field. Two separate trays of surgical equipment were used: one for the recipient site and one for the donor site. In this way, infection contamination of the donor site was avoided. These flaps provided a long vascular pedicle. It also gave plenty of alternatives, in that one of the flaps from the same donor site could be chosen on the basis of the length of pedicle required and the condition of the vascular pedicle. There was also minimal donor site morbidity.

The limitations of this study were that the Wagner–Meggit classification was used instead of the Society for Vascular Surgery's wound ischaemia and foot infection (Wifi) classification. This is because this is a retrospective study, and the Wifi classification was only introduced in the latter part of this study in 2014. Toe pressure and TcPO₂ were not performed, which would further strengthen the diagnosis of critical limb ischaemia and the need for revascularisation. Also, the patients where free tissue transfer was not performed due to extremely calcified vessels, and those where angioplasty were not technically successful could not be included. A further limitation was that the number at risk at five years was very low.

The primary goal in limb salvage treatment is different from many Western countries. Because of cultural differences, the primary end point for limb salvage was not to restore function but rather limb preservation. Many patients regard limb preservation as the final desired result. Whether they were ambulant or not was not important. Many of the elderly patients hold a strong cultural belief that they need to preserve their body as intact as possible. This belief makes it extremely difficult to amputate even minor parts of their body. Therefore for these patients, limb preservation rather than regaining ambulation is the ultimate goal.

CONCLUSION

Management of the critically ischaemic diabetic foot requires close collaboration and teamwork between the different surgical disciplines. As the trend evolves towards

endovascular intervention as the initial form of revascularisation, plastic and reconstructive surgeons have to adapt to performing free tissue transfer to the native diseased vessels. The results of the long-term follow up in this study show that combined endovascular revascularisation and free tissue transfer is a valuable alternative to open bypass revascularisation and free tissue transfer for lower limb salvage in the diabetic patients.

CONFLICT OF INTEREST

None.

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REFERENCES

- Jude EB, Oyibo SO, Chalmers N, Boulton AJ. Peripheral arterial disease in diabetic and nondiabetic patients: a comparison of severity and outcome. *Diabetes Care* 2001;24:1433–7.
- Faglia E, Favales F, Quarantiello A, Calia P, Clelia P, Brambilla G, et al. Angiographic evaluation of peripheral arterial occlusive disease and its role as a prognostic determinant for major amputation in diabetes subjects with foot ulcers. *Diabetes Care* 1998;21:625–30.
- Adler AI, Boyko EJ, Ahroni JH, Smith DG. Lower extremity amputation in diabetes. The independent effects of peripheral vascular disease, sensory neuropathy and foot ulcers. *Diabetes Care* 1999;22:1029–35.
- Lavery LA, Armstrong DG, Wunderlicht RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. *Diabetes Care* 2006;29:1288–93.
- Luther M, Kantonen J, Lepäntalo M, Salenius J. Arterial intervention and reduction in amputation for chronic critical leg ischemia. *Br J Surg* 2000;87:454–8.
- Eskelinen E, Luther M, Eskelinen A, Lepäntalo M. Infra-popliteal bypass reduces amputation incidence in elderly patients: a population based study. *Eur J Vasc Endovasc Surg* 2003;26:65–8.
- Carsten III CG, Taylor SM, Langen EM, Crane MM. Factors associated with limb loss despite a patent infrainguinal bypass graft. *Am Surg* 1998;64:33–8.
- NasirKhan MU, Lall P, Harris LM, Dryjski ML, Dosluoglu HH. Predictors of limb loss despite a patent endovascular-treated arterial segment (PETAS). *J Vasc Surg* 2009;49:1440–5.
- Briggs SD, Banis Jr JC, Kaebnick H, Silverberg B, Acland RB. Distal revascularization and microvascular free tissue transfer: an alternative to amputation in ischemic lesions of the lower extremity. *J Vasc Surg* 1985;2:806–11.
- Vermassen FE, van Landuyt K. Combined vascular reconstruction and free flap transfer in diabetic arterial disease. *Diabetes Metab Res Rev* 2000;16:33–6.
- Moran SL, Illig KA, Green RM, Serletti JM. Free-tissue transfer in patients with peripheral vascular disease: a 10-year experience. *Plast Reconstr Surg* 2002;109:999–1006.
- Tukiainen E, Biancari F, Lepäntalo M. Lower limb revascularization and free flap transfer for major ischemic tissue loss. *World J Surg* 2000;24:1531–6.
- Tukiainen E, Kallio M, Lepäntalo M. Advanced leg salvage of the critically ischemic leg with major tissue loss by vascular and plastic surgeon teamwork : long term outcome. *Ann Surg* 2006;244:949–57.
- Randon C, Jacobs D, De Ryck F, Van Landuyt K, Vermassen F. A 15-year experience with combined vascular reconstruction and

- free flap transfer for limb salvage. *Eur J Vasc Endovasc Surg* 2009;**38**:338–45.
- 15 Serletti JM, Hurwitz SR, Jones JA, Herrera HR, Reading GP, Ouriel K, et al. Extension of limb salvage by combined vascular reconstruction and adjunctive free-tissue transfer. *J Vasc Surg* 1993;**18**:972–80.
 - 16 Faglia E, Dalla PL, Clerici G, Clerissi J, Graziani L, Fusaro M, et al. Peripheral angioplasty as the first choice revascularization procedure in diabetic patients with critical limb ischemia: prospective study of 993 consecutive patients hospitalized and followed between 1999 and 2003. *Eur J Vasc Endovasc Surg* 2005;**29**:620–7.
 - 17 Bosiers M, Hart JP, Deloosse K, Verbist J, Peeters P. Endovascular therapy as the primary approach for limb salvage in patients with critical limb ischemia: experience with 443 infrapopliteal disease. *Vascular* 2006;**14**:63–9.
 - 18 Verzini F, De Rango P, Isernia G, Simonte G, Farchioni L, Cao P. Results of the “endovascular treatment first” policy for infrapopliteal disease. *J Cardiovasc Surg* 2012;**53**:179–88.
 - 19 Nasr MK, McCarthy RJ, Hardman J, Chalmers A, Horrocks M. The increasing role of percutaneous transluminal angioplasty in the primary management of critical limb ischemia. *Eur J Vasc Endovasc Surg* 2002;**23**:398–440.
 - 20 Huang CC, Chang CH, Hsu H, Chiu CH, Lin CM, Lee JT, et al. Endovascular revascularization and free tissue transfer for lower limb salvage. *J Plast Reconstr Aesthet Surg* 2014;**10**:1407–14.
 - 21 Jaft MR, White CJ, Hiatt WR, Fowkes GR, Dormandy J, Razavi M, et al. An update on methods for revascularization and expansion of the TASC lesion classification to include below-the-knee arteries: a supplement to the inter-society consensus for the management of peripheral arterial disease (TASC II). *Ann Vasc Dis* 2015;**8**:343–57.
 - 22 Aboyans V, Ricco JB, Bartelink ML, Bjorck M, Brodmann M, Cohnert T, et al. Editor’s choice – 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases in collaboration with the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2018;**55**:305–68.
 - 23 Illig KA, Moran S, Serletti J, Ouriel K, Orlando G, Smith A, et al. Combined free tissue transfer and infrainguinal bypass graft: an alternative to major amputation in selected patients. *J Vasc Surg* 2001;**33**:17–22.
 - 24 Cronenwett JL, Mcdaniel MD, Zwolak RM, Walsh DB, Schneider JR, Reus WF, et al. Limb Salvage despite extensive tissue loss- free tissue transfer combined with distal revascularization. *Arch Surg* 1989;**124**:609–15.
 - 25 Karp NS, Kasabian AK, Siebery JW, Eidelman JR, Colen S. Microvascular free-flap salvage of the diabetic foot – a 5-year experience. *Plast Reconstr Surg* 1994;**94**:834–40.
 - 26 Shestak KC, Fitz DG, Newton ED, Swartz WM. Expanding the horizons in treatment of severe peripheral vascular disease using microsurgical techniques. *Plast Reconstr Surg* 1990;**85**:406–11.
 - 27 Lorensetti F, Tukiainen E, Alback A, Kallio M, Asko-Seljavaara S, Lepäntalo M. Blood flow in a pedal bypass combined with a free muscle flap. *Eur J Vasc Endovasc Surg* 2001;**22**:161–4.
 - 28 Mimoun M, Hilligot P, Baux S. The nutrient flap – a new concept of the role of the flap and application to the salvage of arteriosclerotic lower-limbs. *Plast Reconstr Surg* 1989;**84**:458–67.
 - 29 Hsu H, Chang CH, Lee CY, Huang CC, Mark Chiu CH, Lin CM, et al. A comparison between combined open bypass revascularization and free tissue transfer versus endovascular revascularization and free tissue transfer for lower limb preservation. *Microsurgery* 2015;**35**:518–27.
 - 30 Jang YJ, Park MC, Hong YS, Won JH, Lim SH, Park DH, et al. Successful lower extremity salvage with free flap after endovascular angioplasty in peripheral arterial occlusive disease. *J Plast Reconstr Aesthet Surg* 2014;**67**:1136–43.
 - 31 DeFazio MV, Han KD, Akbari CM, Evans KK. Free tissue transfer after targeted endovascular reperfusion for complex lower extremity reconstruction: setting the stage for success in the presence of multivessel disease. *Ann Vasc Surg* 2015;**29**:1316. e7–1316.e15.
 - 32 Chou C, Kuo PJ, Chen YC, Huang SH, Chang CH, Wu YC, et al. Combination of vascular intervention surgery and free tissue transfer for critical diabetic limb salvage. *Ann Plast Surg* 2016;**77**:s16–21.
 - 33 Hahn HM, Jeong YS, Hong YS, Won JH, Lim SH, Kim J, et al. Use of revascularized artery as a recipient in microvascular reconstruction of the lower leg: an analysis of 62 consecutive free flap transfers. *J Plast Reconstr Aesthet Surg* 2017;**70**:606–17.
 - 34 Oh TS, Lee HS, Hong JP. Diabetic foot reconstruction using free flaps increases 5-year-survival rate. *J Plast Reconstr Aesthet Surg* 2013;**66**:243–50.