Angiosome-targeted infrapopliteal endovascular revascularization for treatment of diabetic foot ulcers

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Objective: **Because of the prolonged healing time of diabetic foot ulcers, methods for identifying ways to expedite the ulcer healing process are needed. The angiosome concept delineates the body into three-dimensional blocks of tissue fed by specific source arteries. The aim of this study was to evaluate the benefit of infrapopliteal endovascular revascularization guided by an angiosome model of perfusion in the healing process of diabetic foot ulcers.**

Methods: **A total of 250 consecutive legs with diabetic foot ulcers in 226 patients who had undergone infrapopliteal endovascular revascularization in a single center were evaluated. Patient records and periprocedural leg angiograms were reviewed. The legs were divided into two groups depending on whether direct arterial flow to the site of the foot ulcer based on the angiosome concept was achieved (direct group) or not achieved (indirect group). Ulcer healing time was compared between the two groups. A propensity score was used for adjustment of differences in pretreatment covariables in multivariate analysis and for 1:1 matching.**

Results: **Direct flow to the angiosome feeding the ulcer area was achieved in 121 legs (48%) compared with indirect revascularization in 129 legs. Foot ulcers treated with angiosome-targeted infrapopliteal percutaneous transluminal angioplasty healed better. The ulcer healing rate was mean (standard deviation) 72% (5%) at 12 months for the direct group compared with 45% (6%) for the indirect group ($P < .001$). When adjusted for propensity score, the direct group still had a significantly better ulcer healing rate than the indirect group (hazard ratio, 1.97; 95% confidence interval, 1.34-2.90; $P = .001$).**

Conclusions: **Attaining a direct arterial flow based on the angiosome model of perfusion to the foot ulcer appears to be important for ulcer healing in diabetic patients. (J Vasc Surg 2013;57:427-35.)**

Foot ulcers are a common and feared complication of diabetes. Ischemia, neuropathy, and infection are etiologies that lead to diabetic foot complications and frequently occur together. The basic factor preventing healing of a diabetic foot ulcer is often inadequate perfusion.[1]

In diabetics, arterial occlusive disease primarily affects the crural arteries.[2-4] Percutaneous transluminal angioplasty (PTA) is increasingly being used as the first-line revascularization procedure for treatment of peripheral arterial occlusive disease.[5,6] Even in the most challenging areas, such as the infrapopliteal segment, PTA has shown encouraging leg salvage rates.[7]

Foot ulcer healing is of major interest because complications of foot ulcers are the leading cause of hospitalization and amputation among diabetic patients.[8] Studies suggest that a foot ulcer progresses to major amputation in 8% to 29% of patients with diabetes.[9-12] Furthermore, leg ulcers have important effects on quality of life.[13] Ulcer healing time is seldom reported in lower leg revascularization studies.[14] Despite successful revascularization, ulcer healing is a very slow process, especially in diabetics.[15-17] There is a need to identify methods that will enhance the healing process of diabetic foot ulcers. The anatomic location, characteristics of the ulcer, systemic factors, and inadequate local ulcer treatment can partly explain delayed healing despite a patent revascularization.[18-21] Foot ulcers may fail to heal because of inadequate arterial perfusion to the specific ulcer area.[22,23] The aim of this study was to evaluate if infrapopliteal endovascular revascularization guided by an angiosome model of perfusion has a beneficial effect on the healing process of diabetic foot ulcers compared with indirect revascularization.[24]

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ANGIOSOME CONCEPT

The angiosome principle, defined by Ian Taylor in his landmark anatomic study in 1987, divides the body into three-dimensional anatomic units of tissue supplied by specific source arteries.[24] Briefly, the foot can be divided into five distinct angiosomes originating from the three main crural arteries: anterior tibial artery (ATA) and peroneal artery (PA) supply both one angiosome, whereas posterior tibial artery (ATP) supplies three angiosomes. The ATA supplies the dorsal side of the foot and toes, the PA covers the lateral ankle and lateral heel, and the

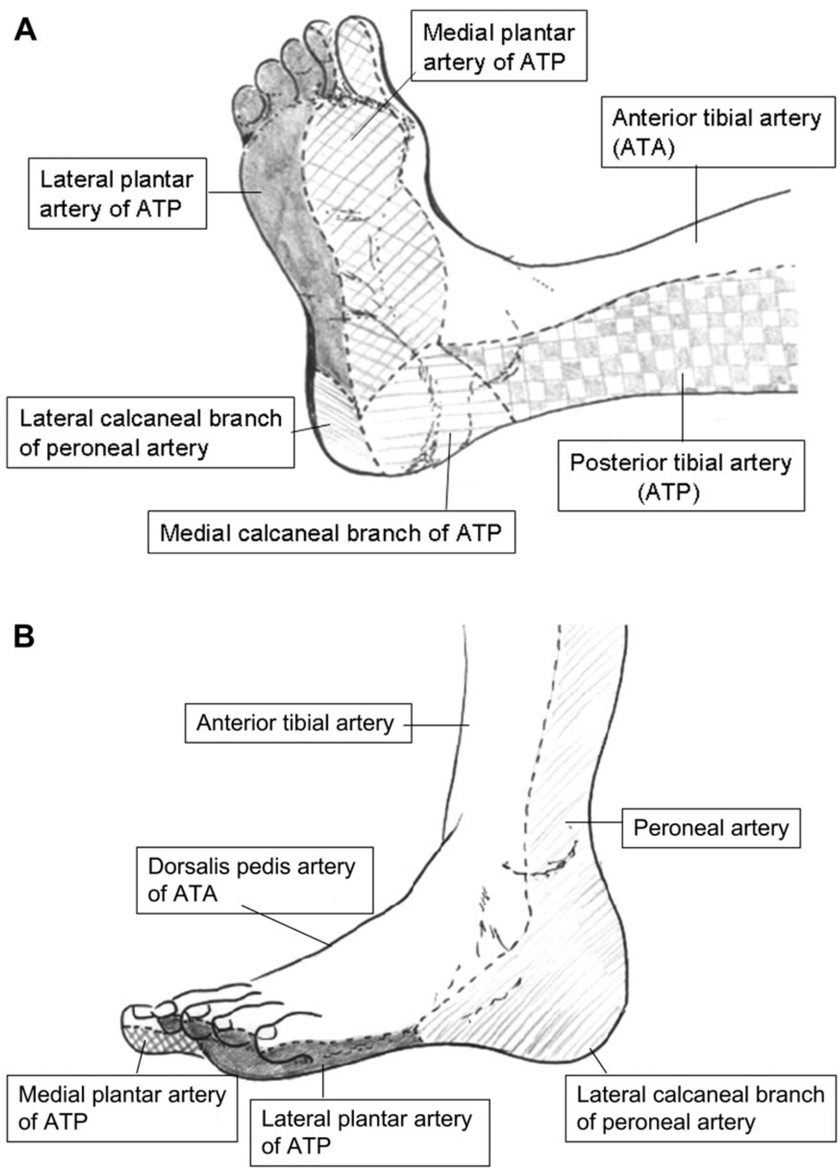

Fig 1. **A** and **B,** The medial calcaneal, medial plantar, and lateral plantar and the arteries angiosomes are derived from the posterior tibial artery (*ATP*) and cover the lateral heel and the plantar surface of the foot. The dorsalis pedis artery angiosome, which prolongs the anterior tibial artery (*ATA*), nourishes the dorsum of the foot, the toes, and the upper anterior perimalleolar area. The lateral calcaneal artery from the peroneal artery supplies the lateral and plantar aspects of the heel. Modified with permission from Alexandrescu V, Söderström M, Venermo M. Angiosome theory: fact or fiction? Scand J Surg 2012;101:125-31.

ATP perfuses the plantar surface of the foot and medial heel and ankle (Fig 1).[22] Neighboring angiosomes are connected to each other by a network of small collateral arteries, "the choke vessels," thus ensuring circulation to an angiosome if its source artery is occluded.[24]

METHODS

The study protocol was approved by the Institutional Review Board of the Department of Surgery, Helsinki University Central Hospital, Finland.

Patients. This retrospective study included all diabetic patients with foot ulcers (226 patients, 250 legs) who underwent a technically successful primary PTA procedure to at least one of the infrapopliteal arteries (ATA, ATP, PA) in our institution during a 3-year period between January 2007 and January 2011. Patients who had undergone a previous infrainguinal revascularization were excluded.

Data collection. The patients were retrospectively collected from our prospectively maintained vascular database (HUSVasc). The HUSVasc database includes demographic data on the patients, indication for revascularization, specific revascularization details, pre- and postprocedural hemodynamic measurements, specific details of vascular reinterventions, type of local ulcer surgery, information on patency, date of ulcer healing, major amputation, and death. Registry data of all patients were manually cross-checked with patients' records, and any missing data were retrieved from the patients' records. Data on major amputations and death were cross-checked with data retrieved from the National Institute of Health and Welfare and the Population Register Centre, respectively.

Definitions and classifications. Patients were considered to have diabetes if they were on a hyperglycemia reducing diet, were undergoing insulin treatment, or were taking oral hypoglycemic medication.

Technical success was defined as PTA of an infrapopliteal (ATA, ATP, or PA) occlusive arterial lesion without residual stenosis of >50%.

A foot ulcer was defined as a full-thickness skin defect distal to the malleolar level present for at least 2 weeks. Ulcer location before PTA was registered. Patients with supramalleolar ulcers were excluded. The University of Texas Wound Classification System (UTWCS) was used for classifying the depth of the foot ulcer (grade 1 = superficial ulcer; grade 2 = ulcer penetrating to muscle, tendon, or joint capsule; grade 3 = ulcer penetrating to joint or bone) and the presence of infection (stage A = nonischemic, noninfected ulcer; stage B = nonischemic, infected ulcer; stage C = noninfected, ischemic ulcer; stage D = infected ischemic ulcer) in the ulcer before PTA.[25]

Ulcer healing was defined as complete epithelialization of the tissue defect by secondary intent or after any additional local ulcer surgery. The foot ulcer was considered nonhealed if it did not heal during follow-up or the patient underwent infrainguinal bypass surgery or a major amputation due to a nonhealing foot ulcer.

Major amputation was defined as an amputation proximal to the ankle level.

Periprocedural angiograms were retrospectively reviewed. The angiographic status of the ATA, ATP, and PA was scored as follows: 0 = normal or <20% stenosis; 1 = 20%-49% stenosis; 2 = 50%-99% stenosis; 3 = less than half of the artery occluded; and 4 = half or more of the artery occluded.[26] The dorsal pedal artery was considered part of the ATA and the plantar artery was considered part of the ATP.

The patients were divided into two groups depending on whether direct in-line flow from the aorta to the foot ulcer based on the angiosome concept was successfully achieved (direct group) or the ulcerated angiosome was fed by collaterals from other angiosomes (indirect group). If the foot ulcer extended over more than one angiosome territory, the leg was considered to belong to the direct group if direct flow to the ulcer from at least one crural artery was achieved with PTA.[27]

PTA. Our policy is to perform intraluminal PTA as a first-line revascularization procedure for occlusions and stenosis >50% whenever possible, except for extensive arterial occlusive disease (eg, TASC [TransAtlantic Inter-Society Consensus] D lesions), as recommended in the newest TASC document.[9] At our institution, if the patient was unfit for infrainguinal bypass surgery or autologous vein grafts were not available, PTA is considered first-line treatment of extensive arterial occlusive disease. Before PTA, all patients were taking aspirin (100 mg/d) if not contraindicated. The PTA techniques conformed to standard principles. All patients continued lifelong aspirin therapy, which was accompanied by clopidogrel (75 mg/d) for 3 months after PTA if not contraindicated.

Wound care. Local wound care was chosen depending on the characteristics of each lesion. Debridement was performed to remove devitalized tissue. Infected ulcers underwent surgical revision and microbial therapy according to bacterial culture results. If primary or secondary closure was not possible, skin grafting or flaps were considered. Complementary methods for addressing local tissue generation were negative-pressure wound therapy and offloading whenever indicated.

Follow-up. The first follow-up visit at our outpatient clinic was 1 month after PTA and at 1- to 3-month intervals thereafter depending on the clinical status of the foot. The surveillance continued until the ulcer healed. In addition to the clinical status, follow-up visits included ankle-brachial index and toe pressure measurements. Duplex scanning and/or angiography was performed in patients with clinical deterioration corroborated by ankle-brachial index and toe pressure findings. Re-PTA was considered for restenosis >50%. For this study, follow-up ended 1 year after the primary infrapopliteal PTA, or death, whichever occurred first.

Outcome measures. The main aim of this study was to investigate if achievement of direct flow to the foot ulcer had an effect on ulcer healing time compared with indirect revascularization according to the angiosome principle. The secondary aim was to assess the rate of patients alive with healed ulcers and salvaged leg in both groups.

Statistical analysis. Statistical software package SPSS version 19.0 (SPSS Inc, Chicago, Ill) was used for statistical analysis. Comparisons of univariate categorical variables in each group were computed using χ^2 test and Fisher exact test when appropriate. Comparisons of univariate continuous variables between the two groups were computed via the Student *t*-test (normal distribution) or Mann-Whitney *U* test (skewed distribution). Kaplan-Meier univariable analysis was used to estimate cumulative ulcer healing, leg salvage, survival, and amputation-free survival. Survival rates are reported as proportion (standard error). Life tables between groups were compared with log-rank test. Cox regression analysis provided risk ratios of clinically relevant factors for ulcer healing. Baseline risk factors having $P < .20$ in univariable analysis were included in the regression analysis. Results are presented as hazard ratio and 95% confidence interval.

The treatment groups were likely to differ with respect to pretreatment covariables. To account for certain differences between the direct and indirect groups, a propensity score was developed for the treatment method. Propensity score analysis is a post hoc statistical method that estimates

Table I. Characteristics of diabetic patients achieving direct flow to the foot ulcer compared with those having indirect revascularization according to the angiosome principle

		Overall series			Propensity score matched pairs		
Comorbidity	*Overall (250 legs)*	*Direct group (121 legs)*	*Indirect group (129 legs)*	P *value*	*Indirect group (84 legs)*	*Direct group (84 legs)*	P *value*
Age, mean (SD)	71.2 (11.8)	68.4 (11.9)	73.8 (11.1)	.001	70.3 (10.9)	71.7 (11.0)	.416
Female gender	90 (36)	32 (26)	58 (45)	.002	26 (31)	25 (30)	.867
Diabetes mellitus	250 (100)	121 (100)	129 (100)	1.000	84 (100)	84 (100)	1.000
Dyslipidemia	162 (65)	78 (65)	84 (65)	.914	60 (71)	50 (60)	.105
Cerebrovascular disease	53 (21)	29 (24)	24 (19)	.300	17 (20)	20 (24)	.576
Chronic pulmonary disease	41 (16)	21 (17)	20 (16)	.693	11 (13)	15 (18)	.394
Coronary artery disease	159 (64)	69 (57)	90 (70)	.044	55 (66)	53 (63)	.747
Hypertension	191 (76)	89 (74)	102 (79)	.305	63 (75)	63 (75)	1.000
Serum creatinine, mean (SD), μmol/L	144 (153)	166 (181)	124 (118)	.303	137 (142)	146 (162)	.978
Estimated glomerular filtration rate <30 mL/min/1.73m^2 or dialysis	39 (16)	26 (22)	13 (10)	.012	12 (14)	14 (17)	.670
Smoking[a]	45 (21)	24 (18)	20 (24)	.281	15 (20)	18 (25)	.442
Bilateral foot ulcers	48 (19)	25 (21)	23 (18)	.570	15 (18)	21 (25)	.259
Gangrene	89 (36)	49 (41)	40 (31)	.106	30 (36)	31 (37)	.873
Heel ulcer	42 (17)	19 (16)	23 (18)	.653	16 (19)	10 (12)	.201
Ulcer extending to bone (UTWCS grade 3)	137 (55)	72 (60)	65 (50)	.148	48 (57)	47 (56)	.876
Infected ulcer (UTWCS stage D)	98 (39)	46 (38)	52 (40)	.710	32 (38)	31 (37)	.873
Carrier of multidrug-resistant bacteria	24 (10)	10 (8)	14 (11)	.330	6 (7)	8 (9)	.577
Ankle-brachial index,[b] mean (SD)	0.68 (0.31)	0.73 (0.33)	0.64 (0.29)	.087	0.69 (0.29)	0.70 (0.31)	.670
Toe pressure, mean (SD), mm Hg	38 (20)	41 (21)	36 (19)	.095	37 (19)	39 (20)	.814
Percutaneous transluminal angioplasty of popliteal or suprapopliteal arteries	74 (30)	34 (28)	40 (31)	.587	27 (51)	26 (49)	.827

SD, Standard deviation; *UTWCS,* University of Texas Wound Classification.
Results are reported for the overall series and for propensity score matched pairs.
Continuous variables are reported as mean (SD), where indicated. Dichotomous variables are reported as count and percentage (in parentheses).
[a]Data available from 219 of 250 patients.
[b]Legs with ankle-brachial index <1.4.

Table II. Description of angiosome arteries and endovascularly treated infrapopliteal arteries in the direct group and the indirect group

Artery	*Direct group, No. of legs (%)*	*Indirect group, No. of legs (%)*	P *value*
Peroneal artery	29 (24)	62 (48)	<.001
Anterior tibial artery	73 (61)	69 (54)	.221
Posterior tibial artery	57 (47)	24 (18)	<.001
Score of the angiosome artery, median	3	4	<.001
Score of the endovascularly treated artery, median	3	3	.987

treatment impact when subjects are not randomly assigned to a specific treatment group.[28,29] It attempts to control for all known patient factors that might influence the decision of whether to perform direct or indirect revascularization and thus potentially affect the outcome. The propensity score was calculated by logistic regression with backward selection by including clinical variables with $P < .20$ in univariable analysis. Receiver operating characteristic curve analysis was used to estimate the area under the curve of the model, predicting the probability of being included in the study groups. The calculated propensity score was used for 1:1 matching and for adjustment of the risk in the overall series. Stratification analysis by propensity score was not performed because of the limited number of patients included in this series. The 1:1 propensity score matching between study groups was done according to a difference in the logit of propensity score of <0.03 between each patient pair in the study groups. Such a caliber width was equal to 0.2 of the standard deviation of the logit of the herein calculated propensity score. $P <$ .05 was considered statistically significant.

RESULTS

Of the 250 consecutive legs undergoing infrapopliteal PTA, direct flow to the foot ulcer based on the angiosome principle was achieved in 121 legs (48%) compared with 129 legs (52%) in which direct perfusion was not achieved (Tables I and II). There were more female patients in the indirect group than in the direct group (26% vs 45%; $P = .002$; Table I). The patients in the indirect group were older than those in the direct group (77 vs 71 years; $P < .001$). There were more patients with end-stage renal disease in the direct group than in the indirect group (22% vs 10%; $P = .012$).

Angiographic scores. The occlusive lesions on the artery perfusing the foot ulcer according to the angiosome principle were more severe as measured by the angiographic

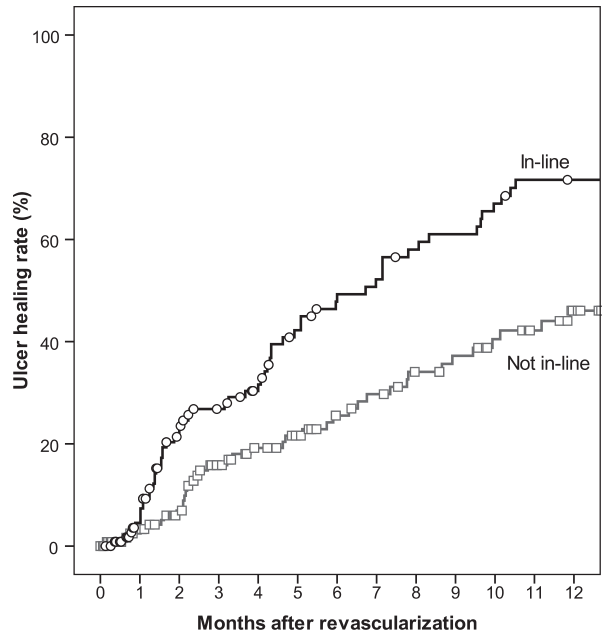

Fig 2. Ulcer healing rates in patients with direct and those with indirect perfusion to the foot ulcer after endovascular revascularization in the overall series (log-rank test, $P < .001$).

Table III. Results of univariable and multivariable factors associated with ulcer healing in the overall series

	Univariate analysis	*Multivariate analysis*		
	P *value*	*HR*	*95% CI*	P *value*
Age	.051	0.99	0.98-1.01	.870
Female gender	.941	—	—	—
Coronary artery disease	.295	—	—	—
Chronic pulmonary disease	.251	—	—	—
Cerebrovascular disease	.350	—	—	—
Estimated glomerular filtration rate <30 mL/min/1.73m^2 or dialysis	.510	—	—	—
Dyslipidemia	.355	—	—	—
Hypertension	.410	—	—	—
Smoking	.528	—	—	—
Ulcer extending to bone (UTWCS grade 3)	.323	—	—	—
Ulcer with signs of infection (UTWCS stage D)	.387	—	—	—
Presence of multidrug-resistant bacteria	.201	—	—	—
Gangrene	.174	0.66	0.44-0.99	.477
Heel ulcer	.165	0.64	0.35-1.14	.129
In-line	<.001	1.90	1.32-2.73	.001

CI, Confidence interval; *HR,* hazard ratio; *UTWCS,* University of Texas Wound Classification.

score in the indirect group compared with the direct group ($P < .001$; Table II). The score of the endovascularly treated infrapopliteal artery was similar in both groups ($P = .987$).

Ulcer healing. The ulcer healing rates were mean (standard deviation) 48% (6%) at 6 months and 72% (5%) at 12 months for the direct group compared with 26% (5%) and 46% (6%) for the indirect group ($P < .001$; Fig 2). Univariable analysis for predictors of ulcer healing for the whole study group is reported in Table III. After multivariable analysis, the achievement of direct in-line perfusion to the ulcer was the only significant independent predictor for ulcer healing (Table III).

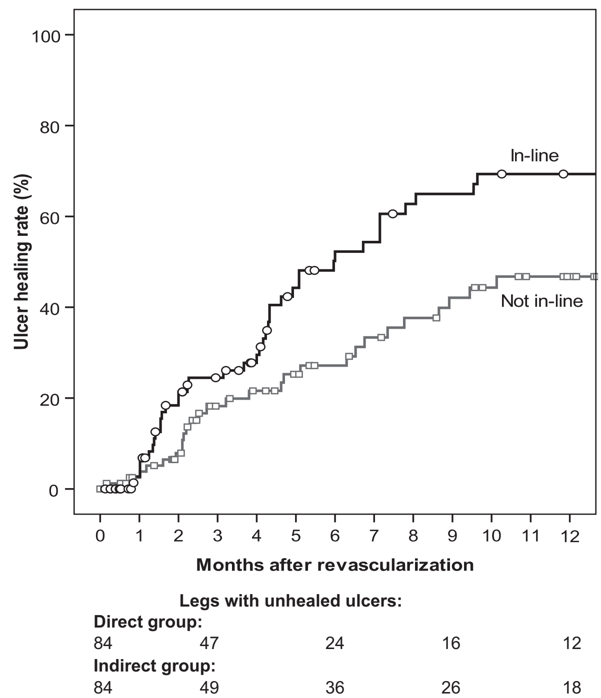

Fig 3. Ulcer healing rates in 84 propensity matched pairs of patients with direct and those with indirect perfusion to the foot ulcer after percutaneous transluminal angioplasty (log-rank test, $P = .021$).

A propensity score was developed by including age, gender, coronary artery disease, gangrene, estimated glomerular filtration rate <30 mL/min/1.73m^2 or dialysis (P = .521 Hosmer-Lemeshow test; area under the receiver operating characteristic curve, 0.689; 95% confidence interval, 0.62-0.76). When adjusted for propensity score, the direct group still had a significantly better healing rate than the indirect group (hazard ratio, 1.97; 95% confidence interval, 1.34-2.90; P = .001; Table I).

Eighty-four propensity-matched pairs with similar baseline characteristics were obtained. Patients who underwent direct perfusion to the ulcer had a significantly higher rate of ulcer healing at 12 months (69% [7%] vs 47% [7%]; median time to healing, 5.9 months vs >1 year; log-rank test, $P = .021$; Fig 3).

Leg salvage. The 1-year leg salvage rates were 86% (3%) for the direct group and 77% (4%) for the indirect group ($P = .086$).

Survival. The 1-year survival rates were 74% (4%) for the direct group and 74% (4%) for indirect group ($P = .646$).

Amputation-free survival. The 1-year amputation-free survival was 65% (4%) for the direct group and 61% (4%) for the indirect group ($P = .360$).

Amputation-free survival with healed ulcers. At 1 year after PTA, 41% of patients in the direct group and 26% of patients in the indirect group had achieved ulcer healing and were alive without a major amputation ($P = .012$).

Vascular reinterventions. Re-PTA to the initially revascularized artery was performed to 18 legs (15%) in the direct group and 21 legs (17%) in the indirect group ($P = .769$).

Ten legs (8%) in the direct group and 16 legs (12%) in the indirect group were treated with a bypass to the infrapopliteal arteries after PTA ($P = .311$).

DISCUSSION

To the best of our knowledge, this study represents the largest study evaluating the influence of revascularization based on the angiosome concept in the healing of foot ulcers.[14,23,30,31]

The results of this study indicate that providing direct blood flow to the specific area of a diabetic foot ulcer has a favorable effect on ulcer healing and should be preferred to indirect revascularization. One reason for the superiority of direct revascularization in this study might be that the choke vessels in diabetics tend to be compromised.[27,32] With indirect revascularization. many diabetic foot ulcers fail to heal because of inadequate perfusion caused by the poor vascular connections between angiosomes.

Our results are in agreement with several other studies evaluating angiosome-guided revascularization in ulcer healing.[6,23,27,30] Alexandrescu et al[36] compared the results of infrapopliteal PTA in diabetics before and after incorporation of the angiosome-targeted revascularization model at their institution. Patients undergoing PTA after introduction of the angiosome concept achieved better ulcer healing and leg salvage compared with those treated before the introduction of the angiosome concept. It is worth noting that both patient groups in the study by

Alexandrescu et al included patients with direct and indirect revascularization. In a personal institutional series of 52 leg revascularizations, Attinger et al[22] reported 9% healing failures when ulcers were treated with angiosome-targeted bypass surgery compared with 38% lack of success in healing of ulcers when treated with non-angiosome-oriented bypass surgery. In another small retrospective surgical series, Neville et al[30] reported an ulcer healing rate of 91% for patients undergoing bypass to the artery directly feeding the ulcerated angiosome vs an ulcer healing rate of 62% for those having indirect revascularization. Seemingly in line with these reports, Varela et al[6] noted significantly better results for ulcer healing (92% vs 73% at 1 year) in the angiosome-guided cohorts of patients in their series, including 76 ischemic ulcers treated by bypass or PTA. The beneficial effect of angiosome-targeted revascularization was not that clear in a retrospective Japanese analysis that included 249 critically ischemic limbs with tissue loss treated with distal bypass surgery.[31] The ulcer healing rate was faster if direct revascularization was possible, but after minimizing the background differences with the propensity score method the positive effect of angiosome-targeted bypass surgery disappeared. The prevalence of patients with end-stage renal disease was high (49%) in the Japanese study. Several publications have suggested that the presence of renal failure interferes with ulcer healing and that patients with renal failure ultimately may require major amputation.[1,33] When performing endovascular revascularization, surgical incisions in the ischemic leg are avoided and thereby also the possible problems with incisional wound healing.

Twenty percent of angiosome-oriented endovascular revascularizations have been reported to be unsuccessful due to technical barriers and lesion severity.[23] Older age is a well-known risk factor for arterial occlusive disease.[9] In our study, the patients in the indirect group were older, and the artery perfusing the ulcer exhibited severer occlusive lesions compared with the direct group. Angiosome-targeted endovascular procedures can be challenging because the artery supplying the ulcer might have more severe atherosclerotic lesions than the other crural arteries. Leg revascularizations in patients who have diabetes already are challenging because of the frequently calcified arterial wall and the distal distribution of arterial occlusive disease.[4,5] In the present series, the PA was the target artery in significantly more legs of the indirect group compared with the direct group. The PA has been reported to be relatively spared from the terminal stage of atherosclerosis and is often the last tibial vessel to become occluded in diabetics.[34]

Reliable data on ulcer healing in diabetic population are scarce.[8] Although the Trans Atlantic Conference on Clinical Trial Guidelines in Peripheral Arterial Occlusive Disease recommended that ulcer healing be a parameter when reporting success of revascularization,[35] only 1% of critical leg ischemia studies have reported information on ulcer healing after leg revascularization.[13] One year after infrainguinal bypass surgery, 63% of diabetic patients have been reported to achieve complete healing of the incisional wounds and ischemic ulcers.[16] Complete ulcer healing after endovascular revascularization was observed in 79% of the limbs during 18-month follow-up in the series by Alexandrescu et al.[36] In another series by Alexandrescu et al,[23] 73% of diabetic patients achieved ulcer healing and returned to ambulation after angiosome-guided infrapopliteal PTA. In a follow-up of diabetic patients undergoing PTA, bypass, or conservative treatment for a mean of 6 years, Faglia et al[37] reported that 86% showed complete healing of the tissue lesions.

In the present study, less than half of the patients in the direct group and only one fourth of the patients in the indirect group achieved ulcer healing and were alive without a major amputation 1 year after PTA. These results indicate that ischemic foot ulcers in diabetics are signs of a severe disease with considerable risk for ulcer chronicity, major amputation, and death. Diabetic patients with arterial insufficiency and foot ulcers should be identified early.[38] It has been suggested that the threshold for revascularization in diabetic patients with foot ulcer should be lower than that for nondiabetics.[8] This may allow surgeons to intervene when the disease has not yet become too extensive for beneficial intervention.

This study had some limitations. First, this was a retrospective, nonrandomized study of a prospectively maintained database. Because there were differences in the baseline characteristics of the groups, adjustment was performed by propensity score analysis. The morphology of the infrapopliteal arterial occlusive lesions was not included in the analysis due to a lack of proper classification.[39,40] Second, the angiosome areas may show individual variations. Third, the wound size could not be retrospectively evaluated and the wound care was not standardized, which might have influenced ulcer healing time. However, there is no evidence that any wound dressing or local ulcer treatment method is better than another for speeding up the ulcer healing process.[19,41] Fourth, glucose levels might interfere with ulcer healing. Due to the retrospective nature of the study, we could not obtain information about how well glucose levels were controlled.

The angiosome concept may be more relevant for endovascular revascularizations than for bypass surgery. Endovascular technique more often offers the option to reopen multiple vessels than bypass surgery. Angiosome-guided bypass surgery is not always possible due to infection, extensive tissue loss, and severe arterial occlusive disease, including absence of runoff.[31] Efforts to opening the feeding artery of the ulcerated angiosome may require more skills, more time, and more redo procedures. A larger clinical experience in randomized and prospective studies is needed to evaluate the potential advantages or drawbacks of angiosome-oriented revascularization.

AUTHOR CONTRIBUTIONS

Conception and design: MS, AA, ML, MV
Analysis and interpretation: MS, AA, FB, MV
Data collection: MS, KL

Writing the article: MS, FB, ML, MV
Critical revision of the article: AA, FB, KL, ML, MV
Final approval of the article: MS, AA, FB, KL, ML, MV
Statistical analysis: MS, FB, MV
Obtained funding: Not applicable
Overall responsibility: MS

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