Concept of Angiosome Does Not Affect Limb Salvage in Infrapopliteal Angioplasty

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Background: The purpose of this study was to evaluate the importance of the "angiosome" concept in patients with critical limb ischemia treated with infrapopliteal angioplasty, analyzing limb salvage, secondary function, and survival rates between those treated with and without reference to the concept of the angiosome (groups 1 and 2, respectively).
Methods: This was a retrospective, consecutive cohort study that evaluated 95 patients with critical limb ischemia who underwent infrapopliteal angioplasty at the Division of Vascular and Endovascular Surgery, São Paulo State Public Servants' Hospital, Brazil, between January 2009 and January 2013. Of the total 92 patients (109 limbs) who underwent angioplasty, 48 (52.2%) patients were in group 1 and 44 (47.8%) patients were in group 2.
Results: There was no difference between groups 1 and 2 in terms of the location, lesion severity, or active infection of the infrapopliteal angioplasty. However, groups 1 and 2 differed in their postoperative ankle-brachial indices, which were 0.95 ± 0.18 and 0.85 ± 0.18, respectively ($P = 0.001$). The estimates of limb salvage were similar in groups 1 and 2 (87% and 92.3%, respectively, at 360 days; $P = 0.241$). The analysis of secondary function did not differ between the 2 groups (65.1% and 58.3%, respectively, within 360 days; $P = 0.92$). Operative mortality was 8.3% in group 1 and 8% in group 2 ($P = 0.60$), and survival at 360 days was 78.5% in group 1 and 78.3% in group 2 ($P = 0.86$), which were not significantly different.
Conclusions: In this study, we found no evidence to support revascularization based on the concept of the angiosome in preference to revascularization of the artery that is most amenable to endovascular treatment for limb salvage and secondary function.

INTRODUCTION

About 20% of the world population suffers chronic peripheral arterial disease, and 1–3% will progress to critical limb ischemia.[1] If not properly treated, 30% of these patients per year will require major amputation, and 25% will die.[2] No available pharmacological treatment has so far proved more effective in limb salvage than arterial revascularization.[1,2] In this context, arterial revascularization is the gold standard treatment, allowing direct arterial perfusion of the foot and good results for limb salvage.[3,4]

A proportion of patients (about 8–29%) with critical limb ischemia will develop nonhealing ulcers and suffer major amputation, despite adequate and technically successful revascularization.[5–8] Many factors have been investigated in an effort to improve the treatment of infrapopliteal lesions and thereby increase the success rates for limb salvage and wound healing. Factors such as the location of the wound and the anatomic regions of the foot angiosomes have been used to explain the failure of limb salvage in patients with patent bypass grafts and technically successful procedures.[9–12]

Lida et al. evaluated the factors associated with limb salvage in a study of the long-term results of

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angiosome-guided angioplasty in 369 patients with critical limb ischemia and isolated infrapopliteal injury. There was a statistically significant difference in limb salvage between the direct group (85% at 12 months) and the indirect group (74% at 12 months; $P = 0.01$), but the groups were not uniform and had different risk factors associated with major amputation.[13] The purpose of this study was to evaluate the importance of the ''angiosome'' concept in patients with critical limb ischemia treated with infrapopliteal angioplasty, analyzing limb salvage, secondary function, and survival rates between those treated with and without reference to the concept of the angiosome (groups 1 and 2, respectively).

METHODS

The study was approved by the ethical committee for research. This was a retrospective, consecutive cohort study that evaluated patients with critical limb ischemia who underwent infrapopliteal angioplasty at the Division of Vascular and Endovascular Surgery, São Paulo State Public Servants' Hospital, Brazil, between January 2009 and January 2013. Patient data were collected from the database of the service using Microsoft Access (Microsoft, Seattle, WA), including their demographic and epidemiologic data and details of the outpatient follow-up program. When necessary, the hospital records were also reviewed. The details of the surgical procedures were obtained from the database and an analysis of the patient records.

The inclusion criterion was that the patient with critical limb ischemia had undergone infrapopliteal angioplasty in at least 1 leg artery (anterior tibial artery, posterior tibial artery, or peroneal artery). Patients who experienced an initial technical failure were excluded. The arteriography procedures of the patients were reevaluated to assure accurate filling of the protocols.

In our department, infrapopliteal angioplasty is performed in the most amenable artery, instead of following the concept of angiosome, preferentially performed with primary ballooning, and stents are reserved for specific situations, such as dissection and when the residual stenosis exceeds 30%. Patients receive 300 mg of clopidogrel as the loading dose immediately after the procedure and continue receiving 75 mg of clopidogrel with aspirin (100 mg/day) for 6 months. The use of aspirin at this dose is indicated for all patients, unless there are contraindications. Therefore, all patients receive some type of statin. The indications for angioplasty are according to 2 important studies, Trans-Atlantic Inter-Society Consensus and BASIL trial.[1,2,15]

Initial technical success of the infrapopliteal angioplasty was defined as no >30% residual stenosis, no dissection after the procedure, and the prompt restoration of blood flow in the previously stenotic or occluded artery. Procedures such as debridement and minor amputations were also performed during hospitalization.

All the patients were followed up with scheduled returns to the hospital at intervals of 15 days, 1, 3, 6, and 12 months after discharge. After the first year, the patients were followed up every 6 months, when the following clinical criteria were evaluated: pulse palpation, ankle-brachial index (ABI), and symptoms. Whenever possible, we undertook surveillance programs with arterial duplex scan (DUS) in the first year, at 1, 3, 6, and 12 months after the procedure. After the first year, arterial Doppler was performed every 6 months. If any clinical or sonographic changes were noted, the case was brought up for discussion at a departmental clinical meeting to assess whether reintervention was required. Occlusion of angioplasty was defined (with DUS) as no flow, segmental, or complete, in the angioplasted artery.

The primary outcome variable was limb salvage. Major amputation was defined as amputation proximal to the ankle. The secondary outcome variables were patency, survival, and operative mortality.

Statistical analyses were performed with SPSS 15.0 for Windows. Frequencies and descriptive statistics were analyzed. The chi-squared test and Student's *t*-test were used to compare the univariate data. Comparisons between groups were made with a multivariate analysis. Survival curves that estimated limb salvage, patency, and survival were constructed with the Kaplan–Meier method and the groups were compared with the log-rank test. A P value < 0.05 was considered statistically significant.

Theory

The ''angiosome'' concept was first defined by Ian Taylor in 1987 and divides the entire body into 3-dimensional anatomic units that are vascularized by specific arteries.[12] In short, the foot is divided into 5 anatomic areas, called angiosomes, according to the derivation of their blood supply from the 3 leg arteries: the anterior tibial and fibular arteries supply 2 angiosomes and the posterior tibial artery is responsible for perfusing 3 angiosomes. The anterior tibial artery perfuses the dorsal region of the foot and toes, whereas the peroneal artery supplies the

Table I. Clinical characteristics of the patients by group

Variable	Total (n = 92)	Group 1 (n = 48, 52.2%)	Group 2 (n = 44, 47.8%)	P value
Age	72.97 ± 8.3	71.83 ± 8.1	74.2 ± 8.4	0.906
Male	50 (54.3%)	25 (52.1%)	25 (56.8%)	0.432
Hypertension	80 (87%)	44 (91.7%)	36 (81.8%)	0.184
Diabetes	70 (76.1%)	36 (75%)	34 (77.3%)	0.66
Dyslipidemia	70 (76.1%)	38 (79.2%)	32 (72.7%)	0.221
Heart disease	42 (45.7%)	23 (47.9%)	19 (43.2%)	0.487
Chronic renal failure	21 (22.8%)	12 (25%)	9 (20.5%)	0.939

Table II. Clinical data for the 2 groups of patients

Variable	Total (n = 92)	Group 1 (n = 48, 52.2%)	Group 2 (n = 44, 47.8%)	P value
Creatinine before	1.51 ± 1.4	1.56 ± 1.1	1.45 ± 1.2	0.689
Creatinine after	1.59 ± 1.47	1.65 ± 1.5	1.53 ± 1.1	0.685
Rutherford 4	4 (4.3%)	1 (4.2%)	2 (4.5%)	0.924
Rutherford 5	57 (62%)	31 (64.6%)	26 (59.1%)	0.638
Rutherford 6	31 (33.7%)	15 (31.3%)	16 (36.4%)	0.223
Infection	77 (83.7%)	41 (85.4%)	36 (81.8%)	0.804
High risk	57 (62%)	29 (60.4%)	28 (63.6%)	0.560

lateral side of the leg and the calcaneus. The posterior tibial artery perfuses the plantar surface of the foot and the medial heel and ankle. These leg arteries send branches to the foot that anastomose with each other to ensure adequate perfusion. The dorsalis pedis artery occurs in the angiosome of the anterior tibial artery, whereas the plantar arteries are classified in the angiosome of the posterior tibial artery.[12–14]

On the basis of the consecutive analysis of the target artery and the topography of the throfic lesion, the patients were identified in 2 groups: the direct group (group 1) consisted of those patients in whom angioplasty was performed with reference to the concept of the angiosome; in the indirect group (group 2), angioplasty was performed without reference to the concept of the angiosome, perfusing the area of the lesion through the communicating arterial branches of the foot.

RESULTS

In total, 114 infrapopliteal angioplasties were performed in 95 patients, with initial technical success in 95.6% of patients and a mean clinical follow-up period of 430 days (±377.5). Analyses were performed at 180 and 360 days. The main cause of technical failure (71.4% of cases) was failure to progress a 0.014-in guidewire through the lesion. These patients were excluded from the study, leaving 92 patients and 109 limbs. The number of reoperations involved 20 limbs, with rates of 16.9% in group 1 and 20% in group 2 (P = 0.890). The mean period without reintervention was 338 days: 247 days in group 1 and 445.74 days in group 2 (P = 0.098). Regarding to the reoperations, there were 11 cases of percutaneous transluminal angioplasty, and 9 patients were submitted to an open surgery.

The clinical characteristics of the patients are summarized in Table I and their clinical data in Table II. The clinical characteristics were similar in both groups, with no statistical difference in the prevalence of cardiovascular disease or the risk factors associated with this condition. Of the total 92 patients (109 limbs) who underwent angioplasty, 48 (52.2%) patients were in group 1 and 44 (47.8%) patients in group 2 (Table III).

There was no difference between groups 1 and 2 in terms of the location, lesion severity, or active infection of the infrapopliteal angioplasty. However, groups 1 and 2 differed in their postoperative ABIs, which were 0.95 ± 0.18 and 0.85 ± 0.18, respectively (P = 0.001). The arteries treated with angioplasty differed significantly between the 2 groups: anterior tibial (group 1 = 55%, group 2 = 18%; P = 0.009), posterior tibial (group 1 = 30%, group 2 = 2%; P = 0.001), and fibular (group 1 = 26%, group 2 = 66%; P = 0.078). The femoropopliteal segment was treated in 72 limbs (66%), without difference between the 2 groups (P = 0.415).

Table III. Profiles of angioplasties in general and stratified by group (multivariate analysis of Cox)

Variable	General (109)	Group 1 (59)	Group 2 (50)	*P* value
ABI before	0.54 ± 0.26	0.56 ± 0.27	0.51 ± 0.23	0.284
ABI after	0.90 ± 0.16	0.95 ± 0.18	0,85 ± 0.18	0.001
Lesion location (%)				
Toes	72.5	76.7	69	0.784
Instep	6.4	1.7	10	0.075
Forefoot	2.7	1.7	4	0.784
Plantar	0.9	0.0	2	0.075
Leg	9.7	13.3	2	0.784
Calcaneus	15.6	8.3	10	0.54
Artery				
Femoropopliteal	72 (66)	40	32	0.415
Anterior tibial	42 (37.7)	33 (55)	9 (18)	0.009
Fibular	51 (48)	20 (26)	31 (66)	0.0078
Posterior tibial	19 (16)	18 (30)	1 (2)	0.001
Tibiofibular trunk	35 (32.1)	13 (21.7)	22 (44)	0.233

The estimates of limb salvage were similar in groups 1 and 2 (87% and 92.3%, respectively, at 360 days; $P = 0.241$; Fig. 1). There was no difference in cumulative patency between the 2 groups (65.1% and 58.3%, respectively, within 360 days; $P = 0.92$) (Fig. 2). Operative mortality was 8.3% in group 1 and 8% in group 2 ($P = 0.60$), and survival at 360 days was 78.5% in group 1 and 78.3% in group 2 ($P = 0.86$), which were not significantly different (Fig. 3).

DISCUSSION

The importance of angiosomes in limb salvage and in wound healing during critical limb ischemia remains controversial in the literature.[16] The concept of angiosomes was initially created by plastic surgeons to program the flaps for wound healing in the lower limbs by subdividing the areas of the foot into anatomic units.[17]

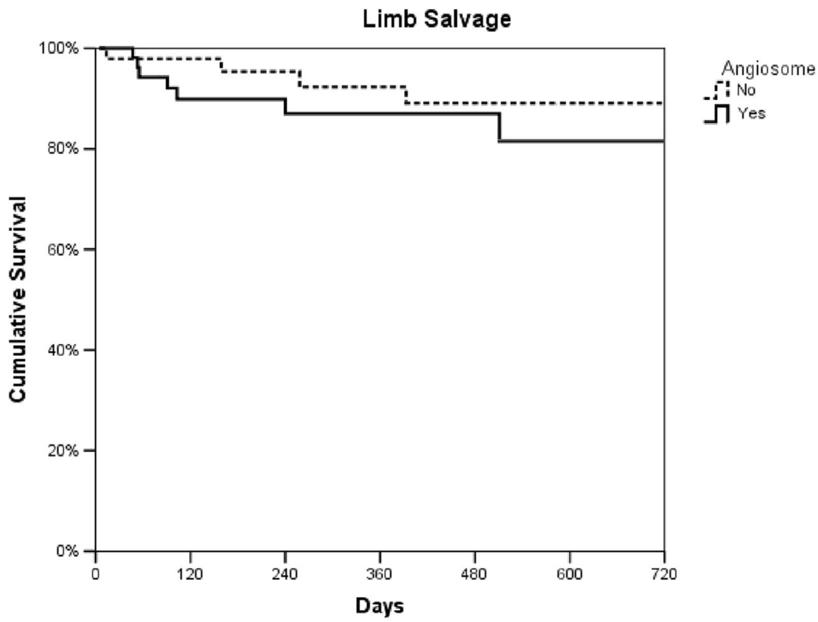
Although the present study was retrospective, there were no differences between the direct and indirect groups in terms of their demographic variables, clinical variables, or comorbidities, demonstrating that the groups were statistically similar. The significant difference between groups was in the postoperative ABI, which was higher in group 1. This can be explained by the direct blood flow to the foot provided by the increased number of tibial arteries treated in this group.[17] In group 2, there was a higher incidence of fibular artery angioplasty, but this did not affect the estimates of limb salvage.

The overall operative mortality rate was 8.6%, which is higher than that reported in the literature, which ranges from 1% to 3%, with an average of 1.8%.[1] This result can be explained by the higher number of patients in the present study who had high cardiac risk factors.

Many factors are involved in limb salvage and wound healing in diabetic patients, including appropriate infection control, constant debridement, dressings, and maintenance of the appropriate level of glycosylated hemoglobin.[18] Poor glycemic control is associated with the progression of diabetic microangiopathy and also depression of the humoral immune system, which are related to inadequately healing wounds and inadequate infection control, with important consequences for the natural course of healing in a diabetic foot.[19–21] It was not possible to properly assess the rates of wound healing in this study because a retrospective analysis of lesion care, dressings, and glucose levels at the time of injury is difficult.

In a study of infrapopliteal angiosome and angioplasty in 250 limbs, Soderstrom et al. reported that the rates of limb salvage in the direct group (86% in 12 months) and indirect group (77% at 12 months) did not differ significantly. Despite this, they found a significant difference in the rates of wound healing (direct group = 72% and indirect group = 46% at 12 months; $P \leq 0.001$).[17]

Lida et al. evaluated the factors associated with limb salvage in a study of the long-term results of angiosome-guided angioplasty in 369 patients with critical limb ischemia and isolated infrapopliteal injury. There was a statistically significant difference in limb salvage between the direct group (85% at 12 months) and the indirect group (74% at 12 months; $P = 0.01$), but the groups were not uniform and had different risk factors associated with



At risk Days	0	120	240	360	480	600	720
Group 1	48	47	46	45	44	44	44
Group 2	44	39	38	38	38	37	37

Fig. 1. Limb salvage. $P = 0.241$. Group 1: 89% at 180 days, 87% at 360 days. Group 2: 95.3% at 180 days, 92.3% at 360 days. Standard error <0.1 until 705 days.

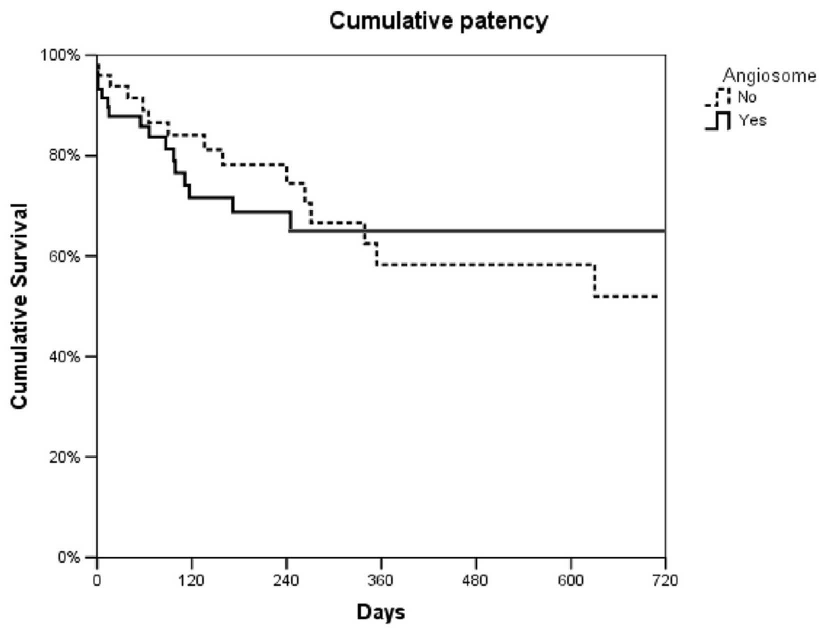
major amputation. The conclusion drawn was that the elevated levels of C-reactive protein in the indirect group were associated with the failure of limb salvage in those patients.[22]

In a recent prospective study comparing infrapopliteal revascularization with reference to the angiosome in 64 patients, Kabra et al. showed similar estimates of limb salvage in the direct and indirect groups (84% and 75%, respectively; $P = 0.06$), compared with the estimates in the present study. The study examined patients undergoing open revascularization (56.2%) or endovascularization (39.1%). The incidence of ischemic coronary disease was higher in the indirect group ($P = 0.01$).[23]

Our estimates of cumulative patency (65.1%) and limb salvage (92.3%) were satisfactory and are consistent with those in other series, such as that of Romiti et al., who undertook a meta-analysis of infrapopliteal angioplasty in 30 articles published between 1990 and 2006. That study showed estimates of 82.4% limb salvage and 62.9% cumulative patency at 36 months. Consequently, our results are consistent with those in the literature.[24]

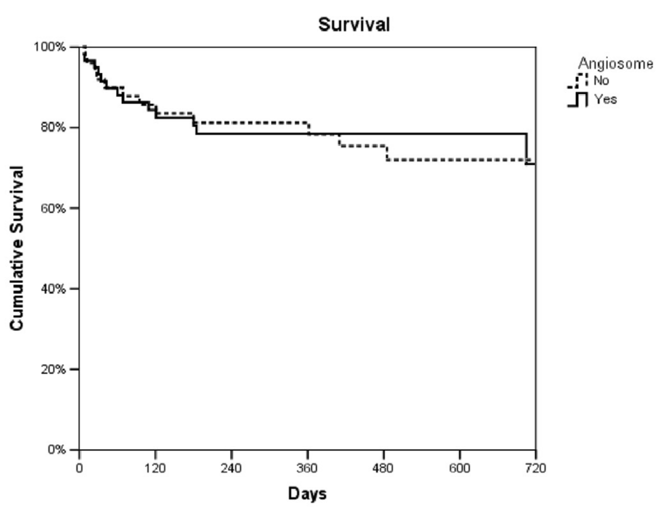
Of note, among the large number of publications available on endovascular procedures, Kret et al. retrospectively evaluated 106 patients who had undergone infrapopliteal bypass-based revascularization with reference to the angiosome, with similar estimates of limb salvage (compared with the present study) for the indirect group (70.9%) and direct group (75.3%; $P = 0.82$) at 11 months. When the groups were defined according to the presence of a full arch and an incomplete arch, the rates of limb salvage were 72% and 65%, respectively ($P = 0.86$).[25]

In recent meta-analysis, Biancari et al. evaluated 9 studies reported on data of interest, showing that the risk of unhealed wound was significantly lower after direct revascularization (hazard ratio [HR], 0.64; 95% confidence interval [CI], 0.52–0.8; I^2 0%, 4 studies included) compared with indirect revascularization. Direct revascularization was also



At Risk Days	0	120	240	360	480	600	720
Group 1	48	41	38	34	34	34	33
Group 2	44	31	29	28	34	34	34

Fig. 2. Cumulative Patency. $P = 0.92$. Group 1: 68.8% at 180 days, 65.1% at 360 days. Group 2: 78.8% at 180 days, 58.3% at 360 days. Standard error <0.1 until 610 days.



At risk days	0	120	240	360	480	600	720
Group 1	48	40	39	38	36	36	35
Group 2	44	34	32	32	32	32	31

Fig. 3. Survival. $P = 0.86$. Group 1: 80.5% at 180 days, 78.5% at 360 days. Group 2: 83.5% at 180 days, 78.3% at 360 days. SE <0.1 until 731 days.

associated with significantly lower risk of major amputation (HR, 0.44; 95% CI, 0.26–0.75; I^2 62%, 8 studies included). Pooled limb salvage rates after direct and indirect revascularization were at 1 year 86.2% and 77.8% and at 2 years 84.9% and 70.1%, respectively.[26]

It is important to note that in most studies, the estimates of limb salvage and cumulative patency are similar in both groups (e.g., direct and indirect), even when the studies show better rates of healing in patients undergoing infrapopliteal angioplasty based on the concept of the angiosome. This supports the idea that even when healing is faster in the direct group, limb salvage is ultimately unaffected. It is also important that most of these studies were performed retrospectively and did not take into account other factors involved in healing, such as the blood glucose levels of patients and the type of dressing used.

This study had some important limitations. It was a retrospective study based on the analysis of consecutive data collected from medical records and a database service. These limitations can be addressed with a prospective study, which is currently in progress in our department.

CONCLUSIONS

In this study, we found no evidence to support revascularization based on the relevant anatomic segment according to the concept of the angiosome in preference to revascularization of the artery that is most amenable to endovascular treatment for limb salvage and secondary function. Future prospective studies are required.

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