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Angiosome Targeted PTA is More Important in Endovascular Revascularisation than in Surgical Revascularisation: Analysis of 545 Patients with Ischaemic Tissue Lesions

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WHAT THIS PAPER ADDS

This paper discusses the importance of angiosome targeted revascularisation in the treatment of critical limb ischaemia. Analysis of 545 patients with diabetes highlights that in endovascular therapy direct revascularisation is superior to indirect in terms of wound healing and leg salvage. If the patient is treated by open bypass surgery, however, the angiosome concept is of less value.

Introduction: This study aimed to evaluate the impact of angiosome targeted (direct) revascularisation according to revascularisation method in patients with diabetes.

Materials and methods: This retrospective study cohort comprised 545 diabetic patients with critical limb ischaemia and tissue loss (Rutherford 5, 6). All patients underwent infrapopliteal endovascular (PTA) or open surgical revascularisation between January 2008 and December 2013. Differences in the outcome after direct revascularisation, bypass surgery, and PTA were investigated by means of Cox proportional hazards analysis. The endpoints were wound healing, leg salvage, and amputation free survival.

Results: Overall, 60.3% of the ischaemic wounds healed during 1 year of follow-up. The highest wound healing rate was achieved after direct bypass (77%) and the worst after indirect PTA (52%). The Cox proportional hazards analysis showed that the number of affected angiosomes <3 (HR 1.37, 95% CI 1.01—1.84) was associated with improved wound healing, whereas wound healing was poorest after indirect PTA ($p = .001$). When Cox proportional hazard analysis was adjusted for the number of affected angiosomes, direct bypass gave the best wound healing ($p = 0.003$).

The overall amputation rate was 25.1% at 1 year of follow-up, and the Cox proportional hazards analysis indicated that haemodialysis compared with patients with no haemodialysis (HR 2.55, 95% CI 1.49—4.38), C-reactive protein ≥10 mg/dL (HR 2.05, 95% CI 1.45—2.90), atrial fibrillation (HR 1.54, 95% CI 1.05—2.26), and number of affected angiosomes >3 (HR 1.75, 95% CI 1.24—2.46) were significantly associated with poor leg salvage. Direct PTA was associated with a lower rate of major amputation compared with indirect PTA (HR 0.57 95% CI 0.37—0.89).

Conclusion: In diabetics, indirect endovascular revascularisation leads to significantly worse wound healing and leg salvage rates compared with direct revascularisation. Therefore, endovascular procedures should be targeted according to the angiosome concept. In bypass surgery, however, the concept is of less value and the artery with the best runoff should be selected as the outflow artery.

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INTRODUCTION

Diabetes mellitus (DM) is one of the strongest predictors of peripheral arterial disease and a significant risk factor for progression of asymptomatic disease or claudication into critical limb ischaemia (CLI).[1] Globally, over 170 million people have been diagnosed with DM, and by the year 2030, the prevalence is estimated to rise 2.5 fold.[2] Diabetic patients who develop CLI are more prone to ischaemic events with an impaired functional status, as nearly 30% will undergo major amputation with a 6 month mortality rate of 20%.[3] Approximately 80% of diabetes related lower limb amputations are preceded by a diabetic foot ulcer (DFU).[4] The aetiology of DFUs is multifactorial, and they are categorised into three groups: neuropathic, ischaemic, and

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neuroischaemic.[5] The proportion of DFUs of ischaemic or neuroischaemic origin has increased compared with neuropathic foot ulcers alone,[4] as ischaemia presents in 50%–60% of all DFUs.[6]

To achieve healing of an ischaemic foot ulcer and save the leg from amputation, revascularisation, endovascular or open surgery, with sufficient wound perfusion is necessary. In recent years, selection of the artery for revascularisation has been the subject of discussion, and a new approach, the angiosome concept, has been introduced.[7,8] Two meta-analyses of the angiosome concept in the treatment of CLI support the idea that the clinical outcome is better when angiosome targeted (direct) rather than non-targeted revascularisation is performed.[9,10] This benefit, especially in terms of wound healing, seems to be more pronounced in diabetic patients, as suggested in recent studies,[11–13] which observed the impact of the angiosome targeted approach in endovascular treatment. To date, there has been no comparative analysis of surgical versus endovascular revascularisation using the angiosome concept in diabetic patients with CLI and tissue loss. Therefore, this was the aim of the present study. In previous studies the significance of collaterals has not been considered, so this study also evaluated the significance of strong collaterals in the case of indirect revascularisation to the outcome of CLI.

MATERIALS AND METHODS

The study plan was approved by the ethical committee of the Helsinki University Central Hospital.

Patients

This retrospective study cohort consisted of 574 consecutive diabetic patients with CLI and tissue loss (Rutherford 5–6) who underwent infrapopliteal endovascular or open surgical revascularisation at the study institution between January 2008 and December 2013. Patients who had undergone a previous infrapopliteal revascularisation, or those without complete information on the status of the foot, were excluded from the cohort ($n = 29$).

Data collection

Operative data and baseline patient characteristics were assembled from a prospectively collected database (HusVasc), and are summarised in Table 1. To evaluate whether a direct procedure had been performed, patient records were reviewed as well as imaging files: digital subtraction angiograms (DSA) from before and after the revascularisation in the endovascular group and pre-operative MRI angiograms and DSAs, if available, in the surgical group. Glomerular filtration rate (eGFR) was estimated by the Modification of Diet in Renal Disease (MDRD) formula (Levey).

Definitions

An ischaemic foot ulcer was defined as a full thickness inframalleolar skin defect present for >2 weeks with decreased arterial flow and toe pressure of <50 mmHg, transcutaneous partial pressure of oxygen of <30 mmHg, or impaired arterial status on imaging (digital subtraction angiography or magnetic resonance angiography).

The diabetes was defined as the patient having diabetes medication (either oral medication and/or insulin treatment) or controlled by diet.

The policy of performing transcutaneous transluminal angioplasty (PTA) as first line revascularisation applied to stenotic lesions and short occlusions, and to patients with an increased risk of bypass surgery or without an available autologous vein. In fit patients with long occlusions and a good autologous vein, the policy was surgical bypass first. Before PTA, all patients were taking aspirin (100 mg/day), and after the procedure the intake continued lifelong, with clopidogrel added for 3 months (75 mg/day). The routine was to administer heparin 5000 IU at the beginning of the procedure, and thereafter 2500 IU hourly. No stents or drug eluting balloons were used for primary infrapopliteal revascularisation. For bypass surgery, a single segment great saphenous vein graft (non-reversed or reversed, placed beneath the fascia) was used in 65.5%, a spliced vein graft in 31.0%, composite vein with prosthesis in 2.6%, and a prosthetic graft in 0.4% as detailed in Table 1. Heparin was administered intra-operatively before clamping the artery. Patients received low molecular weight heparin (1 mg/kg/day) during their hospital stay accompanied by lifelong aspirin therapy (100 mg/day), unless contraindicated. Independently, at the time of the procedure endovascular or surgical, if not on statin therapy (usually initiated by the general practitioner), this was initiated on the first visit to the outpatient clinic before the intervention and the therapy continued lifelong.

The angiosome concept of direct revascularisation was defined according to the conventional method used in previous publications as a procedure to the artery supplying the angiosome affected by tissue loss, with the exception of lesions located in the forefoot or heel.[12,14–17] For a tissue defect located in the forefoot, revascularisation of either the anterior tibial/dorsal pedal artery or the posterior tibial artery/plantar arteries were included in the direct group. If the patient's heel was affected, revascularisation of either the posterior tibial or the fibular artery was classified in the direct group.

In cases of tissue loss spread over several angiosomes elsewhere besides the forefoot or heel, the same approach to direct revascularisation as described in the study by Iida et al. was adopted, where a procedure on the artery supplying the largest surface of the angiosome involved in the lesion was performed.[11,18]

If the patient suffered from multiple foot ulcers located in separate angiosomes, all affected angiosomes had to be revascularised for the case to be classified into the direct group.

Wound location

The location and severity of each ischaemic foot ulcer were ascertained by reviewing patient records, which have been carefully documented ever since research on wound healing

Table 1. Baseline characteristics and operation data of patients who underwent direct or indirect infrainguinal revascularisation.

Patients' characteristics	Overall series Indirect 336 patients	 Direct 408 patients	*p*
Age, years	72.9 ± 11.2	71.5 ± 11.2	.932
Age ≥80 years	72 (32.6)	99 (30.6)	.639
Female	72 (32.6)	98 (30.2)	.922
Smoking	28 (12.7)	41 (12.7)	.996
Diabetes mellitus			
Type I	27 (12.2)	39 (12.0)	.950
Type II	192 (86.9)	283 (87.3)	.897
C-reactive protein	46.7 ± 55.7	49.4 ± 56.1	.354
Dyslipidaemia	56 (25.3)	92 (28.4)	.435
Glomerular filtration rate (mL/min/1.73 m^2)	42.9 ± 16.7	42.9 ± 17.8	.603
Chronic kidney disease class			.364
3A	35 (15.8)	49 (15.1)	
3B	19 (8.6)	35 (10.8)	
4	15 (6.8)	14 (4.3)	
5	9 (4.1)	23 (7.1)	
Dialysis	15 (6.8)	26 (8.0)	.624
Kidney transplantation	6 (2.7)	9 (2.8)	.965
Hypertension	210 (95.0)	306 (94.4)	.768
Atrial fibrillation	56 (25.3)	80 (24.7)	.920
Coronary artery disease	91 (41.4)	133 (41.0)	.976
Heart failure	26 (11.8)	36 (11.1)	.891
Stroke	31 (14.0)	43 (13.3)	.899
Pulmonary disease	24 (10.9)	25 (7.7)	.224
Foot gangrene	53 (24.0)	106 (32.7)	.035
No. of affected angiosomes	2.4 ± 1.0	2.3 ± 0.7	.230
Level of revascularisation			.192
Crural	183 (82.8)	253 (78.1)	
Pedal	38 (17.2)	71 (21.9)	
Type of revascularisation			.003
Endovascular revascularisation	145 (65.6)	171 (52.8)	
Surgical revascularisation	76 (34.4)	153 (47.2)	
Type of bypass graft			.002
Single saphenous vein graft	50 (64.9)	100 (66.2)	
Other vein grafts	26 (33.8)	45 (29.8)	
Composite vein plus prosthesis graft	0 (0.0)	6 (4.0)	
Prosthesis graft	1 (1.3)	0 (0.0)	

was initiated in 2007. The general scheme of angiosomal distribution[12] was adopted to evaluate the number of affected angiosomes. In many cases, the tissue defect was severe and required peri-procedural digit amputation ($n = 157$) or metatarsal amputation ($n = 102$), which led to an increase in the number of affected angiosomes.

Wound healing and follow-up

The wound care depended on the characteristics of each lesion: surgical debridement of necrotic tissue, revision of infected ulcers, and application of a skin graft in cases of impossible primary or secondary closure. Patients with an infected wound received adequate antimicrobial therapy. A healed wound was defined as complete epithelialisation of the tissue defect by secondary intent or after any additional local ulcer surgery. If the wound remained open at the end of the follow-up, it was considered to be unhealed. Also, if the wound was open at the time of major amputation, it was considered to be unhealed at the end of the follow-up.

After the revascularisation, patients remained under routine outpatient surveillance. A vascular nurse carried out duplex ultrasound examinations of the revascularised artery and followed the foot status; a vascular surgeon was consulted if necessary. After PTA, the visits were scheduled at 1, 3, and 6 months, and in the case of a bypass graft at 1, 3, 6, and 12 months. If the wound remained open at the last routine duplex surveillance examination, the patient continued to visit the outpatient clinic until the wound healed fully. The follow-up ended if the patient underwent a new infrainguinal bypass because of failure of the primary intervention (endovascular or surgical), or a major amputation because of a non-healing foot ulcer, or if the patient died.

Outcome measures

The outcome was compared in four groups: direct and indirect surgical revascularisation, and direct and indirect endovascular revascularisation. The primary outcome measures were wound healing and leg salvage; amputation free survival was a secondary outcome measure.

Statistical analysis

For statistical analysis, SPSS v. 22.0 statistical software was used (IBM SPSS Inc., Chicago, IL, USA). No attempt was made to replace missing values. Fisher's exact and chi-square tests, as well as the Mann-Whitney and Kaplan-Meier tests were used for univariate analysis. Twenty-one variables were included; only those with a p value $<.2$ were included in the multivariate analysis (Appendix 1). Multivariate analysis for assessing the impact of baseline variables on late outcome was performed using the Cox proportional hazards method. All tests were two sided, with the alpha level set at .05 for statistical significance. Post-hoc Cox proportional hazard sample size calculation (alpha value: 5%, beta value 20%) showed and confirmed that an overall series of 315 patients was needed with the current proportion of samples to confirm the superiority of direct PTA over indirect PTA in terms of leg salvage.

Sub-analysis of collaterals

The importance of collaterals was analysed by reviewing the DSA and MRA before the procedure. The presence of collaterals was graded as good or non-existent by two independent observers. In each revascularisation group, endovascular and surgical, the patients were divided into three groups depending on the presence or absence of collaterals and the angiosome approach: direct revascularisation, indirect revascularisation with good collaterals, and indirect revascularisation with no collaterals. The univariate analysis using the Cox proportional hazards method was performed with the alpha level set at .05 for statistical significance.

RESULTS

In total, 545 patients were included in the study, 316 in the PTA group and 229 in the surgical group. Most of the patients ($n = 479$) had type II diabetes with medication (having either oral medication and/or insulin treatment started over the age of 40 years), only five patients had diet controlled diabetes mellitus (Table 1).

The mean follow-up was 24 months (SD 17.7; 0.7–76.4). Direct revascularisation (DR) was achieved in 54.1% of the endovascular group and 66.8% of the surgical group. The toe pressure was available from 347 (63.0%) patients and the mean value in the surgical group was 29 and in the PTA group 37. The wound affected more than two angiosomes in 209 cases (38.3%).

In the endovascular group, 33 patients (10.4%) underwent one or more re-interventions – a new additional PTA in 18 cases and distal bypass in 15 cases. Only six patients (2.6%) in the surgical group had a re-intervention – an additional PTA in three cases and a jump graft to one or more other crural arteries in three cases.

Wound healing

The overall 1 year wound healing rate was 60.3%. The highest wound healing rate was achieved after direct bypass (77%) and the worst after indirect PTA (52%) (Table 2). In the univariate analysis the C-reactive protein $\leq$10 mg/dL ($p = .041$), type of procedure ($p = .001$), and number of affected angiosomes <3 ($p = .020$) were associated with improved wound healing while rheumatoid arthritis was associated with decreased wound healing ($p = .095$). The Cox proportional hazards analysis showed that number of affected angiosomes <3 (HR 1.37, 95% CI 1.01–1.84) and type of procedure were independently associated with wound healing, and the poorest wound healing was seen after indirect PTA ($p = .001$) (Table 3). When Cox proportional hazard analysis was adjusted for number of affected angiosomes, direct bypass gave the best wound healing (Fig. 1).

Leg salvage

The overall amputation rate at 1 year was 25.1%. In the univariate analysis the C-reactive protein $>$10 mg/dL ($p < .0001$), number of affected angiosomes >3 ($p < .001$),

Table 2. Outcome of patients who underwent infrapopliteal revascularisation by endovascular or open bypass for critical limb ischaemia.

	DR PTA 171 patients	IR PTA 145 patients	DR bypass surgery 153 patients	IR bypass surgery 76 patients	p value
Wound healing					.001
30 day	3.3%	0.0%	3.8%	17.8%	
6 month	44.0%	29.5%	51.6%	43.7%	
1 year	52.0%	52.4%	77.0%	68.5%	
Survival					.312
30 day	2.9%	4.8%	3.9%	5.3%	
6 month	17.0%	21.4%	15.8%	22.4%	
1 year	24.1%	25.5%	21.3%	32.3%	
Leg salvage					.038
30 day	7.1%	15.6%	9.9%	5.3%	
6 month	8.8%	27.7%	18.4%	14.4%	
1 year	20.3%	32.8%	20.3%	18.0%	
Amputation free survival					.011
30 day	10.6%	19.6%	7.2%	9.3%	
6 month	32.7%	44.3%	28.9%	29.3%	
1 year	39.7%	48.7%	37.3%	42.2%	

Table 3. Cox proportional hazard analysis outcomes for each variable.

Variable	Wound healing *p* value	HR (95% CI)	Leg salvage *p* value	HR (95% CI)
Type of procedure vs. IR PTA:	.003		.024	
Direct PTA	.025	1.64 (1.06—2.51)	.013	.57 (.36—.89)
Direct bypass	.000	2.19 (1.45—3.30)	.055	.65 (.42—1.01)
Indirect bypass	.025	1.73 (1.07—2.89)	.013	.47 (.26—.85)
Number of affected angiosomes<3	.041	1.37 (1.01—1.84)	.001	1.75 (1.24—2.46)
CRP≤10 mg/dL	.565	1.10 (.80—1.50)	.000	2.05 (1.45—2.90)
CKD	.212	.77 (.54—1.15)		
Gout	.160	.49 (.18—1.33)		
Rheumatoid arthritis	.198	1.71 (.76—3.88)		
Coronary heart disease			.083	.73 (.51—1.04)
Hypercholesterolaemia			.058	.67 (.44—1.01)
Atrial fibrillation			.029	1.54 (1.05—2.26)
Haemodialysis			.001	2.55 (1.49—4.38)

and haemodialysis ($p = .009$) were associated with decreased leg salvage and hypercholesterolaemia was associated with improved leg salvage ($p = .033$). Cox proportional hazards analysis indicated that haemodialysis compared with no haemodialysis (HR 2.55, 95% CI 1.49—4.38), C-reactive protein ≥10 mg/dL (HR 2.05, 95% CI 1.45—2.90), atrial fibrillation (HR 1.54, 95% CI 1.05—2.26), and number of affected angiosomes>3 (HR 1.75, 95% CI 1.24—2.46) were significantly associated with poor leg salvage (Table 3). The indirect PTA predicted poorest leg survival (Fig. 2).

Amputation free survival

In the univariate analysis the C-reactive protein <10 mg/dL ($p < .001$), hypercholesterolaemia ($p = .033$), type of procedure ($p = .039$), and number of affected angiosomes<3 ($p = .021$) were associated with amputation free survival. In turn, increased age ($p < .001$), chronic heart failure ($p = .004$), chronic kidney disease ($p < .001$), haemodialysis ($p = .002$), atrial fibrillation ($p < .001$), and chronic obstructive pulmonary disease ($p < .004$) were associated with decreased amputation free survival. Cox proportional hazards analysis indicated that direct bypass (HR 0.58, 95% CI 0.43—0.79), indirect bypass (HR 0.66, 95% CI 0.45—0.96), and direct PTA (HR 0.66, 95% CI 0.49—0.91) as opposed to indirect PTA were independent predictors of amputation free survival. In contrast, atrial fibrillation (HR 1.87, 95% CI 1.45—2.42), chronic kidney disease (HR 1.44, 95% CI 1.04—1.20), haemodialysis (HR 2.12, 95% CI 1.30—3.44), C-reactive protein <10 mg/dL (HR 1.54, 95% CI 1.20—

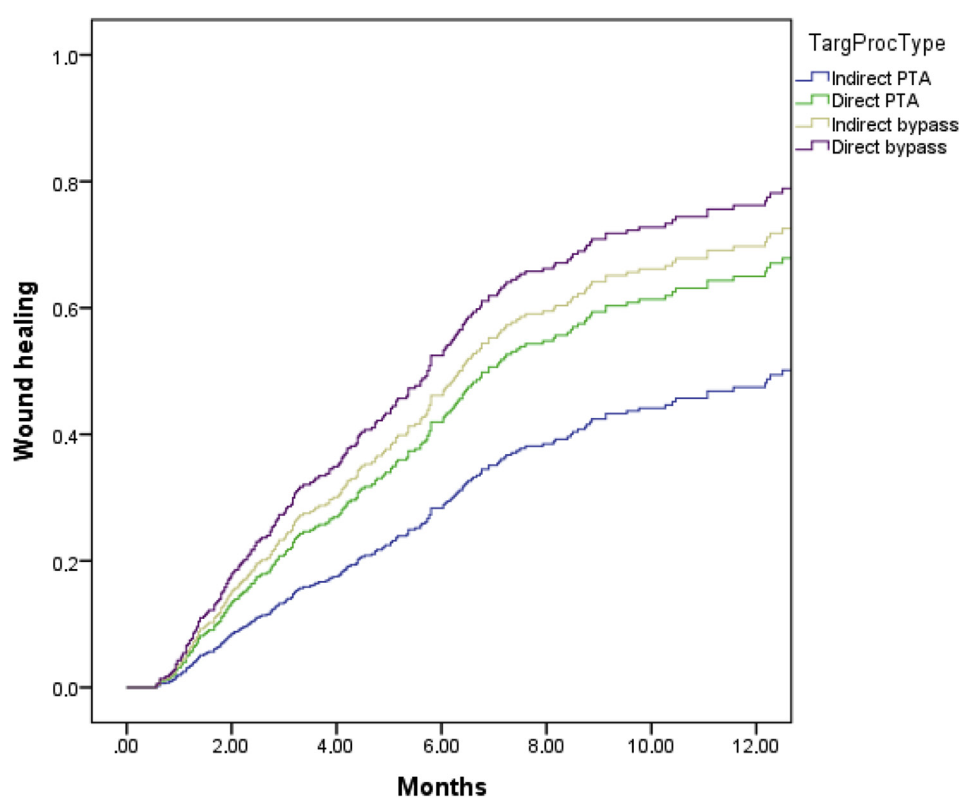

Figure 1. Cox proportional hazards analysis adjusted for number of affected angiosomes ($p = .003$).

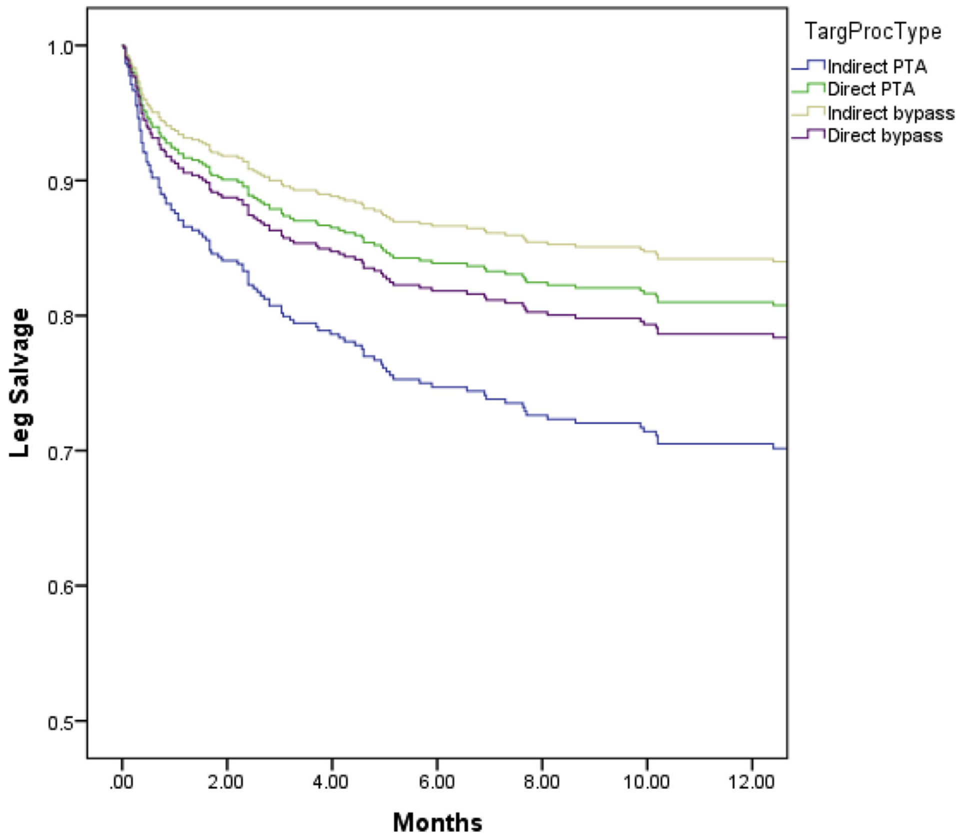

Figure 2. Cox proportional hazards analysis on leg salvage adjusted for number of affected angiosomes, atrial fibrillation, CRP>10, and haemodialysis ($p = .04$).

2.99) and age ≥80 (HR 1.02, 95% CI 1.01—1.04) were predictors of worse amputation free survival.

Sub-analysis of collaterals

In the surgical group, direct revascularisation was performed in 153 (66.8%) cases, indirect revascularisation with good collaterals in 28 (12.2%), and indirect revascularisation with no collaterals in 48 (21.0%). No significant difference was found between the groups with regard to wound healing or leg salvage. In the endovascular group, direct revascularisation was performed in 178 (56.5%) cases, indirect revascularisation with good collaterals in 97 (30.8%), and indirect revascularisation with no collaterals in 40 (12.7%). The Cox proportional hazards model showed only a trend towards better wound healing ($p = .244$) in the presence of good collaterals when indirect revascularisation was performed (Fig. 3); however, the leg salvage rate at the 1 year follow-up was significantly better, $p = .008$ (HR 0.45, 95% CI 0.25—0.814) (Fig. 3).

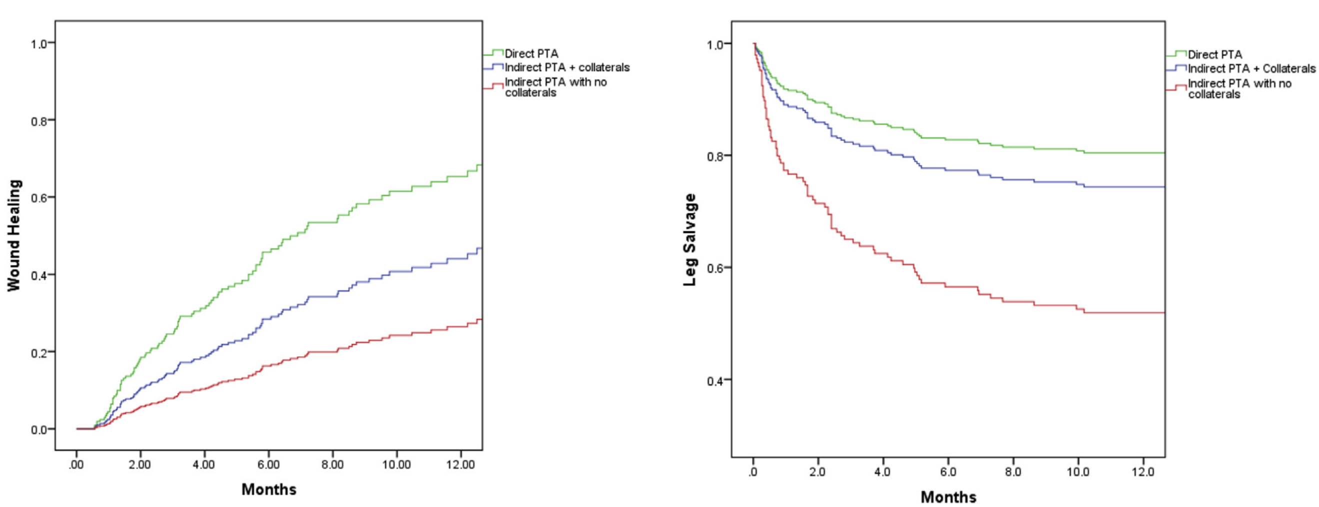

Figure 3. Cox proportional hazards model for the presence of collaterals. Wound healing, $p = .004$ (left), and leg salvage, $p \leq .001$ (right).

DISCUSSION

The prevalence of ischaemic and neuroischaemic diabetic foot ulcers is increasing, and relates to the increasing number of older diabetic patients in the population.[19] Furthermore, continuous education of general practitioners and foot therapists on the importance of ischaemic aetiology behind wound healing problems has increased referrals to vascular surgeons. However, the biggest problem in diabetics is ‘patient related delay’: because of neuropathy, the feet are usually pain free and patients do not seek help until there is significant infection or advanced tissue lesions, which makes eventual treatment very challenging. Once an ischaemic foot ulcer is detected, revascularisation is mandatory. The latest reports suggest that angiosome oriented revascularisation is favoured in patients with an ischaemic tissue lesion, and some reports emphasise its importance in diabetic patients,[11,13] because of the different pathophysiology of atherosclerosis. In diabetic patients the tunica media is affected rather than the intima,[20] which leads to diffuse disease of the source artery as well as the collaterals and true anastomoses between angiosomes. Nevertheless, Acín et al. showed that, also in diabetic patients with CLI and tissue loss, restoration of blood flow in the presence of good medium size or large collaterals seems to be similar to that via the source artery.[17] The present study suggests that when treating a diabetic foot with an ischaemic ulcer, direct revascularisation is of greater importance than endovascular revascularisation. However, after surgical bypass, there were no significant differences between direct and indirect revascularisation in wound healing and leg salvage. Wound healing was better after surgical revascularisation than after endovascular revascularisation. Leg salvage was similar after direct endovascular revascularisation and direct or indirect surgical bypass, and was significantly better than after indirect PTA.

This study compared endovascular revascularisation with surgical revascularisation using multivariate analysis. Interestingly, the results in this cohort of only diabetic patients are comparable with results from a previous large study in which most of the patients were not diabetic.[21] These two studies show, quite convincingly, that wound healing is better after bypass surgery than after PTA, independent of the angiosome orientation. Furthermore, indirect PTA is associated with the poorest leg salvage (Fig. 1) and, together with wound infection, indirect PTA increases the risk of major amputation. In the sub-analysis on the importance of collaterals, it was found that after bypass surgery, wound healing was not associated with the presence of collaterals. After PTA, there was a trend towards better wound healing in the indirect group with good collaterals compared with the indirect group with poor collaterals. However, wound healing was superior with an angiosome oriented strategy. The results may be seen as preliminary because of the limited numbers of patients in the groups.

A few studies have suggested that the success of wound healing is related more to the quality of the pedal arch than to angiosome guided revascularisation.[22,23] This can be explained by the argument that the better the quality of the arch, the better the perfusion of the ischaemic area via true anastomoses. However, as mentioned above, the probability of the arch and the links between the pedal arteries being impaired by tunica media calcinosis is high. The importance of the pedal arch was checked in this study and, surprisingly, no significant difference was found between a complete and an incomplete arch. The univariate analysis as well as the Kaplan-Meier test resulted in a tendency towards poorer wound healing and leg salvage in cases of a completely missing pedal arch. The number of patients, however, was small ($n = 36$), and no further analysis was performed because of poor statistical reliability. The absence of a pedal arch should not be taken as a contraindication to bypass surgery.[24]

Rapid advances in endovascular technology, improved vascular imaging, and the expanding skill level related to the endovascular approach allow for endovascular treatment of the most complex anatomies. This evolution has shifted the treatment of CLI towards an “endovascular first” strategy, and the number of patients primarily referred for open surgical revascularisation has decreased significantly.[25] Furthermore, most diabetic patients with CLI and a tissue lesion are fragile with other comorbidities, and for them the aim of as non-invasive an intervention as possible leads to a shorter hospital stay and faster rehabilitation. Despite the evolution in endovascular technology, long infrapopliteal occlusions remain challenging for endovascular therapy because of the high risk of failure and a need for repeated revascularisation attempts. A failure of endovascular therapy, usually after two PTAs, results in a delay of revascularisation by surgical bypass. Such a delay, especially in diabetic patients, may lead to poorer leg salvage rates.[26] Therefore, in cases of long infrapopliteal occlusion, the policy at the study clinic is changing to opt for surgical bypass first. This strategy is supported by the present results, showing that, especially in patients with several affected angiosomes and elevated C-reactive protein levels, it seems to be significantly better to perform bypass as a first line treatment and skip the indirect angioplasty. However, in cases of a lesion suitable for direct endovascular treatment, “endovascular first” would be the first option.

The other criteria for the decision regarding revascularisation method are that the wound is rarely localised to a single angiosome and, in nearly one in three patients, the anatomy of the revascularisation cannot be chosen as there is only one crural vessel with patent outflow.[27,28] In such cases, where endovascular therapy would lead to indirect flow, it seems the patient would benefit from surgical bypass, unless contraindicated.

The possible reasons behind the differences between the surgical and endovascular groups can only be speculated upon, as described previously.[20] It is believed that with surgical bypass using a good autologous vein, the arterial pressure is transferred effectively to the foot, which is not the case in indirect PTA.

A number of limitations may affect the results of this study. The retrospective character of the study meant that evaluation of some angiograms was problematic because of the poor quality of the images in the examined region. Also, in the surgical group pre-operative DSA was available in only 17% of all cases; MRI angiography which is the baseline imaging technique does not provide such detailed information of distal perfusion. Furthermore, the definition of angiosome targeted revascularisation in cases where the wound spreads over several angiosomes is not clear. Also, because of anatomical vessel variation, more than one scheme of angiosome distribution exists,[28] which is problematic for evaluation of the affected angiosomes, as it cannot be known which one applies to each patient. The wound healing time in the study may have been overestimated because the status was checked intermittently, and wound care was not standardised and took place at a number of other facilities outside Helsinki University Hospital.

The retrospective nature of the study made it difficult to get two equal groups as the patients who were selected for the surgical group had worse foot perfusion at baseline and more extensive atherosclerotic lesions, whereas patients with endovascular revascularisation were usually older with more comorbidities.

On the other hand, a strength of the study is comprehensive follow-up for most patients and reliable data on amputations and deaths. Furthermore, the number of patients included is high, allowing for a strong statistical analysis.

Without doubt, a well planned prospective study with precisely defined wound location and size, high quality angiograms with information on collaterals as well as the patency of the pedal arch, and carefully standardised wound healing follow-up is needed to confirm the usefulness of the angiosome concept in the treatment of CLI and tissue loss.

CONCLUSION

In diabetic patients, indirect endovascular revascularisation leads to the poorest wound healing and leg salvage rates. Therefore, endovascular procedures should be targeted according to the angiosome concept. In bypass surgery, however, the concept is of less value and the artery with the best runoff should be selected as the outflow artery.

FUNDING

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CONFLICT OF INTEREST

None.

APPENDIX 1. ALL VARIABLES USED IN UNIVARIATE ANALYSIS. VARIABLES WITH *P* VALUE ≤.2 WERE INCLUDED (SHADE HIGHLIGHTED) IN THE MULTIVARIATE ANALYSIS.

Variable	Wound healing		Leg salvage		Amputation free survival	
	p–value	HR (95% CI)	*p*–value	HR (95% CI)	*p*–value	HR (95% CI)
Gender	.500	1.101 (.827–1.466)	.692	1.075 (.751–1.539)	.356	1.120 (.881–1.424)
Type of the procedure	.001		.101		.039	
Direct surg vs. IR PTA	.000	2.314 (1.547–3.463)	.118	.710 (.462–1.091)	.004	.638 (.470–.865)
Indirect surg vs. IR PTA	.011	1.826 (1.149–2.904)	.049	.557 (.311–.998)	.254	.811 (.566–1.163)
Direct pta vs. IR PTA	.014	1.683 (1.111–2.549)	.041	.637 (.413–.982)	.138	.797 (.590–1.076)
Krea class	.141	.757 (.523–1.096)	.388	1.201 (.792–1.820)	.000	1.633 (1.255–2.125)
Age	.578	1.004 (.991–1.016)	.558	.996 (.981–1.011)	.000	1.020 (1.009–1.031)
CRP10	.041	.972 (.945–.999)	.000	1.066 (1.042–1.091)	.000	1.033 (1.015–1.052)
DM I	.968	1.008 (.669–1.519)	.889	1.038 (.616–1.748)	.417	1.164 (.807–1.680)
DM II	.778	.945 (.635–1.404)	.889	.964 (.580–1.603)	.410	.861 (.602–1.230)
Hypertension	.789	.953 (.832–1.092)	.739	1.129 (.553–2.306)	.370	.768 (.431–1.369)
Coronary heart disease	.873	1.022 (.783 1.334)	.117	1.326 (.932–1.888)	.542	.931 (.739–1.172)
Chronic heart failure	.303	1.281 (.800–2.050)	.720	1.110 (.627–1.967)	.004	.627 (.455–.864)
Stroke	.456	.862 (.583–1.274)	.588	.877 (.546–1.409)	.308	.847 (.615–1.165)
Hypercholesterolaemia	.596	1.081 (.810–1.443)	.033	1.564 (1.038–2.357)	.033	1.332 (1.024–1.731)
Smoking	.351	1.196 (.821–1.743)	.186	1.471 (.831–2.606)	.155	1.301 (.905–1.870)
COPD	.767	.931 (.582–1.492)	.450	1.317 (.644–2.693)	.004	.589 (.409–.847)
Atrial fibrilation	.767	1.051 (.765–1.462)	.044	.682 (.470–.990)	.000	.491 (.385–.626)
Gout	.198	.520 (.192–1.407)	.771	1.231 (.305–4.974)	.421	.735 (.347–1.556)
Chronic kidney disease	.341	1.209 (.818–1.785)	.363	1.274 (.756–2.146)	.230	.829 (.610–1.126)
Kidney transplatation	.453	.749 (.352–1.594)	.623	1.332 (.424–4.186)	.153	2.053 (.765–5.511)
Asthma	.600	1.243 (.552–2.800)	.938	.965 (.395–2.357)	.212	.710 (.415–1.215)
Haemodialysis	.190	1.499 (.818–2.749)	.009	.500 (.297–.844)	.002	.550 (.377–.803)
Rheumatism	.095	1.997 (.886–4.503)	.135	.597 (.304–1.174)	.164	.699 (.422–1.157)

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