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Peripheral Vascular Disease

Effect of Limb Salvage by Excimer Laser Angioplasty Plus Low-Pressure Balloon Inflation in Chronic Limb-Threatening Ischemia Patients with Infrapopliteal Vessel Disease

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Background: Patients with chronic limb-threatening ischemia (CLTI) often exhibit long, diffuse, totally occluded and heavily calcified infrapopliteal (IP) lesions. This study evaluated limb salvage after peripheral excimer laser atherectomy (PELA) plus low-pressure balloon inflation (LPBI) without stent deployment in CLTI patients with severe IP disease.

Methods: We retrospectively evaluated 70 consecutive patients with 109 IP vessels who underwent PELA plus LPBI from 2010 to 2013. Technical success was defined as at least one IP straight-line flow being achieved below the malleolus. Binary logistic regression was performed to identify factors associated with 6-month limb salvage.

Results: Of the 109 IP vessels, 100 (91.7%) were totally occluded, and none of the patients received a stent. Of the 70 patients, 20% were octogenarians, and 85.8% had a Rutherford-Becker class 5 and 6. The technical success rate was 87.1% and 6-month limb salvage rate was 78.6%. Rutherford score was negatively correlated with clinical success (adjusted odds ratio 0.24; p = 0.028). No immediate major cardiovascular events were recorded during admission.

Conclusions: PELA plus LPBI may be a treatment option for complex IP lesions in patients with CLTI. Higher Rutherford class was correlated with a lower 6-month limb salvage rate. However, a large-scale study with a control group is needed to clarify our results.

Key Words: Chronic total occlusion • Infrapopliteal artery • Laser

INTRODUCTION

Patients with critical limb-threatening ischemia (CLTI) often experience poor wound healing and require vary-

Abbreviations	
aORs	Adjusted odds ratios
CLTI	Chronic limb-threatening ischemia
EVT	Endovascular therapy
IP	Infrapopliteal
LPBI	Low-pressure balloon inflation
PELA	Peripheral excimer laser atherectomy
QCA	Quantitative coronary angiography
WIFI	Wound, ischemia, foot infection

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ing degrees of debridement or even amputation. These patients are often frail and have multiple co-morbidities, such as coronary artery disease, diabetes mellitus, stroke, or chronic kidney disease. Furthermore, these patients occasionally have a suboptimal quality of self-care, and the 1-year mortality rate is approximately 25%.[1] In many cases, the infrapopliteal (IP) lesions are complex, calcified, long, diffuse, and totally occluded. These characteristics make most of these lesions unsuitable for surgical bypass and are also challenging to treat with catheter-based therapy.[2-6]

Many devices and techniques have been used in an attempt to achieve better outcomes among various patient groups. These devices include excimer laser, drug-eluting stents, drug-eluting balloons, and bio-absorbable vascular scaffolds.[7-13] Peripheral excimer laser atherectomy (PELA) has been demonstrated to increase treatment success for complex IP lesions.[14] In this context, debulking of the occluded artery is thought to change the vessel's compliance, prevent dissection, reduce distal embolization, and minimize bail-out stent deployment, even in cases with IP vessels.[15] The Laser Angioplasty for Critical Limb Ischemia trial reported technical success and 6-month limb salvage rates of 86% and 93%, respectively, when the patients were treated using PELA and adjunctive balloon angioplasty with or without stent deployment.[3,16,17] However, data are scarce for the use of PELA plus low-pressure balloon inflation (LPBI) in patients with IP-related CLTI, and especially in patients with totally occluded lesions. The avoidance of amputation remains the treatment target for these patients even if patency is not achieved.[18] Therefore, the present study aimed to investigate limb salvage after PELA plus LPBI for CLTI patients with IP disease.

METHODS

Ethics approval was granted by the Institutional Review Board of Chang-Hua Christian Hospital (Approved No. 190119). No informed consent forms were signed because the data were analyzed anonymously (retrospective study).

Patient population

This single-center retrospective study included 70 patients who underwent PELA plus LPBI between January 2010 and December 2013. Patients were enrolled if they had a Rutherford-Becker class of ≥ 4 and > 50% stenosis of any IP artery with or without femoropopliteal lesions. We excluded patient who required high-pressure balloon inflation (above the nominal pressure) or stenting, patients with intervention failure at the inflow vessel (the femoral or popliteal arteries), patients in whom the subintimal technique was used for IP vessels, and patients who did not complete 6 months of outpatient follow-up. The patients' demographic characteristics were obtained from their medical records, and the angiographic results were reviewed by another physician who did not perform the initial intervention. All endovascular therapy (EVT) and medical treatments complied with the American College of Cardiology/American Heart Association guidelines.[19] All study procedures complied with the tenets of the Declaration of Helsinki and its revisions. Informed consent was obtained from the patients before laser atherectomy.

Peripheral excimer laser angioplasty

We used quantitative coronary angiography (QCA) to assess the IP vessels. A xenon chloride excimer laser unit (CVX-300^{TM}; Spectranetics, Colorado) was used for all patients, and the laser's energy was delivered through concentric multifiber catheters (diameters: 0.9-2.2 mm; Vitesse^{TM}-E; Spectranetics, Colorado).[20] All patients received oral aspirin (300 mg) and clopidogrel (300 mg) loading, and intravenous heparin (5,000-10,000 units) was administered before PELA to maintain an activated clotting time of 250-300 seconds during the procedure. A 0.035-in or 0.014-in wire system was used, depending on the size of the device, and we attempted to pass the wire through any totally occluded lesions into the distal vessels. If there were inflow lesions in the femoropopliteal region, we initially performed EVT with balloon angioplasty alone or laser debulking plus balloon angioplasty, and the IP intervention was started after we successfully completed the inflow procedure. The laser catheter was advanced at a speed of 0.5 mm/s across the lesion, with the simultaneous intra-aretry infusion of a 0.9% saline solution. The lesion was debulked in sequential 5-mm segments using the multiple pass technique, with a fluence of 45-60 mJ/mm^2 and a frequency of 2,500. The laser catheter size was selected to be 50-60% of the target

vessel's diameter, although we selected smaller catheters or attempted balloon pre-dilation if the laser catheter could not pass though the lesions. Adjunctive balloon angioplasty with lower balloon pressure was performed once the lesion had been ablated.

Adjunctive low-pressure balloon inflation

We inflated the balloon slowly and used the minimum amount of pressure to successfully dilate the lesion (i.e., less than the nominal pressure). Furthermore, we stopped increasing the pressure if we reached the nominal balloon pressure or if the balloon became fully expanded (even with a low balloon pressure), in order to avoid distal embolization and vessel dissection. Patients who required a provisional stent or the use of high-pressure inflation to dilate the lesion were excluded from the study. After PELA and LBPI, the patients took aspirin only for secondary prevention of cardiovascular disease according to the 2017 European Society of Cardiology and 2018 American Heart Association guidelines. After discharge, the patients were followed-up at the outpatient department, and their limb status was confirmed at the 6-month follow-up visit.

Definitions

Technical success was defined as at least one IP straight-line flow being achieved below the malleolus in the angioplasty-treated vessel.[21] Clinical success was defined as limb salvage without major amputation at 6 months of follow-up.

Statistical analysis

All statistical analyses were performed with SPSS 18.0 software (SPSS, Chicago, IL). Categorical data were reported as count and percentage. Continuous data were reported as mean ± standard deviation. The chi-square test was used to compare categorical variables, and the Student's t-test was used to compare continuous variables. Logistic regression was performed to identify independent predictors of 6-month limb salvage. Adjusted odds ratios (aORs) were calculated usinga multivariate logistic regression model for variables with p values < 0.25 in the univariate model, including gender, age, smoking history, Rutherford classification, and technical success. Differences with a p value < 0.05 were considered statistically significant.

RESULTS

Patient characteristics and peripheral artery disease risk factors

Seventy patients with CLTI underwent PELA plus LPBI for 109 IP vessels. A representative case is shown in Figures 1 and 2. The patients included 33 men (47.1%) and 14 octogenarians (20%), and the mean age was 71.9 ± 10.1 years (range: 44-93 years). Among the 109 vessels, 100 (91.7%) showed total occlusion. Twenty percent of the patients had a history of cigarette smoking, 54.2% had advanced chronic kidney disease (> stage 4; 12.8% had end-stage renal disease with hemodialysis or peritoneal dialysis), 68.5% had diabetes mellitus, 68.5% had hypertension, 37.1% had hyperlipidemia, 18.5% had a history of stroke, and 25.7% had coronary artery disease. Rutherford-Becker classes of 4, 5, and 6 were observed in 14.2%, 32.9%, and 52.9% of the patients, respectively. All 70 patients successfully completed 6 months of outpatient follow-up, and no deaths occurred during follow-up.

Technical results and 6-month outcomes

The technical success rate was 87.1% (61/70 pati-

Figure 1. *Percutaneous transluminal angioplasty for an 88-year-old woman with gangrene at several toes. (A) The woman underwent successful peripheral excimer laser atherectomy and low-pressure balloon inflation. Improvements were observed at (B) 3 months, (C) 12 months, and (D) 24 months after the procedure.*

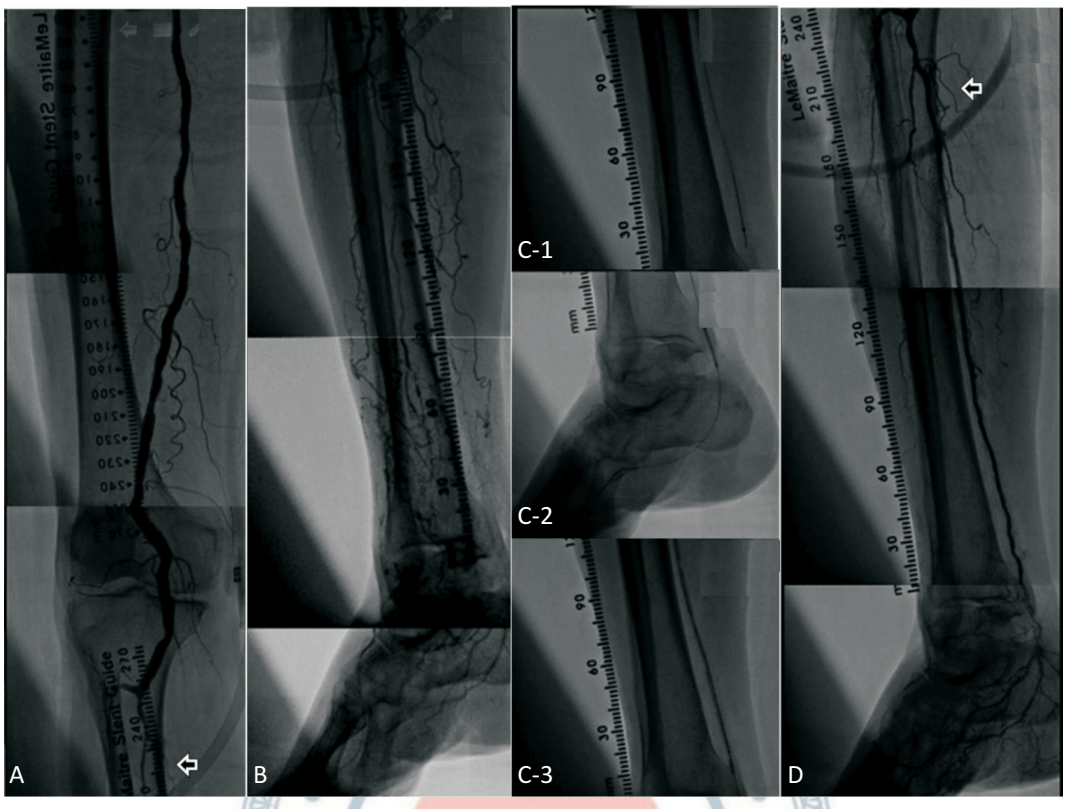

Figure 2. *Angiograms before the endovascular therapy (arrowhead to the beginning of the total occlusion of the posterior tibial artery) (A & B). A 1.4-mm laser was used to for the ablation (C-1). Low-pressure balloon inflation was performed after laser debulking (C-2 & C-3). The review angiograms reveal adequate antegrade flow into the plantar arteries (D).*

ents, 9 failure). A total of 138 laser catheters were used, and the catheter diameters were 0.9 mm, 1.4 mm, 1.7 mm, 2.0 mm, and 2.2 mm. Twenty-five vessels required 2 laser catheters, and 2 vessels required 3 laser catheters. A total of 94 balloons were used, and the mean inflation pressure was 6.27 ± 3.00 bars in the limb-salvage group. The minimum lumen diameters increased from 0.21 ± 0.59 mm and 0.23 ± 0.76 before treatment to 4.44 ± 5.58 mm and 3.61 ± 2.24 mm after PELA plus LPBI in the amputation and limb salvage groups, respectively.

The baseline characteristics between the patients with and without 6-month limb salvage are shown in Table 1. Compared to the patients without 6-month limb salvage, those with 6-month limb salvage were younger (70.93 ± 10.32 vs. 75.4 ± 8.83 years) and had higher smoking and technical success rates (23.64% vs. 6.67% and 90.9% vs. 73.3%, respectively). There was no significant difference in Rutherford classification between the two groups (p = 0.147).

The characteristics of the intervention are shown in Table 2. The limb-salvage group had a higher technical success rate (90.9%) than the non-limb salvage group (73.3%), although the difference was not significant (p = 0.09). The technical success group (total 61 patients) had a higher 6-month limb salvage rate (81.9%) than the technical failure group (55.5%).

The univariate and multivariate logistic regression models for 6-month limb salvage are showed in Table 3. With regards to clinical success, the aOR of age was 0.95 (p = 0.050) per 1 year increase in age. The higher the Rutherford class, the lower the clinical success rate (aOR: 0.26, p = 0.024). There was no significant difference in technical success rate between the two groups (aOR: 5.03, p = 0.091).

DISCUSSION

Patients with diabetes mellitus and end-stage renal

Table 1. Comparison of baseline characteristics between the patients with and without 6-month limb salvage

6-month limb salvage Parameters	(–) (n = 15)	(+) (n = 55)	Total (n = 70)	p value
Gender				
Male	7 (46.67%)	26 (47.27%)	33 (47.1%)	0.967
Female	8 (53.33%)	29 (52.73%)	37 (52.9%)	
Age	75.4 ± 8.83	70.93 ± 10.32		0.131
≥ 80 years-old	4	10	14 (20%)	
CKD (> Stage 4)	8 (53.33%)	30 (54.55%)	38 (54.2%)	0.933
DM	11 (73.33%)	37 (67.27%)	48 (68.5%)	0.654
Hypertension	10 (66.67%)	38 (69.09%)	48 (68.5%)	0.858
Hyperlipidemia	5 (33.33%)	21 (38.18%)	26 (37.1%)	0.730
CVA	3 (20%)	10 (18.18%)	13 (18.5%)	0.872
Smoking	1 (6.67%)	13 (23.64%)	14 (20.0%)	0.145
CAD	5 (33.33%)	13 (23.64%)	18 (25.7%)	0.446
Rutherford classification				
4	0 (0%)	10 (18.18%)	10 (14.2%)	0.147
5	7 (46.67%)	16 (29.09%)	23 (32.9%)	
6	8 (53.33%)	29 (52.73%)	37 (52.9%)	

CAD, coronary artery disease; CKD, chronic kidney disease; CVA, cerebrovascular accident; DM, diabetes mellitus.

Table 2. Comparison of the intervention of lower limb between the patients with and without 6-month limb salvage

6-month limb salvage	(–) (n = 15)	(+) (n = 55)	Total	p value
Numbers of intervention vessels (ATA, PTA, PA)				
1	7 (46.67%)	30 (54.55%)	37 (52.9%)	0.721
2	6 (40%)	21 (38.18%)	27 (38.6%)	
3	2 (13.33%)	4 (7.27%)	6 (8.5%)	
Pre-intervention				
Vessel diameter (mm)	2.32 ± 3.91	2.36 ± 1.65		0.964
Lesion length (mm)	158.57 ± 115.88	171.05 ± 92.34		0.555
Intervention				
Pre-dilated for laser (n)	6 (40.00%)	20 (36.34%)		0.623
Balloon diameter (mm)	3.48 ± 0.95	3.23 ± 0.73		0.244
Balloon length (mm)	34.2 ± 26.44	25.61 ± 13.52		0.034
Balloon pressure (ATM)	6.38 ± 2.1	6.27 ± 3.00		0.837
Technical success (%)				
Success	11 (73.3%)	50 (90.9%)		0.09
Failure	4 (26.7%)	5 (9.1%)		

ATA, anterior tibial artery; ATM, atmosphere pressure; PA, peroneal artery; PTA, posterior tibial artery.

Table 3. Univariate and multivariate logistic regression model for clinical success and technical success

	cOR (95% CI)	p value	aOR (95% CI)	p value
Clinical success (6-month limb salvage)				
Age (per 1 yr increase)	0.95 (0.90, 1.01)	0.133	0.92 (0.85, 1.00)	0.050
Gender, male	0.98 (0.31, 3.06)	0.967	--	--
CKD	1.05 (0.33, 3.30)	0.933	--	--
DM	0.75 (0.21, 2.68)	0.655	--	--
HTN	1.12 (0.33, 3.77)	0.858	--	--
Lipid	1.24 (0.37, 4.12)	0.731	--	--
CVA	0.89 (0.21, 3.75)	0.873	--	--
CAD	0.62 (0.18, 2.14)	0.449	--	--
Smoking	4.33 (0.52, 36.17)	0.176	3.77 (0.29, 48.39)	0.309
Rutherford score (per increase 1 category)	0.68 (0.29, 1.60)	0.376	0.26 (0.08, 0.84)	0.024
Technical success	3.64 (0.84, 15.78)	0.085	5.03 (0.77, 32.74)	0.091

aOR, adjusted odds ratio; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; cOR, crude odds ratios; CVA, cerebrovascular accident; DM, diabetes mellitus; HTN, hypertension.

disease frequently have IP vessel-related CLTI, and these lesions are typically long (> 10 cm), diffuse, heavily calcified, have a small diameter, and may be totally occluded.[22] Furthermore, these patients typically have co-morbidities, with high perioperative risk, and no suitable distal vessel for bypass.[23-26] Excimer laser treatment can debulk the pre-existing lesions including hard plaques or calcified tissue, change the vessel's compliance, and allow for easier device delivery or inflation of the balloon. This technique also prevents distal emboli and allows LBPI to be used to treat previously undilatable lesions. In addition, the combination of PELA plus LBPI has been shown to reduce the incidence of balloon barotrauma, dissection, vessel wall proliferation, and the need for stent implantation.[15,16,27]

In our group, 91.7% of the cases had total occlusion, and therefore the use of a balloon alone without prior debulking may have increased the risks of distal embolization, dissection, and treatment failure. Moreover, 85.8% of the patients had a Rutherford-Becker class of 5-6, indicating lesions that were more calcified, diffuse, and complex. Such conditions may require a high balloon pressure for dilation and subsequently increase the risks of dissection, distal embolization, and bail-out stent deployment.[28] However, without visible and clear collateral circulation in these complex lesions, it is also difficult to identify the proximal and distal ends of the lesion, which can complicate the selection of appropriate stent length and landing zones. In addition, a single stent may not be sufficient to cover these long and diffuse lesions, eventually making the procedure more complex and unappreciated. Thus, debulking may be useful as preparation for LPBI to canalize the occluded vessels, and we found that this technique provided a 6-month limb salvage rate of 81.9%.

In our study, Rutherford class was the only one of multiple factors which affected the clinical outcome. The complexity of peripheral artery disease and clinical condition are the major factors affecting clinical success. Wound healing requires increased blood supply to the distal vessels compared to typical baseline metabolism. Good control of wound infection is also an important factor influencing clinical success. Previous studies have demonstrated that delayed wound healing is associated with a high Rutherford-Becker class and the time between symptom onset to the intervention.[29-31] Antonopoulos et al. reported that differences in vascular supply (i.e., the angiosome and quantity of collateral circulation) and inflammation status could affect wound healing and limb salvage.[32] In this context, a high Rutherford-Becker grade with gangrenous toes implies that there has been irreversible tissue damage that requires amputation, regardless of any successful recanalization. Moreover, infection status and small-vessel disease with microcirculation dysfunction could influence the likelihood of wound healing and limb salvage. Nevertheless, even indirect flow restoration during the early stage of wound healing may help preserve the limb.[31] Therefore, for limb salvage, it is important to perform early interventions to improve the prognosis.

In daily practice, octogenarians are an important group of patients, as they typically do not exhibit symptoms until the vessel is occluded. Brosi et al. enrolled 376 patients with CLTI (39.9% octogenarians and 63.9% with IP lesions) and reported a 1-year limb salvage rate of 81.8%, with no significant differences between the octogenarians and non-octogenarians.[23] However, 20% of the patients in our study were octogenarians, and 92.8% of them had total IP occlusion. The 6-month salvage rate was lower among the octogenarians compared to that among the non-octogenarians (71.4% vs. 80.4%, $p = 0.024$), which was likely related to a worse general condition, co-morbidities and disease severity/duration. Hypertension, diabetes, and chronic kidney disease in older patients is always associated with a worse prognosis.[33,34] Moreover, almost all of our patients had totally occluded IP lesions, and many patients had a higher Rutherford-Becker class. In such severe IP CLTI patients, EVT in younger patients is more likely to succeed; however, our procedure still resulted in a 6-month limb salvage rate of 71.4% in the octogenarian group. We believe that it is riskier to perform surgery at an older age, and that later surgery is associated with much more complex medical situations and care needs. Thus, PELA with LBPI offers an alternative method in older patients with totally occluded IP-CLTI. However, we did not collect data of conventional angioplasty (balloon inflation only), so we cannot conclude whether or not the strategy of PELA plus LBPI is better than a conventional procedure.

Smoking was not an independent predictor of limb salvage in this study. The "smoking paradox" has been noted in patients with coronary atherosclerosis,[35] how-

ever it was not seen in our study. Possible reasons may include that the morphology of peripheral artery disease is always located over proximal arteries such as the iliac artery or superficial femoral artery instead of IP vessels. A younger age at therapy, less atherosclerotic or complex lesions, and fewer co-morbidities have been proposed, although evidence of long-term outcomes still favors non-smokers. Similar results have been seen in studies of EVT for CLTI, however, the reasons for these results are unclear.[36,37] Further studies are needed to elucidate the real significance of the "smoking paradox" in peripheral interventions.

In this study, some vessels required more than 2 laser catheters, and the cost was expensive for these vessels. The cost-effectiveness of such interventions (multiple laser catheters) should be investigated in further studies.

Limitations

First, this is a single-center study with a retrospective design which may have led to selection bias, and there was no control group (conventional balloon angioplasty) for comparison. Second, given the absence of any angiographic follow-up, we could not calculate the patency rate for PELA plus LPBI or elucidate the relationship between the intervention and clinical outcomes, despite our observation of a good 6-month limb salvage rate in our complex patient group. Third, we only evaluate patients after 6 months of follow-up, and studies with a longer follow-up period may be useful to determine the long-term outcomes of PELA plus LPBI. Fourth, our procedure success and limb salvage rates included both direct and indirect angioplasty, and it is possible that using only direct angioplasty for the corresponding angiosome could further increase the limb salvage rate. Fifth, we did not record the wound condition according to the wound, ischemia, foot infection (WIFI) classification system, and these factors may have influenced the clinical success of amputation. Finally, we lacked imaging findings for intra-vessel evaluation, such as intravascular ultrasound. In the current concept, vessel calcification has a poor prognosis after any type of intervention.

CONCLUSION

PELA plus LPBI may be an effective treatment for patients with a high Rutherford class with CLTI and complex IP vessels. Using the combination of these techniques, we achieved adequate debulking of the lesion and increased the vessel lumen without dissection, distal emboli, or subsequent stent deployment. However, a large-scale study with a control group is warranted to verify our results.

DECLARATION OF CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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REFERENCES

1. Norgren L, Hiatt WR, Dormandy JA, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg* 2007;45 Suppl S:S5-67.
2. Abdelhamid MF, Davies RS, Rai S, et al. Below-the-ankle angioplasty is a feasible and effective intervention for critical leg ischaemia. *Eur J Vasc Endovasc Surg* 2010;39:762-8.
3. Bosiers M, Peeters P, Elst FV, et al. Excimer laser assisted angioplasty for critical limb ischemia: results of the LACI Belgium Study. *Eur J Vasc Endovasc Surg* 2005;29:613-9.
4. Das T. Optimal therapeutic approaches to femoropopliteal artery intervention. *Catheter Cardiovasc Interv* 2004;63:21-30.
5. Siablis D, Karnabatidis D, Katsanos K, et al. Sirolimus-eluting versus bare stents after suboptimal infrapopliteal angioplasty for critical limb ischemia: enduring 1-year angiographic and clinical benefit. *J Endovasc Ther* 2007;14:241-50.
6. Slovut DP, Sullivan TM. Critical limb ischemia: medical and surgical management. *Vasc Med* 2008;13:281-91.
7. Das TS. Excimer laser-assisted angioplasty for infrainguinal artery disease. *J Endovasc Ther* 2009;16:II98-104.
8. Dattilo PB, Casserly IP. Critical limb ischemia: endovascular strategies for limb salvage. *Prog Cardiovasc Dis* 2011;54:47-60.
9. Rogers JH, Laird JR. Overview of new technologies for lower extremity revascularization. *Circulation* 2007;116:2072-85.
10. Serino F, Cao Y, Renzi C, et al. Excimer laser ablation in the treatment of total chronic obstructions in critical limb ischaemia in

diabetic patients. Sustained efficacy of plaque recanalisation in mid-term results. *Eur J Vasc Endovasc Surg* 2010;39:234-8.
11. Siablis D, Diamantopoulos A, Katsanos K, et al. Subintimal angioplasty of long chronic total femoropopliteal occlusions: long-term outcomes, predictors of angiographic restenosis, and role of stenting. *Cardiovasc Intervent Radiol* 2012;35:483-90.
12. Singh GD, Armstrong EJ, Yeo KK, et al. Endovascular recanalization of infrapopliteal occlusions in patients with critical limb ischemia. *J Vasc Surg* 2014;59:1300-7.
13. Varcoe RL, Thomas SD, Rapoza RJ, Kum S. Lessons learned regarding handling and deployment of the absorb bioresorbable vascular scaffold in infrapopliteal arteries. *J Endovasc Ther* 2017; 24:337-41.
14. Garnic JD, Hurwitz AS. Endovascular excimer laser atherectomy techniques to treat complex peripheral vascular disease: an orderly process. *Tech Vasc Interv Radiol* 2005;8:150-9.
15. Shammas NW, Aasen N, Bailey L, et al. Two blades-up runs using the JetStream navitus atherectomy device achieve optimal tissue debulking of nonocclusive in-stent restenosis: observations from a porcine stent/balloon injury model. *J Endovasc Ther* 2015;22:518-24.
16. Laird JR, Zeller T, Gray BH, et al. Limb salvage following laser-assisted angioplasty for critical limb ischemia: results of the LACI multicenter trial. *J Endovasc Ther* 2006;13:1-11.
17. Sultan S, Tawfick W, Hynes N. Cool excimer laser-assisted angioplasty (CELA) and tibial balloon angioplasty (TBA) in management of infragenicular arterial occlusion in critical lower limb ischemia (CLI). *Vasc Endovascular Surg* 2013;47:179-91.
18. Todd KE Jr, Ahanchi SS, Maurer CA, et al. Atherectomy offers no benefits over balloon angioplasty in tibial interventions for critical limb ischemia. *J Vasc Surg* 2013;58:941-8.
19. Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC Guideline on the management of patients with lower extremity peripheral artery disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *Circulation* 2017;135: e686-725.
20. Chen CP, Huang CL, Fong CC, et al. Six-month angiographic and clinical outcomes after successful eccentric excimer laser coronary angioplasty with adjunctive cutting balloon angioplasty for recurrent in-stent restenosis. *Acta Cardiol Sin* 2008;24:15-20.
21. Arain SA, White CJ. Endovascular therapy for critical limb ischemia. *Vasc Med* 2008;13:267-79.
22. Thukkani AK, Kinlay S. Endovascular intervention for peripheral artery disease. *Circ Res* 2015;116:1599-613.
23. Brosi P, Dick F, Do DD, et al. Revascularization for chronic critical lower limb ischemia in octogenarians is worthwhile. *J Vasc Surg* 2007;46:1198-207.
24. Graziani L, Silvestro A, Bertone V, et al. Vascular involvement in diabetic subjects with ischemic foot ulcer: a new morphologic categorization of disease severity. *Eur J Vasc Endovasc Surg* 2007; 33:453-60.
25. Pua U, Wong DE. Angioplasty in critical limb ischaemia: one-year limb salvage results. *Ann Acad Med Singapore* 2008;37:224-9.
26. Wu R, Yao C, Wang S, et al. Percutaneous transluminal angioplasty versus primary stenting in infrapopliteal arterial disease: a meta-analysis of randomized trials. *J Vasc Surg* 2014;59:1711-20.
27. Scheinert D, Laird JR Jr, Schroder M, et al. Excimer laser-assisted recanalization of long, chronic superficial femoral artery occlusions. *J Endovasc Ther* 2001;8:156-66.
28. Mustapha J, Diaz-Sandoval LJ. Arterial deposition of calcium and outcomes of peripheral interventions: is it time to redefine the "gold standard?". *Vascular Disease Management* 2013;10:E208-11.
29. Gray BH, Laird JR, Ansel GM, Shuck JW. Complex endovascular treatment for critical limb ischemia in poor surgical candidates: a pilot study. *J Endovasc Ther* 2002;9:599-604.
30. Huang HL, Chou HH, Wu TY, et al. Endovascular intervention in Taiwanese patients with critical limb ischemia: patient outcomes in 333 consecutive limb procedures with a 3-year follow-up. *J Formos Med Assoc* 2014;113:688-95.
31. Tsetis D, Belli A. The role of infrapopliteal angioplasty. *Br J Radiol* 2004;77:1007-15.
32. Antonopoulos AG, Thomopoulos M, Trikas A. The role of the angiosome model in percutaneous intravascular and surgical reperfusion treatment of peripheral artery disease of the lower limbs. *Hellenic J Cardiol* 2014;55:52-7.
33. Boutitie F, Gueyffier F, Pocock S, et al. J-shaped relationship between blood pressure and mortality in hypertensive patients: new insights from a meta-analysis of individual-patient data. *Ann Intern Med* 2002;136:438-48.
34. Myers OB, Adams C, Rohrscheib MR, et al. Age, race, diabetes, blood pressure, and mortality among hemodialysis patients. *J Am Soc Nephrol* 2010;21:1970-8.
35. Venkatason P, Salleh NM, Zubairi Y, et al. The bizzare phenomenon of smokers' paradox in the immediate outcome post acute myocardial infarction: an insight into the Malaysian National Cardiovascular Database-Acute Coronary Syndrome (NCVD-ACS) registry year 2006–2013. *SpringerPlus* 2016;5:534.
36. Bosevski M, Meskovska S, Tosev S, et al. Risk factors for development of critical limb ischemia--a survey of diabetic vs. nondiabetic population. *Prilozi* 2006;27:89-96.
37. Rastan A, McKinsey JF, Garcia LA, et al. One-year outcomes following directional atherectomy of popliteal artery lesions: subgroup analysis of the prospective, multicenter DEFINITIVE LE trial. *J Endovasc Ther* 2018;25:100-8.