Original Article

Impaired pedal arch affects the treatment effect in patients with single tibial artery revascularization demonstrated by intraoperative perfusion

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Background: The treatment strategy for patients with multiple infrapopliteal artery occlusions remains controversial. In this study, we investigated how anatomic factors affect the treatment effect of infrapopliteal artery intervention and identified suitable intervention strategies for patients with multiple infrapopliteal artery occlusions.

Methods: This was a prospective, single-center, observational cohort study. For each patient, the intrainterventional blood volume improvement of the dorsum and plantar surface was measured and classified into the direct perfused region (DR) or indirect perfused region (IR) on the basis of whether the supplying artery was revascularized. Digital subtraction angiography was performed to analyze how pedal arch patency affects blood communication between DR and IR.

Results: A total of 38 patients treated with infrapopliteal intervention at the Department of Vascular Surgery of Peking Union Medical College Hospital from November 2016 to November 2020 were considered for inclusion in this study. Finally, 26 patients were included in the analysis. In patients with type III pedal arch, blood volume improvements for DR and IR were 70.50 (17.50, 191.75) and 11.25 (–10.25, 50.25) mL/1,000 mL, respectively (P=0.018). No significant difference was found between DR and IR in patients with type I pedal arch (P=0.208) and type II pedal arch (P=0.110).

Conclusions: Impaired pedal arch has an adverse impact on foot collateral circulation. Patients with these conditions are more suitable for direct revascularization than other patients.

Trial Registration: ClinicalTrials.gov identifier: NCT03248323.

Keywords: Peripheral arterial disease; blood volume; perfusion imaging; collateral circulation; pedal arch

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Introduction

Peripheral artery disease (PAD) affects approximately 202 million people globally and causes a heavy disease burden on society (1). The restoration of blood supply, including endovascular treatment and bypass surgery, is critical for patients with PAD.

The infrapopliteal arteries are often involved in patients with PAD. Considering that it is unclear how the patency of three infrapopliteal arteries and their communication contribute to the blood supply of the foot, it can be difficult to find the best treatment strategy for patients with multiple infrapopliteal artery occlusions. According to the angiosome proposed by Taylor and Palmer (2) in 1987, the blood supply to the foot is mainly affected by major arteries, and blood communication among angiosomes is limited. This means that revascularizing the occluded artery directly can improve perfusion compared with supplying blood via collateral circulation. However, this strategy is still under debate. On one hand, it can be difficult to treat arteries with complete occlusion. On the other hand, evidence concerning angiosomes has not reached the same conclusion (3-12). The role of foot collateral circulation requires further investigation.

The blood volume delivered to the tissue is affected by the pedal arch, which connects the anterior and posterior tibial arteries. Therefore, anatomic abnormalities in the pedal arch may impair blood supply to the ischemic area after endovascular intervention. Previous studies have shown that an impaired pedal arch leads to worse wound healing in patients with PAD (13-17). It can be assumed that impaired perfusion restoration may play an important role in resolving the adverse outcome.

Flat panel detector CT (FD-CT) was deemed promising in assessing tissue perfusion in recent years (18). Given that FD-CT can be performed during endovascular intervention and can reconstruct the 3D perfusion status of an organ, it can measure intrainterventional blood volume changes in different foot areas and evaluate treatment effects immediately. This technique has presented excellent correlation coefficient with conventional multislice perfusion CT in several previous studies concerning liver and brain perfusion (19-22). In this study, we measured the intrainterventional blood volume of different foot regions by using FD-CT and assessed whether pedal arch patency affects the outcome of infrapopliteal revascularization.

We present the following article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-21-801/rc).

Methods

Study design and patient population

This study was a single-center, prospective, observational cohort study. Patients who were treated at the Department of Vascular Surgery of Peking Union Medical College Hospital between November 2016 and November 2020 were included in this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of our hospital. All participants in this study provided written informed consent. Patients were included if they (I) had a diagnosis of infrapopliteal artery occlusion or stenosis (>70%) confirmed by CT angiography or duplex ultrasonography, (II) had a Rutherford classification of stage 3 or higher, and (III) consented to participate in this study. Patients who met the following exclusion criteria were excluded from the study: (I) having less or more than one tibial artery treated, (II) infection or ulcers in the puncture area, (III) life-threatening disease, (IV) allergy to iodinated contrast, (V) taking medicine that may influence study creditability, and (VI) other conditions that should merit exclusion as decided by the investigators.

Image acquisition and measurement

At the beginning of endovascular treatment, the operator injected 8 mL iodixanol (320 mg of iodine per milliliter, Visipaque; GE Healthcare) at a rate of 1.5 mL/s via a catheter placed in the common femoral artery (Cordis, 5F VER). The condition of the lower extremity arteries was evaluated to determine the treatment strategy via digital subtraction angiography (DSA) performed with a flat panel detector angiographic system (Artis Zeego; Siemens Healthcare). Before infrapopliteal intervention, DSA was performed again after the injection of 8 mL iodixanol. The images acquired in this process were transferred to a workstation (syngo X-Workplace, Siemens Healthcare GmbH) and then processed to calculate the time from contrast injection to arrival time at the ankle level. This time was used to estimate when to start the CT scan by using the following procedure.

The parameters for the CT scan were as follows: 70 kV tube voltage, 8 s acquisition time, 30 cm × 40 cm flat panel detector size, 616×480 matrix, 200° rotation angle, 0.5°/frame,

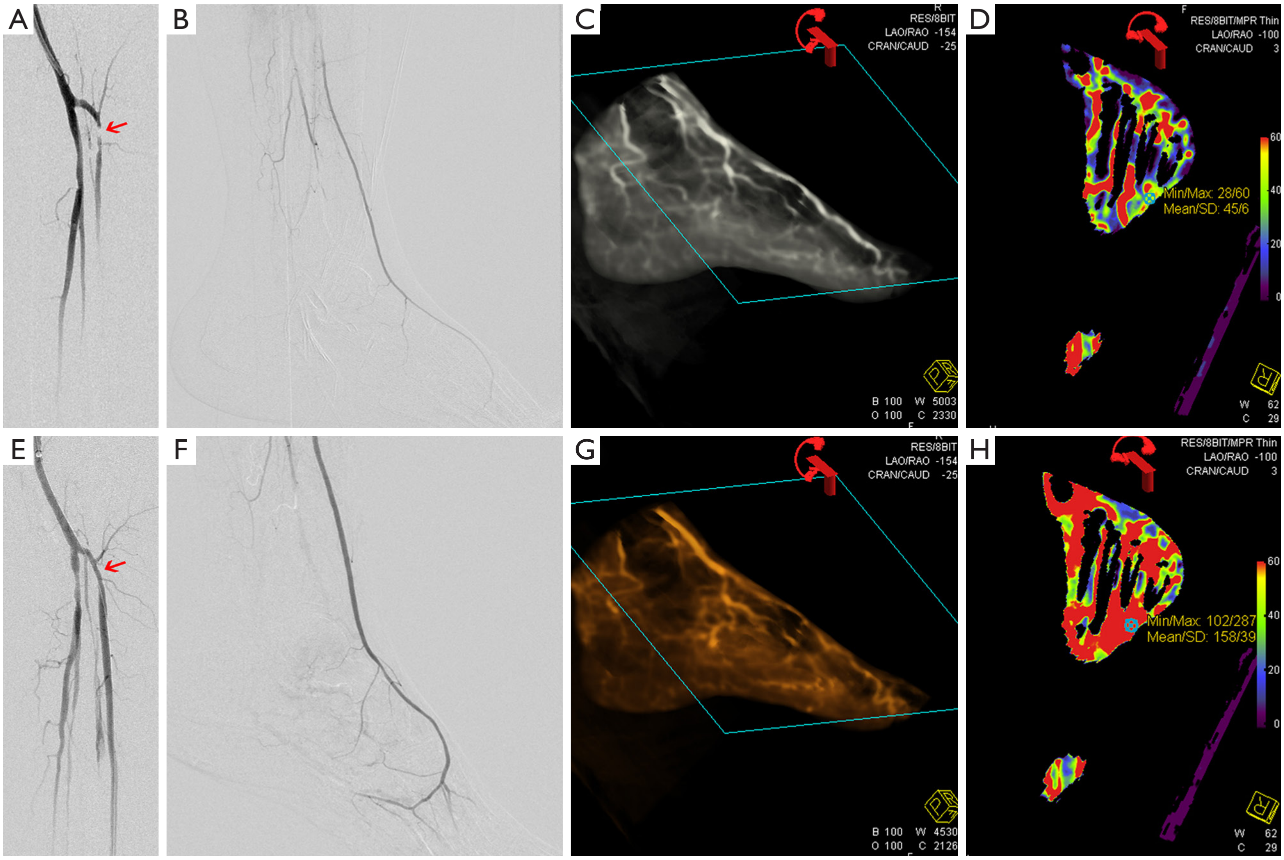

Figure 1 Blood volume measurement. Preoperative anterior tibial artery occlusion (A), pedal arch (B), 3-dimentional reconstruction (C) and perfusion image of a certain interface of dorsum (D). Postoperative anterior tibial artery occlusion (E), pedal arch (F), 3-dimentional reconstruction (G) and perfusion image of a certain interface of dorsum (H). Red arrow indicates occlusion site. Blue circle indicates region of interest. Reprint from Ma *et al*.

0.36 μGy/frame dose. The scan area contained the ankle and the foot. Before the contrast injection, a mask scan lasting 8 s was performed to obtain a background image of the foot. The operator then injected 15 mL iodixanol diluted with 15 mL normal saline at a rate of 1.5 mL/s. When the contrast reached the ankle, a fill scan lasting 8 s was performed to obtain the distribution of the contrast. The images were then transferred to a workstation for 3D reconstruction. The above process, including estimating delay time, was repeated within 10 min after infrapopliteal endovascular intervention performed with uncoated balloon.

If the operator judged that a spasm occurred during the intervention, the operator would use drug to alleviate spasm. Besides, the operator would also wait for a while for the spasm to recover before perfusion measurement. To avoid the influence of foot movement, corrections were made to ensure that the preinterventional and postinterventional reconstructions stayed at the same position. Thereafter, planes with a thickness of 0.5 mm were used to obtain a color-coded perfusion map of the intersecting area. The blood volume in the cylinder was calculated after selecting a region of interest (ROI) in the perfusion map (*Figure 1*).

The decision of ROIs was in accordance with the angiosome concept. The parenchymal blood volume (PBV) of the dorsum and plantar surface was used to represent the perfusion status of the anterior tibial artery (ATA) and posterior tibial artery (PTA), which are indicated as PBV_{dor} and PBV_{pla}, respectively. To calculate the PBV of each area, we selected four ROIs with a diameter of 5 mm and used the average blood volume of the four ROIs to indicate the blood volume of the area (*Figure 2*). The ROIs were at the same position on the preinterventional and postinterventional perfusion maps. Blood vessels were avoided during measurement. The person who measured

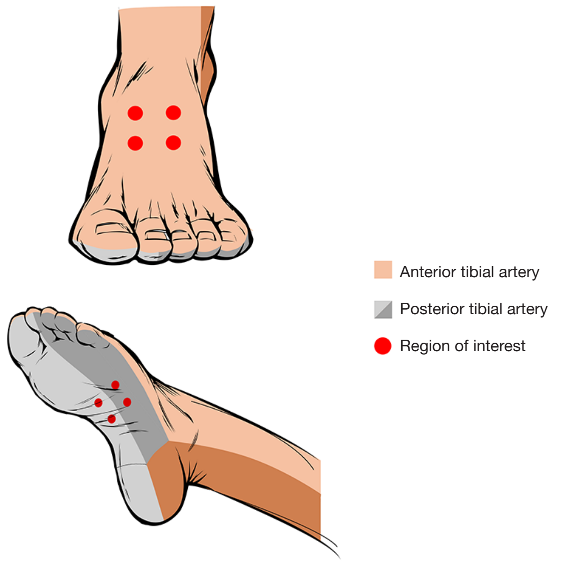

Figure 2 Illustration of region of interests (ROIs). Parenchymal blood volumes of dorsum and plantar surface were used to represent perfusion status of anterior tibial artery (ATA) and posterior tibial artery (PTA) separately. For each area, 4 ROIs with a diameter of 5 mm were selected and average blood volume of 4 ROIs was used to represent blood volume of the area. Reprint from Ma *et al*.

the blood volume was unaware of the clinical condition of the patients before measurement.

On the basis of the condition of supplying the infrapopliteal artery, each foot area was classified into either the direct perfused region group (DR) or indirect perfused region group (IR). The supplied area was classified as DR if an artery was revascularized, and the area was classified as IR if the supplying artery was not treated and if the area was perfused by the other revascularized tibial artery via collateral circulation.

Pedal arch patency evaluation

The pedal arch was classified into one of three types on the basis of the presence of plantar arteries and the dorsalis pedis artery in DSA (14). The type I pedal arch showed both the plantar arteries and dorsalis pedis artery. The type II pedal arch had either plantar arteries or the dorsalis pedis artery. If neither of the two arteries was patent, the pedal arch would be categorized as type III (*Figure 3*).

Statistical analysis

Qualitative data, such as baseline characteristics, were

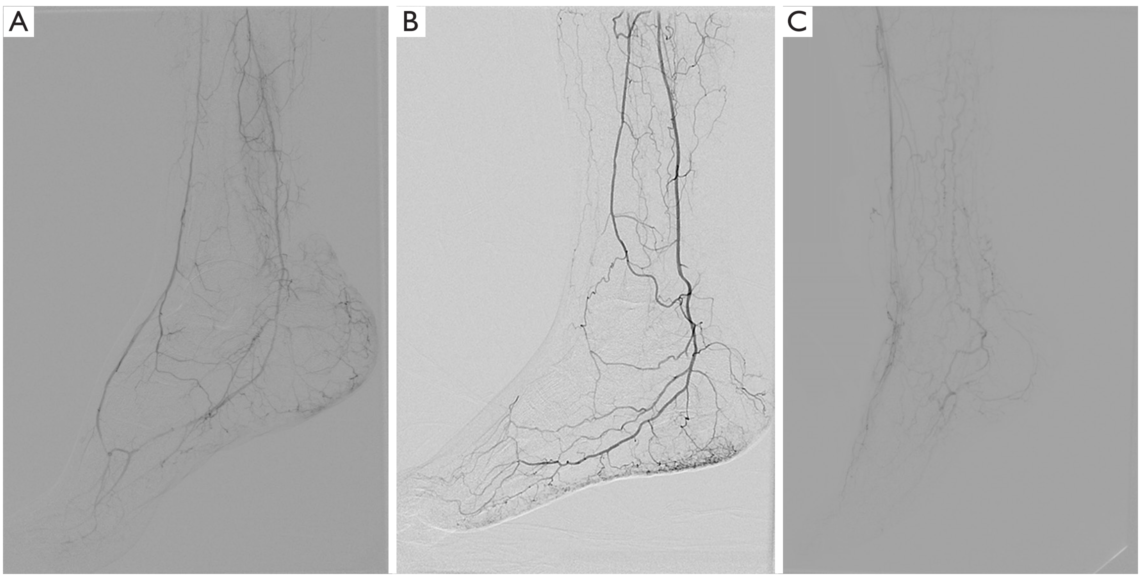

Figure 3 Pedal arch classification. Type I pedal arch showed both plantar arteries and dorsalis pedis (A). Type II pedal arch had either plantar arteries or dorsalis pedis (B). Type III pedal arch showed no plantar arteries or dorsalis pedis (C).

Table 1 Occlusions and interventions of infrapopliteal arteries

Category	n
Diseased artery	
3 arteries	21
2 arteries	15
ATA + PTA	10
ATA + PA	2
PTA + PA	3
1 artery	2
ATA	2
PTA	0
PA	0
Disposed artery	
3 arteries	1
2 arteries	8
ATA + PTA	2
ATA + PA	2
PTA + PA	4
1 artery	26
ATA	11
PTA	9
PA	6
No disposed artery	3

Among the 38 patients considered for inclusion, 21 of them had occlusions in all 3 infrapopliteal arteries, 15 patients had 2 occluded arteries and 2 patients possessed 1 occluded artery. Most patients only had 1 occluded artery treated (26/38). ATA, anterior tibial artery; PA, peroneal artery; PTA, posterior tibial artery.

presented as frequencies and percentages. Continuous data were presented as means (standard deviations) or medians (quartiles) depending on their normality. Missing data was removed from analysis. Student's *t*-test or the Wilcoxon signed-rank test was performed to test the differences between two groups. In this study, the blood volume of different groups is distributed abnormally, so we used medians (quartiles) to display the data and Wilcoxon signed-rank test to test the difference between different groups. The tests were two-tailed, and the results were considered significant at $P<0.05$. Statistical analyses were performed using SPSS version 25 (SPSS Inc.).

Table 2 Baseline characteristics

Characteristics	Data
Age, years, mean [range]	68.8 [53–86]
Men	17 (65%)
Hypertension	22 (85%)
Diabetes mellitus	20 (77%)
Dyslipidemia	17 (65%)
Smoking	13 (50%)
Coronary artery disease	11 (42%)
Cerebral infarction	10 (38%)
Ankle-brachial index	0.31 (0, 0.60)
Preoperative Rutherford symptom classification	
Stage 3	5
Stage 4	10
Stage 5	7
Stage 6	4

Results

In total, 38 patients (mean age: 67.9 years, range: 48–86 years), including 24 males (mean age: 65.3 years, range: 48–80 years) and 14 females (mean age: 72.1 years, range: 58–86 years), were included in this study. Among the 38 patients with infrapopliteal artery occlusion, 45 arteries from 35 patients, including 16 ATAs, 16 PTAs, and 13 peroneal arteries (PAs), were treated with angioplasty. Intervention was unsuccessful in three patients. *Table 1* shows the occlusion and intervention conditions of the patients. Finally, 26 patients were included in the analysis (*Table 2*, Figure S1).

Perfusion difference in patients with types I, II, and III pedal arch

Considering that the pedal arch is composed of plantar arteries and the dorsalis pedis artery, we selected patients with either ATA or PTA intervention. Because the patient only had single tibial artery treatment and was measured blood volume in 2 foot areas, there would be one area belonging to DR and the other area belonging to IR, which means DR was paired with IR for each patient. We then divided these patients into 3 groups on the basis of the pedal arch type: 8 patients had type I pedal arch, 11 patients

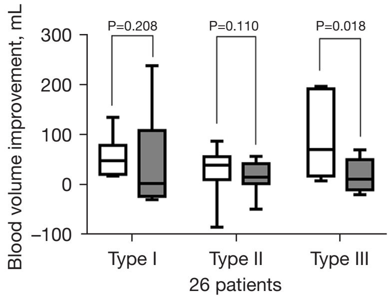

Figure 4 Subgroup analysis in patients with different type of pedal arch. In patients with type III pedal arch, blood volume improvements for direct perfused region (DR) and indirect perfused region (IR) were 70.50 (17.50, 191.75) and 11.25 (–10.25, 50.25) mL/1,000 mL, respectively (P=0.018). No significant difference was found between DR and IR in patients with type I (P=0.208) and type II (P=0.110) pedal arch.

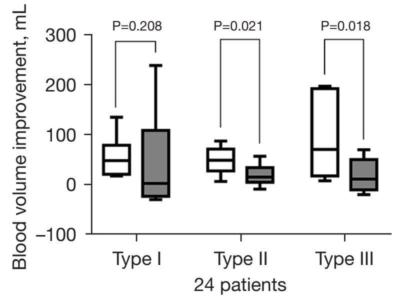

Figure 5 Subgroup analysis in patients with different type of pedal arch. After excluding patients with decreased overall blood volume, result remained the same in patients with type I and type III pedal arch. In patients with type II pedal arch, direct perfused region (DR) resulted in better blood volume improvements than indirect perfused region (IR) (P=0.021).

had type II pedal arch, and 7 patients had type III pedal arch. In patients with type III pedal arch, the blood volume improvements for DR and IR were 70.50 (17.50, 191.75) and 11.25 (–10.25, 50.25) mL/1,000 mL, respectively. There was a significant difference between the two groups (P=0.018). No significant difference was found between DR and IR in patients with type I pedal arch [48.00 (20.69, 78.81) *vs.* 2.38 (–23.06, 108.50) mL/1,000 mL, P=0.208] and type II pedal arch [39.25 (10.25, 56.25) *vs.* 15.00 (2.00, 42.25) mL/1,000 mL, P=0.110] (*Figure 4*).

Among the 26 patients who underwent single tibial artery intervention, 2 patients had decreased overall blood volume, which may have been caused by plaque shedding or spasm. After excluding patients with decreased overall blood volume, 24 patients were analyzed for differences between DR and IR, including 8 patients with type I pedal arch, 9 patients with type II pedal arch, and 7 patients with type III pedal arch. The results remained the same in patients with types I and III pedal arch. However, the results were slightly different in patients with type II pedal arch. Blood volume improvements for DR and IR were 48.75 (27.38, 71.13) and 15.00 (4.88, 34.13) mL/1,000 mL, respectively. The results showed a significant difference (P=0.021) (*Figure 5*).

Discussion

In this study, we focused on the impact of pedal arch patency on the infrapopliteal intervention strategy. By establishing a method to evaluate the treatment effect directly within the intervention, we can avoid the influence of confounding factors and evaluate the treatment effect directly. Our results show that impaired pedal arch has an adverse impact on foot collateral circulation, and direct revascularization needs to be performed in patients with these conditions. By contrast, in patients with patent pedal arches, it may be feasible to supply an ischemic area with collateral circulation. Our study provides more options for patients with infrapopliteal artery occlusion.

The angiosome concept has drawn a lot of attention since it was put forward. However, this concept is still controversial. Many studies with various designs have found that angiosome-guided treatment can result in better clinical outcomes (3-7), including a higher wound healing rate and shorter wound healing time in different populations, thus suggesting that it is valid to determine a treatment strategy on the basis of this theory. However, several studies have drawn opposing conclusions regarding the feasibility of angiosomes (8-10,12). Some factors may underlie this controversy, and some pieces of evidence have been raised (16,23,24). Rashid *et al.* (16) concluded that the quality of the pedal arch influences wound healing. Špillerová *et al.* (23) found differences between DR and IR in patients undergoing endovascular intervention but not in patients with surgical revascularization. Stimpson *et al.* (24) considered that the classical angiosome concept is not appropriate for patients with PAD.

In our previous study, we have already proved the correctness of the angiosome concept and concluded that direct revascularization to the ischemia region should be performed (11). However, we also noticed that collateral circulation can achieve similar perfusion restoration compared with direct revascularization in some patients. We assumed that some underlying reason may result in the phenomenon and further designed the current study to explore whether anatomic abnormities would affect the blood communication between different foot regions.

The blood volume delivered to the tissue is affected by the major arteries. Therefore, anatomical abnormalities may impair blood communication among angiosomes. Given that most previous studies investigating DR and IR are retrospective and have limited sample sizes, the ratio of patients with anatomic abnormalities may vary in different studies. The negligence of these abnormalities may cause heterogeneity among different studies and influence the accuracy of the results, thus accounting for the discrepancy in previous evidence.

Several studies have indicated the significance of the pedal arch (13,15-17,25,26). Jung *et al.* (13) and Nakama *et al.* (15) proved that pedal arch angioplasty is beneficial for wound healing in patients with critical limb ischemia. Rashid *et al.* (16) and Troisi *et al.* (17) evaluated the quality of the pedal arch in patients with surgical revascularization and endovascular revascularization, respectively, and found that it was relevant to clinical outcomes. Ricco *et al.* (25) investigated patients with only a patent PA and discovered that the patency of the peroneal branches and the pedal arch was related to better outcomes regardless of angiosome. Varela *et al.* (26) found that restoring blood supply via collateral circulation may achieve similar outcomes as revascularizing the source artery. These studies suggest that the pedal arch plays an important role in patients with critical limb ischemia and may function by affecting the collateral circulation.

In our study, blood volume showed a significant difference between DR and IR in patients with impaired pedal arch, but no difference existed in patients with complete pedal arch. This finding proved the significance of the pedal arch from the perfusion level. According to our study, pedal arch quality is an important factor that affects blood communication in different foot areas and should be considered in future clinical practice and research on angiosomes. Compared with classical angiosomes, whether the ischemia area is reperfused may be more important in determining the treatment effect. In other words, in addition to the direct revascularization of the source artery, we should also focus on major collateral arteries, including the pedal arch and newly formed vessels, because these arteries also bring blood to the ischemic area.

Our study has several limitations. First, the sample size of this study was limited, thus restricting the quality of evidence. In addition, foot deformation and movement during treatment may not be completely eliminated despite the fusion of preinterventional and postinterventional reconstructions. Besides, we can not observe microvascular occlusion in the DSA, which will also affect the blood supplied to the tissue. Finally, there would be several technics for assessment of perfusion and intrainterventional perfusion values should be correlated with other imaging technics in future studies (11,27-29).

Conclusions

We investigated the factors affecting intrainterventional blood volume communication between different angiosomes by using FD-CT. Our results demonstrated that impaired pedal arch has an adverse impact on foot collateral circulation and should be considered in future clinical practice and scientific research.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-21-801/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-21-801/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of our hospital. All participants in this study provided written informed consent.

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Supplementary

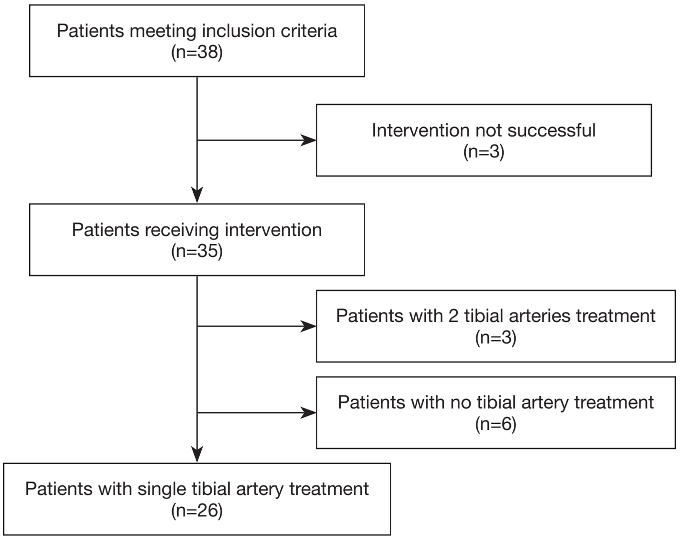

Figure S1 Flowchart of patients inclusion.

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