Clinical Investigation

Interventional Treatment Options for the Prevention of Amputation in Patients With Lower Extremity Wounds From Peripheral Arterial Disease

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Abstract

Background: Peripheral arterial disease and related lower extremity wounds are prominent causes of amputation. Revascularization may reduce amputation rates or the amputation margin more distally in patients with peripheral arterial disease who have wounds resulting from critical limb ischemia. This study examined the association of risk factors and intervention types with amputation rates in patients with critical lower extremity arterial disease.

Methods: A total of 211 patients who underwent peripheral intervention because of foot wound were followed up for 12 months after the intervention. All patients had lower extremity wounds resulting from peripheral arterial disease. The effects of treatment approaches were compared in patients who underwent and did not undergo amputation.

Results: Revascularization of the anterior tibial artery reduced the amputation rate by 6.52 times compared with occlusion. Posterior tibial artery revascularization reduced the amputation rate by 49.95 times.

Conclusion: In this study of percutaneous intervention methods for prevention of amputation, the most effective option was revascularization of the posterior tibial artery and anterior tibial artery. Considering these results, treatment of critical peripheral arterial disease can be cost-effective and efficient and may shorten procedure time.

Introduction

Lower extremity peripheral arterial disease (PAD) affects more than 230 million adults worldwide and is associated with an increased risk of various adverse clinical outcomes, including other cardiovascular diseases such as coronary heart disease and stroke, and leg outcomes such as amputation.[1] Critical risk factors for PAD are hyperlipidemia, hypertension, diabetes, chronic kidney disease, and smoking; the presence of 3 or more factors confers a 10-fold increase in PAD risk.[2] Critical limb ischemia (CLI) (also known as chronic limb-threatening ischemia) is a severe form of PAD typically associated with pain at rest, nonhealing wounds, and tissue loss.[3] The 1-year cumulative incidence for both mortality and amputation in patients with CLI is almost 20%.[4] Providing optimal medical treatment and risk factor control is a priority in all patients, but patients with CLI require revascularization to improve limb perfusion and limit the risk of amputation.[5] There is a focus on eliminating the risk of amputation

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or reducing the amputation margin, especially with interventions to the popliteal artery, anterior tibial artery, posterior tibial artery, and peroneal artery. This study examined the relationship between the risk of amputation and the arteries that underwent intervention in patients with foot wounds resulting from PAD. The aim was to observe the effect of arterial localizations in reducing the risk of amputation.

Key Points

- An endovascular treatment approach should be considered to prevent amputation in patients with CLI.
- The tibialis anterior and tibialis posterior arteries have been identified as the most efficacious revascularization targets for the purpose of amputation prevention.
- During the 12-month follow-up period, it was observed that revascularization of the anterior tibial artery resulted in a 6.52-fold decrease in the risk of amputation compared with patients with occlusion. Similarly, revascularization of the posterior tibial artery was associated with a 49.95-fold decrease in the risk of amputation.

Abbreviations and Acronyms

CLI	critical limb ischemia
OR	odds ratio
PAD	peripheral artery disease

Patients and Methods

This observational study was conducted in a single clinic. Patients who underwent lower extremity arterial intervention between January 2015 and December 2020 were examined. Patients older than 18 years of age and those with wounds resulting from PAD were included in the study. Patients without CLI-related wounds and patients with PAD resulting from trauma were excluded.

Patient demographic characteristics, chronic diseases, and risk factors were examined. For the treatment options, popliteal artery, anterior tibial artery, posterior tibial artery, and peroneal artery interventions were examined. The effects of thrombectomy and atherectomy were also evaluated. The SilverHawk Peripheral Plaque Excision System (Medtronic) was used in these cases. All patients were followed up for 12 months under optimal medical treatment. Patients were separated into 2 groups: those who underwent amputation during postintervention follow-up and those who did not require amputation. The risk of amputation was compared between the 2 groups according to risk factors, treatment approach, and choice of artery for revascularization.

Statistical Analysis

The normal distribution of continuous data was evaluated by visual analysis of histograms and the Shapiro-Wilk test. Normally distributed continuous data were reported as mean (SD), and non-normally distributed continuous data were reported as frequency and percentage. The independent *t* test was used when comparing 2 groups with continuous variables assumed to fit normal distribution, and the χ^2 test or Fisher exact test was used when comparing the categorical data in the 2 groups. The logistic regression method was used when examining the factors affecting the dependent variable, amputation. When adding the independent variables to the model, the stepwise selection method was used, and the appropriateness of the independent variables selected with the forward and backward methods was observed. For the goodness of fit of the model, the Hosmer-Lemeshow test was used. SPSS, version 21, software (IBM Corp) was used, and $P < .05$ was considered statistically significant.

To mitigate the influence of selection bias and establish equitable groups for subsequent analysis, the propensity score method was used to achieve balance between patients who underwent amputation and those who did not. Of the total sample size of 211 individuals, lower extremity amputation was observed in 87 patients, whereas the remaining 124 patients did not undergo such amputation. Following a 1:1 propensity matching procedure, both study groups consisted of 87 participants. The nearest-neighbor matching methodology was used for matching, and the mean difference method was used for balancing assessment. The use of propensity score matching, however, results in the generation of additional outliers in the CIs because when the 2 groups are dispersed in a 1:1 ratio, the overall number of observations is further reduced. Therefore, propensity score matching results were not used in the final analysis.

The study complied with the principles of the Declaration of Helsinki and was approved by the local ethics committee.

Results

A total of 211 patients who underwent peripheral intervention because of a foot wound were evaluated. The mean (SD) age was 65.2 (11.8) years, and 77 (36.5%) of the patients were female. The chronic diseases and risk factors of the entire patient group are shown in Table I.

At least 1 artery was targeted for intervention in the study. The preintervention and postintervention data for the popliteal artery, anterior tibial artery, posterior tibial artery, and peroneal artery are shown in Table II.

Table III shows the risk factors and chronic diseases of patients who did and did not undergo amputation in their follow-up after percutaneous intervention. The frequency of hyperlipidemia was found to be higher in patients who underwent amputation (18.4%) than in patients who did not undergo amputation (8.1%) ($P = .03$).

Intervention characteristics in patients who did and did not undergo amputation are shown in Table IV. Revascularization of the anterior tibial artery and the posterior tibial artery was found to be statistically significant in preventing the risk of amputation ($P = .008$ and $P < .001$, respectively). It was observed that popliteal artery and peroneal artery revascularization, atherectomy, thrombus aspiration, and number of attempts did not reduce amputation risk during follow-up.

The logistic regression method was used to model whether the independent variables would protect patients against amputation. In this model, opening of the anterior tibial artery (odds ratio [OR], 6.52 [95% CI, 3.84-14.32]) and opening of the posterior tibial artery (OR, 49.95 [95% CI, 28.02-136.95]) were associated with lower amputation rates. Diagnoses of diabetes (OR, 0.31 [95% CI, 0.10-0.91]) and hyperlipidemia (OR, 0.28 [95% CI, 0.08-0.89]), however, were associated with higher amputation rates. The Hosmer-Lemeshow test showed that the created model was a compatible model ($P = .79$) (Table V).

In summary, anterior tibial artery revascularization was found to reduce the risk of amputation by 6.52 times compared with occlusion, while posterior tibial artery revascularization reduced the rate of amputation by 49.95 times. In addition, the presence of hyperlipidemia and diabetes was associated with a higher risk of amputation in patients with wounds related to PAD.

TABLE I. Patient Demographic Characteristics and Risk Factors

Factor	Value
Age, mean (SD), y	65.2 (11.8)
Female sex, No, (%)	77 (36.5)
Diabetes, No, (%)	74 (35.1)
Hypertension, No, (%)	81 (38.4)
Coronary artery disease, No, (%)	100 (47.4)
Chronic kidney disease, No, (%)	50 (23.7)
Hyperlipidemia, No, (%)	26 (12.3)
Heart failure, No, (%)	22 (10.4)
Peripheral artery disease history, No, (%)	61 (28.9)
Burger disease, No, (%)	8 (3.8)
Active smoker, No, (%)	5 (26.1)

TABLE II. Vascular Patency Status Before and After Intervention and Artery Revascularization

Artery	No. (%) Preintervention, patent	Preintervention, occluded	Revascularization	Postintervention, patent	Postintervention, occluded
Popliteal	104 (49.3)	107 (50.7)	100 (93.4)	204 (96.7)	7 (3.3)
Anterior tibial	29 (13.7)	182 (86.3)	99 (54.4)	128 (60.7)	83 (39.3)
Posterior tibial	16 (7.6)	195 (92.4)	95 (48.7)	111 (52.6)	100 (47.4)
Peroneal	51 (24.2)	160 (75.8)	90 (56.2)	121 (57.3)	70 (33.2)

TABLE III. Comparison of Demographic and Risk Factors of Patients Who Did and Did Not Undergo Amputation

Variable	Patients undergoing amputation (n = 87)	Patients not undergoing amputation (n = 124)	*P* value[a]
Age, mean (SD), y	65.8 (11.8)	64.8 (11.7)	.55
Female sex, No. (%)	33 (42.9)	44 (35.5)	.77
Diabetes, No. (%)	61 (70.1)	76 (61.3)	.19
Hypertension, No. (%)	53 (60.9)	77 (62.1)	.89
Coronary artery disease, No. (%)	41 (47.1)	59 (47.6)	.87
Chronic kidney disease, No. (%)	24 (27.6)	26 (21.0)	.32
Hyperlipidemia, No. (%)	16 (18.4)	10 (8.1)	.03
Heart failure, No. (%)	8 (9.2)	14 (11.3)	.66
Peripheral artery disease history, No. (%)	27 (31.0)	34 (27.4)	.64
Burger disease, No. (%)	3 (3.4)	5 (4.0)	>.99
Active smoker, No. (%)	18 (20.7)	37 (29.8)	.15

[a] $P < .05$ was considered statistically significant.

TABLE IV. Intervention Characteristics in Patients Who Did and Did Not Undergo Amputation

Variable	Patients undergoing amputation (n = 87)	Patients not undergoing amputation (n = 124)	*P* value[a]
No. of interventions, mean (SD)	3.3 (1.4)	3.4 (1.1)	.77
Popliteal artery revascularization, No. (%)	40 (46.0)	60 (48.4)	.78
Anterior tibial artery revascularization, No. (%)	31 (35.6)	68 (54.8)	.008
Posterior tibial artery revascularization, No. (%)	8 (9.1)	87 (70.1)	<.001
Peroneal artery revascularization, No. (%)	38 (43.7)	52 (41.9)	.89
Atherectomy, No. (%)	34 (39.1)	48 (38.7)	>.99
Thrombus aspiration, No. (%)	4 (4.6)	8 (6.5)	.77

[a] $P < .05$ was considered statistically significant.

TABLE V. Analysis of Variables' Associations With Amputation Rates

Variable	Odds ratio (95% CI)	*P* value[a]
Anterior tibial artery revascularization	6.52 (3.84-14.32)	<.001
Posterior tibial artery revascularization	49.95 (28.02-136.95)	<.001
Diabetes	0.31 (0.10-0.91)	.04
Hyperlipidemia	0.28 (0.08-0.89)	.04

[a] $P < .05$ was considered statistically significant.

Discussion

This study examined the effects of risk factors and intervention types on amputation risk in patients with critical lower extremity arterial disease. Clinical findings in PAD occur due to ischemia secondary to stenosis and occlusions in the arterial system. Although PAD may be asymptomatic, it may also show a clinical course with loss of limb and death. The healing potential of the PAD wound is severely limited because of the reduced perfusion of the area.[6] In these patients, effective revascularization may prevent limb loss or reduce the surgical margin more distally.

In this study, the observation period in terms of amputation risk was 12 months. A 12-month follow-up period is sufficient to observe the need for amputation in these patients because amputation is usually required within this time frame for patients with foot wounds related to CLI.

Approximately 60% of people who undergo lower limb amputation will require a wheelchair and may experience reduced physical capability, independence, and quality of life,[7] which can also increase the risk of cardiovascular events. Therefore, percutaneous transluminal angioplasty or open vascular surgery options should be considered before amputation for patients with critical peripheral disease.

Several meta-analyses have compared outcomes after direct and indirect revascularization strategies and suggest that there may be a benefit for patients undergoing direct vs indirect revascularization for wound healing.[8] In the present study, intervention in the anterior tibial artery and posterior tibial artery was effective in preventing amputation. Revascularization of the peroneal artery, which is the other artery of the below-knee arterial system, did not have a positive effect in the follow-up of these patients. In the foot, these 3 arteries provide perfusion of the extremity with various perforator branches and arches. In patients with PAD, the wound is mostly located in the heel and lateral arch. Additionally, diabetic ulcers are typically located on the toes or the plantar aspect of the metatarsal heads.[9] Intervention in the posterior tibial artery had an especially protective effect on amputation risk, which may be related to these localizations. The posterior tibial artery travels distally toward the ankle. The artery can be located posterior to the malleolus supplying the medial ankle and eventually dividing into its 3 main branches: the medial plantar, the lateral plantar, and calcaneal arteries.[10] This distribution increases the importance of the posterior tibial artery in wound healing. A similar situation may apply to the anterior tibial artery.

In addition, the anterior and posterior tibial arteries make a significant contribution to distal anastomoses. Perforators of the posterior tibial artery are the largest in diameter, and the anterior tibial artery has double the number of perforators of the peroneal artery.[10] In this study, revascularization of the anterior tibial artery reduced the amputation risk by 6.52 times compared with occlusion, and posterior tibial artery revascularization reduced the amputation risk by 49.95 times. Considering these data, it is reasonable to prioritize the posterior and anterior tibial arteries in patients with CLI. This approach was seen as an effective method in the prevention of amputation in patients in this study. In addition, this approach is more cost-effective and efficient.

Popliteal artery revascularization alone does not improve outcomes without revascularizing the posterior or anterior tibial artery. There were no documented beneficial outcomes in the revascularization of the popliteal artery among patients with occlusion of the anterior or posterior tibial arteries.

Atherectomy offers the potential advantage of eliminating stretch on arterial walls and reducing rates of restenosis.[11] In the present study, however, atherectomy did not reduce the risk of amputation in patients with lower extremity wounds. Similarly, embolectomy had no positive contribution. Both approaches should be considered only in select cases rather than in routine practice.

Statistically significant risk factors in this study were diabetes and hyperlipidemia, which are the main etiologic factors in the pathophysiology of PAD. The results observed in this study are consistent with the literature.[12,13]

Limitations

The limitations of the study are its retrospective design and the absence of wound classification. Detection of wound classification would have allowed subgroup analysis and provided more specific data. Wound localization was considered in the interventional procedures performed on all patients, but no data have been created regarding wound localization on this subject.

Conclusion

Amputation is a serious consequence of PAD. Revascularization may reduce amputation rates or reduce the amputation margin more distally. This study evaluated percutaneous intervention methods and found that the most effective options are revascularization of the posterior tibial artery and anterior tibial artery. Considering these results, treatment of critical PAD can be cost-effective and efficient and can shorten procedure time.

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