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Review Article

Lower limb peripheral arterial diseases: diagnosis, management and the effect of pedal arch reconstruction on the overall outcomes

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ABSTRACT

Peripheral arterial diseases (PAD) are a significant cause of morbidity and limb loss. PAD is estimated to affect 237 million people worldwide. Atherosclerosis accounts for 95% of the cases of PAD. The progression of atherosclerosis gradually narrows the vascular lumen and leads to ischemia. Of the several risk factors implicated in PAD, smoking is most significant. The diagnosis of PAD requires a high index of suspicion. Over 50% of the patients are asymptomatic. A sizeable portion attributes their mild to moderate symptoms to general ageing rather than PAD and fails to seek medical advice. Claudication is a classical symptom of PAD. With the progression of the disease, rest pain, ulcerations, or gangrene can develop. PAD can be diagnosed by thorough history-taking, detailed physical examination (including objective measures like an ankle-brachial index) and imaging modalities such as duplex ultrasonography, contrast-enhanced ultrasound, magnetic resonance angiography, computed tomography angiography, and digital subtraction angiogram. Early identification and risk factor modification are crucial for improving the outcomes in PAD patients. Treatment strategies include lifestyle modifications, pharmacotherapy and revascularisation (surgical or endovascular). With the recent technological advances, coupled with its minimally invasive nature, the popularity of Endovascular therapy (ET) is increasing. However, the procedure of pedal arch reconstruction and the role ET can play in improving the outcomes of patients with poor pedal vascularity is still debated. The aim of the study was to find answer some of the queries on the topic of ET for the management of PAD of the lower limbs.

Keywords: Peripheral arterial disease, Critical limb ischemia, Endovascular therapy, Below knee angioplasty, Below ankle angioplasty, Pedal arch reconstruction

INTRODUCTION

Peripheral arterial disease (PAD) is a chronic progressive atherosclerotic disease leading to incomplete or total vascular occlusion. The abdominal aorta, iliac and lower limb arteries are typically affected. Involvement of the upper extremities is relatively infrequent.[1] PAD is estimated to affect 237 million people worldwide, with an annual prevalence of 10.7% among hospital admissions.[2,3] PAD remains asymptomatic or unrecognised in a sizable portion of the population.[4] The disease presentation is variable and can manifest as intermittent claudication, resting limb pain, ulceration, gangrene or limb loss.[5] PAD is associated with other cardiovascular diseases. 90% of PAD patients show coronary artery disease on angiography. Carotid artery stenosis of >70% can be demonstrated in 25% of PAD patients.[6] The crude five-year all-cause mortality rate of PAD is 33.2%.[7] A multidisciplinary team approach is essential for improving patient outcomes.

ETIOLOGY

Atherosclerosis accounts for 95% of the cases of PAD.[8] Progression of atherosclerosis causes gradual narrowing of the vascular lumen and leads to end-organ ischemia.[9]

Several modifiable and non-modifiable risk factors are implicated in the progression of atherosclerosis.[5,10-12] They are smoking, diabetes, family history of cardiovascular diseases, hypertension, dyslipidemia, age >50 years, obesity (BMI>30 kg/m^2), and increased homocysteine levels.

EPIDEMIOLOGY

PAD affects 237 million people worldwide. It is infrequent in the younger age groups. However, the incidence increases to 20% in individuals over 70 years.[13,14] The role of gender in PAD is confounding. In the Framingham and Rotterdam studies, men were more likely to have intermittent claudication than women.[15,16] However, there were no statistically significant gender discrepancies in the Rotterdam Study, and Cardiovascular Health Study on an Ankle-brachial index (ABI) based diagnosis.[9,14] PAD may be significantly underdiagnosed at the primary care level, as most patients do not present with the characteristic claudication symptoms.[14] Smoking is the most significant risk factor for PAD.[17] Smokers have shorter lifespans than non-smokers and are more prone to progress to critical limb ischemia.[18]

PATHOPHYSIOLOGY

The progression of atherosclerosis affects both macro-and microvascular circulation. Lower extremity vasculature is typically affected. However, the larger iliac arteries and abdominal aorta are also frequently involved. In severe disease, the affliction can be multi-level or diffuse.

Reactive oxygen species or free radicals (ROS) escalate the expression of Cell adhesion molecules (CAM). Monocyte adherence to the endothelial cells is mediated through CAM. Low-density lipoprotein cholesterol (LDL-C) is oxidised to minimally modified LDL (MM-LDL), which stimulates the endothelial cells and smooth Muscle cells to produce chemoattractant protein-1 (MCP-1).[19] MM-LDL is further oxidised to fully oxidised LDL (OX-LDL).[20] OX-DL and MCP-1 accelerate the migration of monocytes to the subendothelial area.[21-23]

OX-LDL is a ligand for the scavenger receptor expressed in monocyte differentiated into tissue macrophage.[24,25] This monocyte/macrophage differentiation is facilitated by releasing Monocyte colony-stimulating factor (MCSF) from the endothelial cells under the influence of MM-LDL.[19]

The differentiated macrophage develops receptors for OX-LDL, which receptors take up to produce foam cells. Foam cells also generate ROS.[26]

Macrophages generate a host of growth-regulating molecules and cytokines that affect neighbouring cells. Gene expression and transcription in the smooth muscle cells could result in smooth muscle cell proliferation and migration, synthesis of connective tissue and its matrix, migration of monocytes and formation of foam cells that results in the development and progression of atherosclerosis.[27]

Atherosclerotic plaque gradually builds up within the vessel wall. This results in vascular stenosis and reactive dilation to maximise end-organ perfusion. Once the vessel dilation capacity is exceeded, the continuous plaque accumulation leads to critical narrowing of the artery. Collateral circulation develops to preserve distal perfusion and tissue viability; however, these collaterals cannot match the blood supply of a typical healthy vessel. When the oxygen requirement of the tissue exceeds this fixed oxygen supply, intermittent claudication, resting limb pain or tissue loss ensues as the tissues crave oxygen.[28,29]

Sudden vascular occlusion occurs with the development of in-situ vascular thrombosis or an embolism from a cardiac source.[30] In-situ thrombosis secondary to progressive atherosclerosis represents 40% of Acute limb ischemia (ALI) cases. In comparison, embolic causes account for 30% of ALI cases.[31] Atherosclerotic plaque rupture leads to the exposure of subendothelial collagen and other inflammatory cells, causing platelet adhesion, aggregation with the development of in-situ thrombosis within the vessel lumen.

Patients with in-situ thrombosis tend to have better outcomes than embolic causes due to extensive collateral circulation.[31] ALI is a vascular emergency that requires immediate intervention to prevent limb loss.[9]

CLINICAL FEATURES

Diagnosis of PAD requires a high index of suspicion. Many patients are asymptomatic (over 50%).[32] Some mild to moderate PAD patients rarely exert themselves to a level that requires increased blood flow to the lower extremity muscles.

Other patients attribute the symptoms of discomfort to the natural consequences of ageing and do not report them. Comorbidities such as advanced diabetes mellitus, spinal disease, or lumbosacral disease may alter the pain perception and lead to atypical presentations.[8]

Claudication is the most classic symptom. It is initiated by walking and relieved with rest. It is often described as cramping, aching, pressure, weakness or leg fatigue. On exertion, symptoms occur in the muscle groups distal to the narrowed artery.[14] In severe PAD, patients can develop ischemic rest pain, which worsens at night. The symptoms are exacerbated by limb elevation and relieved by placing the limb in a dependent position. In some cases, oedema may develop from keeping the leg in a dependent position

which may be mistakenly attributed to venous thrombosis. Non-healing wounds are also complained about by some patients.[33]

The physical exam may reveal the following: (a) reduced or absent pulses; (b) tenderness; (c) pallor with limb elevation, dependent rubor; (c) cool and cyanotic skin; (d) muscle atrophy; (e) loss of hair; (f) audible bruits; (g) non-healing ulcers; (h) delayed capillary refill time; and (i) lower limb gangrene.[14,33] Critical limb ischemia (CLI) is a severe form of PAD characterised by clinical findings of (1) ischemic rest pain; and/or (2) ischemic tissue loss (ulceration or gangrene).[34]

DIAGNOSIS

PAD diagnosis depends on the patient risk profile, history, clinical presentation and objective tests.[35]

ABI is a non-invasive, cost-effective, objective measure for PAD diagnosis. It is the ratio of systolic ankle pressure to the highest systolic brachial pressure. A healthy ABI ratio ranges from 0.9 to 1.2. Values lower than 0.9 are diagnostic of PAD. Noncompressible vessels (as seen in advanced renal diseases or diabetes) have falsely elevated ratios. These patients tend to have higher all-cause mortality.[36] Further evaluation of a toe-brachial index (the ratio of the systolic toe pressure to the highest brachial systolic pressure) is warranted in these patients.[28]

Duplex ultrasonography (DUS) is a non-invasive, safe and relatively cost-effective imaging modality. It can determine the length, location, plaque characteristics and hemodynamic severity of the stenosis. DUS is helpful in the initial diagnosis, decision-making when planning for other diagnostics or interventions, or post-procedure follow-up.[37] Contrast-enhanced ultrasound (CEUS) imaging using microbubble contrast agents is another emerging concept with considerable potential for diagnostic and therapeutic applications. There is enhanced overall contrast and quality, and accuracy of ultrasound images. However, proper technician training and widespread adoption are needed to reap the full benefits.[38] Digital subtraction angiography (DSA) is considered the gold standard for PAD decision-making.

It has both diagnostic and therapeutic implications.[39] MRA has 90% sensitivity and 97% specificity compared to DSA. However, MRA can delineate small runoff vessels, missed on DSA. The diagnostic accuracy of CTA is comparable to MRA.[37]

TREATMENT/MANAGEMENT

Management is aimed at improving symptoms and decreasing cardiovascular events. PAD patients are at an increased risk of coronary artery disease mortality (CAD) (RR=6.6), cardiovascular mortality (RR=5.9), and all-cause mortality (RR=3.1).[40]

Lifestyle/risk factor modification

Smoking cessation

It is achieved by patient education, behavioural therapy, nicotine replacement, or pharmacological therapy (varenicline and bupropion).[9,41] Failure to quit might limit the improvement obtained from exercise and pharmacological treatment.[42]

Exercise therapy

Exercise improves pain-free walking distance and total walking distance. However, there is no effect on overall mortality. Exercise programs typically consist of 30 to 45-minute sessions conducted 4 to 5 times a week over three months.[43]

Glycemic control

A multidisciplinary team approach is preferable for the optimal management of diabetes in PAD patients.[41] A combination of a well-balanced diet, weight control, and pharmacotherapy are prerequisites for optimal glycemic control and is associated with reduced amputation rates and improved post-revascularisation patency.[44,45]

Antihypertensive therapy

It is indicated for all hypertensive patients with PAD. The choice of therapeutic agent required depends on the patient comorbidities.[41] Angiotensin-converting enzyme inhibitors (ACEIs) and Angiotensin II receptor blockers (ARBs) are considered first-line therapy because they significantly reduce adverse cardiovascular events in patients with PAD.[46-48] Calcium channel blockers, beta-blockers and diuretics are reliable alternatives.[33]

Statin therapy

Early statin initiation is associated with a reduction of adverse cardiovascular events and mortality. Hence it is indicated for all PAD patients.[41,48-51]

Antiplatelet therapy

Single-antiplatelet therapy with aspirin alone (75-325 mg/day) or clopidogrel alone (75 mg/day) is associated with a reduction in adverse cardiovascular events, non-fatal strokes and vascular deaths among patients with symptomatic PAD on antiplatelet therapy. Clopidogrel is superior to aspirin for monotherapy in PAD patients.[52,53]

Dual-antiplatelet therapy demonstrated a reduction in adverse limb-related events and the need for repeat revascularisation procedures in patients with PAD who underwent endovascular intervention or below-knee bypass prosthetic grafting.[54-56]

Cilostazol, naftidrofuryl and pentoxifylline

Cilostazol (phosphodiesterase type 3 inhibitor) significantly improves pain-free and total walking distances.[57] In addition, it also demonstrates antiplatelet, vasodilatory, and anti-smooth muscle cell proliferation properties.[57] Naftidrofuryl (5-hydroxytryptamine-2-receptor antagonist) has lesser adverse effects than cilostazol and is more likely to be cost-effective than cilostazol or pentoxifylline.[58,59] Due to the lack of high-quality evidence, the role of pentoxifylline (competitive nonselective phosphodiesterase inhibitor) in managing intermittent claudication is uncertain.[60]

Revascularisation

Revascularisation is typically employed in patients with burdening symptoms unresponsive to conventional approaches like lifestyle modification, exercise therapy and pharmacotherapy. Indications include severe claudication causing marked limitation of activities of daily living, to prevent tissue loss in CLI. Depending on the patient profile and the decision of the healthcare team, the modalities of recanalisation include endovascular, surgical or a combined approach.[61]

The goal of revascularisation is to restore perfusion of the extremity with CLI.[41] In CLI without revascularisation, amputation rates reach 20% to 40%, and 6-month mortality exceeds 20%.[58,62-65] The four-year amputation and mortality rates approach two-thirds.[66,67]

Open surgical techniques for CLI primarily consist of endarterectomy and bypass. Bypass is favoured over endarterectomy for the management of aortoiliac segment disease.[68] Endarterectomy is favoured for the treatment of disease in the femoral arteries. The five-year patency rates as high as 91% have recently been reported.[69] Distal stenoses are generally treated via bypass.[70]

Endovascular techniques used for the management of CLI include percutaneous balloon angioplasty (using conventional plain, drug-coated or cutting balloons), laser or mechanical atherectomy and stenting with bare metal or drug-eluting stents.[71,72] In the past 20 years, the rate of lower limb endovascular interventions has more than quadrupled.[73-77] Recent advancements in technologies have resulted in the ever-expanding utilisation of these interventions in patients with disease characteristics once thought to preclude endovascular interventions. Albeit with limited data, these newer applications have met some success in CLI.[78-82] Treatment biases among the various provider specialities impact the decision-making as to which modality is offered to patients with CLI.[71,83-85]

In the Bypass versus angioplasty in severe ischaemia of the leg (BASIL) trial, the amputation free survival at 1 and 3 years for the bypass surgery cohort was 68% and 57%, and 71% and 52% for the angioplasty first group, which was not statistically significant.[86] Surgery had lower re-intervention rates (18% vs 26%). Bypass surgery was associated with higher early morbidity than angioplasty.

However, there were no differences in overall mortality. Health-related quality of life was similar in both cohorts. Hospital expenses were higher during the first year for the surgery-first group.[86] The limitations of the study were the small sample size, non-randomisation, retrospective design, failure to distinguish intermittent claudication from CLI, poorly defined interventions, failure to restrict to infrainguinal anatomic disease pattern, and/or inadequate follow-up.[71,87,88]

The ongoing Best endovascular versus best surgical therapy for patients with critical limb ischemia (BEST-CLI) trial attempts to address many of the limitations of the BASIL trial and may provide further data about issues previously unexplored in randomised studies (e.g., angiosome-directed outcomes vs conventional in-line revascularisation strategies, as well as anatomic predictors of outcome).[41,87,89,90] Two additional randomized controlled trials in the United Kingdom promise to complement the findings of BEST-CLI.[71] The BASIL-2 trial aims to compare primary vein bypass versus primary best endovascular treatment focused on infrageniculate disease.[91] The BASIL-3 trial seeks to compare the efficacy of endovascular options with three randomisation arms: 1) plain angioplasty, 2) drug-coated balloon angioplasty, and 3) drug-eluting stents.[92]

ROLE OF PEDAL ARCH RECONSTRUCTION (INFRAMALLEOLAR ANGIOPLASTY)

The development of endovascular techniques and advances in guidewire and stent design have facilitated Below-the-ankle (BTA) revascularisation strategies.[93] Jung et al reported a higher freedom major amputation significant (96.3% vs 84.2%; p=009) in the Pedal arch revascularisation (PAR) at one-year follow-up. Wound healing rate was higher in the successful PAR group compared to the non-PAR subgroup (p=0.031). PAR was an independent factor related to improved wound healing rate (p=0.015).

Pre-procedural absence of pedal arch was associated with impaired wound healing.[94] Teymen et al reported a decrease in major and minor lower limb amputation in the BTA angioplasty arm in comparison to the Above the ankle (ATAn) angioplasty alone arm (0.0% vs 8.0%, and 15.0% vs 24.0%, respectively) at 12-month follow-up; however, this failed to reach statistical significance.[95] Nakama et al reported a significant increase in the rate of wound healing at 12-month follow-up in the BTA angioplasty arm in comparison to the ATAn angioplasty alone arm (59.3% vs 38.1%, p<0.05). Time to wound healing was also significantly shorter in the BTA angioplasty arm (211 days vs 365 days, p=0.008).[96] Kawarada et al reported that 83% of participants achieved the composite outcome of improvement in rest pain or wound healing at follow-up.[97]

Kawarada et al reported a composite outcome of improvement of rest pain and wound healing.[97] Wei et al used improvement in rest pain as an outcome but did not report symptomatology at follow-up.[98]

Dua et al saw an overall increase in QoL scores (1.3 pre-study to 0.7 at six months follow-up) and significant increases in activity ('fairly' to 'well', p=0.014) and mood parameters (0 to 0.1, p=0.033).[99] Lower restenosis rates were observed in the BTA angioplasty arm in comparison to the ATAn angioplasty alone arm, which approached significance at one year (15.8% vs 47.8%, p.0.059).[95] The post-BTA angioplasty arm represented an 80.3% overall freedom from re-intervention at follow-up.[13] Complications between the BTA and ATAn cohorts do not vary significantly. The pooled complication rate is 12.5%. Some commonly encountered complications include puncture site hematoma, vessel rupture, distal embolisation, dissection, balloon rupture, bleeding, or vasospasm.[13,94]

OUR INSTITUTION APPROACH

The procedure is performed under local anaesthesia following strict aseptic protocol. The patient is placed in the supine position on the angiographic table. An ipsilateral transfemoral arterial access is taken. A 7F sheath [Cook Medical, USA] is placed into the Common femoral artery (CFA) anterogradely towards the Popliteal artery (PA). An angiogram is done to assess the vascularity of the foot. The Superficial femoral artery (SFA), PA and Below-knee arteries (BKA), including the Anterior tibial artery (ATA), Posterior tibial artery (PTA) and the common peroneal arteries are examined. The pedal arch is studied (Figure 1).

Once the pedal arch disease is confirmed, pedal arch angioplasty is planned. It could be associated with the disease of the BKA, PA, SFA, or it could be an isolated problem in itself. The pedal arch is accessed with a distal access catheter (DAC- Stryker Neurovascular, USA) placed from the groin into the PA or selectively into the ATA or PTA when feasible. A 2×100 mm balloon, Whisper wire was navigated into the ATA, and the pedal arch was accessed at the base of the first metatarsal. Then the wire was slowly navigated through the arch, and a path was created into the PTA through the foot.

The 2×100 mm balloon was navigated across the arch, and angioplasty was commenced (Figure 2). The balloon was inflated for 90 seconds. A Post-angioplasty angiogram was done to assess the result of the angioplasty (Figure 3).

In case of focal stenosis or slow flow, the angioplasty was repeated at the particular segment. After achieving adequate pedal arch flow, the procedure was completed by removing the catheter, wire and the balloon, and hemostasis was achieved for the groin puncture site after removing the sheath.

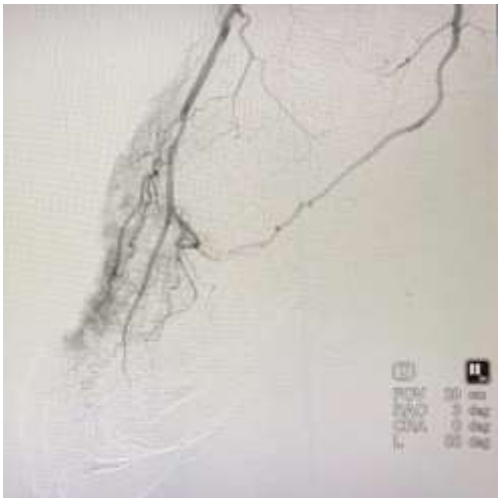

Figure 1: A DSA of the right foot with a non-healing ulcer on the dorsum of the foot and poor below the ankle blood supply.

Figure 2: The balloon-wire combination is navigated across the pedal arch and angioplasty was done.

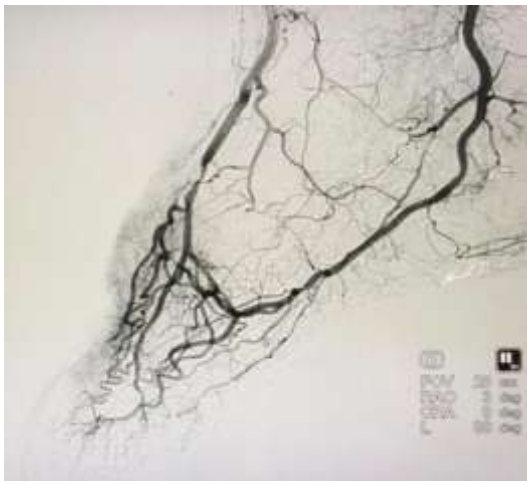

Figure 3: Post-procedural angiogram demonstrating enhanced blood supply of the foot.

CONCLUSION

PAD are a significant cause of morbidity and limb loss. A significant majority are atherosclerosis related. Physicians should have a high index of suspicion to diagnose PAD. Various modalities of radiological investigations can be employed to establish the diagnosis. Treatment is centered around lifestyle modification, pharmacotherapy and revascularisation. The use of endovascular therapy is gaining significant traction in the recent years to technological advances and product development. Timely interventions and pedal arch reconstructions are vital in achieving the best possible outcomes.

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REFERENCES

1. European Stroke Organisation, Tendera M, Aboyans V, Bartelink ML, Baumgartner I, Clément D, et al. ESC Guidelines on the diagnosis and treatment of peripheral artery diseases: Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: the Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2011;32(22):2851-906.
2. Song P, Rudan D, Zhu Y, Fowkes FJI, Rahimi K, Fowkes FGR, et al. Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis. Lancet Glob Health. 2019;7(8):1020-30.
3. Nehler MR, Duval S, Diao L, Annex BH, Hiatt WR, Rogers K, et al. Epidemiology of peripheral arterial disease and critical limb ischemia in an insured national population. J Vasc Surg. 2014;60(3):686-95.
4. Signorelli S, Anzaldi M, Fiore V, Catanzaro S, Simili M, Torrisi B, et al. Study on unrecognized peripheral arterial disease (PAD) by ankle/brachial index and arterial co-morbidity in Catania (Sicily, Italy). Angiology. 2010;61:524-9.
5. Krishna SM, Moxon JV, Golledge J. A review of the pathophysiology and potential biomarkers for peripheral artery disease. Int J Mol Sci. 2015;16(5):11294-322.
6. Malyar N, Fürstenberg T, Wellmann J, Meyborg M, Lüders F, Gebauer K, et al. Recent trends in morbidity and in-hospital outcomes of in-patients with peripheral arterial disease: a nationwide population-based analysis. Eur Heart J. 2013;34(34):2706-14.
7. Caro J, Walle K, Ishak KJ, Proskorovsky I. The morbidity and mortality following a diagnosis of peripheral arterial disease: long-term follow-up of a large database. BMC Cardiovasc Disord. 2005;5:14.
8. Dhaliwal G, Mukherjee D. Peripheral arterial disease: Epidemiology, natural history, diagnosis and treatment. Int J Angiol. 2007;16(2):36-44.
9. Gul F, Janzer SF. Peripheral Vascular Disease. StatPearls. Treasure Island. 2022.
10. Wakabayashi I, Sotoda Y. Alcohol drinking and peripheral arterial disease of lower extremity. Nihon Arukoru Yakubutsu Igakkai Zasshi. 2014;49(1):13-27.
11. Periard D, Cavassini M, Taffé P, Chevalley M, Senn L, Taillard C, et al. High prevalence of peripheral arterial disease in HIV-infected persons. Clin Infect Dis. 2008;46(5):761-7.
12. Khandanpour N, Loke YK, Meyer FJ, Jennings B, Armon MP. Homocysteine and peripheral arterial disease: systematic review and meta-analysis. Eur J Vasc Endovasc Surg. 2009;38(3):316-22.
13. Machin M, Younan HC, Guéroult AM, Onida S, Shalhoub J, Davies AH. Systematic review of inframalleolar endovascular interventions and rates of limb salvage, wound healing, restenosis, rest pain, reintervention and complications. Vascular. 2021.
14. Zemaitis MR, Boll JM, Dreyer MA. Peripheral Arterial Disease. StatPearls. Treasure Island. 2022.
15. Kannel WB, McGee DL. Update on some epidemiologic features of intermittent claudication: the Framingham Study. J Am Geriatr Soc. 1985;33(1):13-8.
16. Murabito JM, Evans JC, Nieto K, Larson MG, Levy D, Wilson PW. Prevalence and clinical correlates of peripheral arterial disease in the Framingham Offspring Study. Am Heart J. 2002;143(6):961-5.
17. Sampson UKA, Fowkes FGR, Naidoo NG, Criqui MH. Peripheral Artery Disease. In: Prabhakaran D, Anand S, Gaziano TA, Mbanya JC, Wu Y, Nugent R, eds. Cardiovascular, Respiratory, and Related Disorders. 3rd ed. Washington, DC: The International Bank for Reconstruction and Development /The World Bank; 2017.
18. Jelani QU, Petrov M, Martinez SC, Holmvang L, Al-Shaibi K, Alasnag M. Peripheral Arterial Disease in Women: an Overview of Risk Factor Profile, Clinical Features, and Outcomes. Curr Atheroscler Rep. 2018;20(8):40.
19. Cushing SD, Berliner JA, Valente AJ, Territo MC, Navab M, Parhami F, et al. Minimally modified low density lipoprotein induces monocyte chemotactic protein 1 in human endothelial cells and smooth muscle cells. Proc Natl Acad Sci U S A. 1990;87(13):5134-8.
20. Steinberg D. Oxidized low density lipoprotein--an extreme example of lipoprotein heterogeneity. Isr J Med Sci. 1996;32(6):469-72.
21. Wang GP, Deng ZD, Ni J, Qu ZL. Oxidized low density lipoprotein and very low density lipoprotein enhance expression of monocyte chemoattractant protein-1 in rabbit peritoneal exudate macrophages. Atherosclerosis. 1997;133(1):31-6.
22. Navab M, Imes SS, Hama SY, Hough GP, Ross LA, Bork RW, et al. Monocyte transmigration induced by

modification of low density lipoprotein in cocultures of human aortic wall cells is due to induction of monocyte chemotactic protein 1 synthesis and is abolished by high density lipoprotein. J Clin Invest. 1991;88(6):2039-46.
23. Hashimoto K, Kataoka N, Nakamura E, Tsujioka K, Kajiya F. Oxidized LDL specifically promotes the initiation of monocyte invasion during transendothelial migration with upregulated PECAM-1 and downregulated VE-cadherin on endothelial junctions. Atherosclerosis. 2007;194(2):9-17.
24. Nagy L, Tontonoz P, Alvarez JG, Chen H, Evans RM. Oxidized LDL regulates macrophage gene expression through ligand activation of PPARgamma. Cell. 1998;93(2):229-40.
25. Henriksen T, Mahoney EM, Steinberg D. Enhanced macrophage degradation of biologically modified low density lipoprotein. Arteriosclerosis. 1983;3(2):149-59.
26. Rajagopalan S, Meng XP, Ramasamy S, Harrison DG, Galis ZS. Reactive oxygen species produced by macrophage-derived foam cells regulate the activity of vascular matrix metalloproteinases in vitro. Implications for atherosclerotic plaque stability. J Clin Invest. 1996;98(11):2572-9.
27. Prasad K. Pathophysiology and Medical Treatment of Carotid Artery Stenosis. Int J Angiol. 2015;24(3):158-72.
28. Olin JW, Sealove BA. Peripheral artery disease: current insight into the disease and its diagnosis and management. Mayo Clin Proc. 2010;85(7):678-92.
29. Varu VN, Hogg ME, Kibbe MR. Critical limb ischemia. J Vasc Surg. 2010;51(1):230-41.
30. Kim HO, Kim W. Elucidation of the Diagnosis and Treatment of Peripheral Arterial Disease. Korean Circ J. 2018;48(9):826-7.
31. Olinic DM, Stanek A, Tătaru DA, Homorodean C, Olinic M. Acute Limb Ischemia: An Update on Diagnosis and Management. J Clin Med. 2019;8(8).
32. Høyer C, Sandermann J, Petersen LJ. The toe-brachial index in the diagnosis of peripheral arterial disease. J Vasc Surg. 2013;58(1):231-8.
33. Tummala S, Scherbel D. Clinical Assessment of Peripheral Arterial Disease in the Office: What Do the Guidelines Say? Semin Intervent Radiol. 2018;35(5):365-77.
34. Patel MR, Conte MS, Cutlip DE, Dib N, Geraghty P, Gray W, et al. Evaluation and treatment of patients with lower extremity peripheral artery disease: consensus definitions from Peripheral Academic Research Consortium (PARC). J Am Coll Cardiol. 2015;65(9):931-41.
35. Hennion DR, Siano KA. Diagnosis and treatment of peripheral arterial disease. Am Fam Physician. 2013;88(5):306-10.
36. Resnick HE, Lindsay RS, McDermott MM, Devereux RB, Jones KL, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. Circulation. 2004;109(6):733-9.
37. Olin JW, Kaufman JA, Bluemke DA, Bonow RO, Gerhard MD, Jaff MR, et al. Atherosclerotic Vascular Disease Conference: Writing Group IV: imaging. Circulation. 2004;109(21):2626-33.
38. Mehta KS, Lee JJ, Taha AG, Avgerinos E, Chaer RA. Vascular applications of contrast-enhanced ultrasound imaging. J Vasc Surg. 2017;66(1):266-74.
39. Koshy CG, Chacko BR, Keshava SN, Stephen E, Agarwal S. Decision making in the treatment of peripheral arterial disease - A single-institution comparative study using information from color doppler and digital subtraction angiogram studies. Indian J Radiol Imaging. 2011;21(4):294-7.
40. Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. N Engl J Med. 1992;326(6):381-6.
41. Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2017;69(11):71-126.
42. Nicolaï SP, Hendriks EJ, Prins MH, Teijink JA, EXITPAD Study Group. Optimizing supervised exercise therapy for patients with intermittent claudication J Vasc Surg. 2010;1226-33.
43. Lane R, Harwood A, Watson L, Leng GC. Exercise for intermittent claudication. Cochrane Database Syst Rev. 2017;12:CD000990.
44. Singh S, Armstrong EJ, Sherif W, Alvandi B, Westin GG, Singh GD, et al. Association of elevated fasting glucose with lower patency and increased major adverse limb events among patients with diabetes undergoing infrapopliteal balloon angioplasty. Vasc Med. 2014;19(4):307-14.
45. Takahara M, Kaneto H, Iida O, Gorogawa S, Katakami N, Matsuoka TA, et al. The influence of glycemic control on the prognosis of Japanese patients undergoing percutaneous transluminal angioplasty for critical limb ischemia. Diabetes Care. 2010;33(12):2538-42.
46. Heart Outcomes Prevention Evaluation Study Investigators, Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med. 2000;342(3):145-53.
47. Yusuf S, Teo KK, Pogue J. Telmisartan, ramipril, or both in patients at high risk for vascular events N Engl J Med. 2008;35:1547-59.
48. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document

covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2018;39(9):763-816.
49. Aung PP, Maxwell HG, Jepson RG, Price JF, Leng GC. Lipid-lowering for peripheral arterial disease of the lower limb. Cochrane Database Syst Rev. 2007;2007(4):CD000123.
50. Antoniou GA, Fisher RK, Georgiadis GS, Antoniou SA, Torella F. Statin therapy in lower limb peripheral arterial disease: Systematic review and meta-analysis. Vascul Pharmacol. 2014;63(2):79-87.
51. Heart Protection Study Collaborative Group. Randomized trial of the effects of cholesterol-lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions. J Vasc Surg. 2007;45(4):645-54.
52. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002;324(7329):71-86.
53. Berger JS, Krantz MJ, Kittelson JM, Hiatt WR. Aspirin for the prevention of cardiovascular events in patients with peripheral artery disease: a meta-analysis of randomized trials. JAMA. 2009;301(18):1909-19.
54. Tepe G, Bantleon R, Brechtel K, Schmehl J, Zeller T, Claussen CD, et al. Management of peripheral arterial interventions with mono or dual antiplatelet therapy--the MIRROR study: a randomised and double-blinded clinical trial. Eur Radiol. 2012;22(9):1998-2006.
55. Strobl FF, Brechtel K, Schmehl J, Zeller T, Reiser MF, Claussen CD, et al. Twelve-month results of a randomized trial comparing mono with dual antiplatelet therapy in endovascularly treated patients with peripheral artery disease. J Endovasc Ther. 2013;20(5):699-706.
56. Belch JJ, Dormandy J, CASPAR Writing Committee, Biasi GM, Cairols M, Diehm C, et al. Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (CASPAR) trial. J Vasc Surg. 2010;52(4):825-33.
57. Thompson PD, Zimet R, Forbes WP, Zhang P. Meta-analysis of results from eight randomized, placebo-controlled trials on the effect of cilostazol on patients with intermittent claudication. Am J Cardiol. 2002;90(12):1314-9.
58. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg. 2007;45:5-67.
59. Meng Y, Squires H, Stevens JW, Simpson E, Harnan S, Thomas S, et al. Cost-effectiveness of cilostazol, naftidrofuryl oxalate, and pentoxifylline for the treatment of intermittent claudication in people with peripheral arterial disease. Angiology. 2014;65(3):190-7.
60. Salhiyyah K, Forster R, Senanayake E, Hadi M, Booth A, Michaels JA. Pentoxifylline for intermittent claudication. Cochrane Database Syst Rev. 2015;9(9):CD005262.
61. Comerota AJ. Endovascular and surgical revascularization for patients with intermittent claudication. Am J Cardiol. 2001;87(12A):34-43.
62. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg. 2007;33(1):1-75.
63. Teraa M, Conte MS, Moll FL, Verhaar MC. Critical Limb Ischemia: Current Trends and Future Directions. J Am Heart Assoc. 2016;5(2):002938.
64. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. Circulation. 2004;110(6):738-43.
65. Dabrh AM, Steffen MW, Undavalli C, Asi N, Wang Z, Elamin MB, et al. The natural history of untreated severe or critical limb ischemia. J Vasc Surg. 2015;62(6):1642-51.
66. Reinecke H, Unrath M, Freisinger E, Bunzemeier H, Meyborg M, Lüders F, et al. Peripheral arterial disease and critical limb ischaemia: still poor outcomes and lack of guideline adherence. Eur Heart J. 2015;36(15):932-8.
67. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, et al. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: Analysis of amputation free and overall survival by treatment received. J Vasc Surg. 2010;51(5):18-31.
68. Brewster DC, Darling RC. Optimal methods of aortoiliac reconstruction. Surgery. 1978;84(6):739-48.
69. Kang JL, Patel VI, Conrad MF, Lamuraglia GM, Chung TK, Cambria RP. Common femoral artery occlusive disease: contemporary results following surgical endarterectomy. J Vasc Surg. 2008;48(4):872-7.
70. Darling RC, Linton RR. Durability of femoropopliteal reconstructions. Endarterectomy versus vein bypass grafts. Am J Surg. 1972;123(4):472-9.
71. Farber A, Eberhardt RT. The current state of critical limb ischemia: a systematic review. JAMA Surg. 2016;151:1070-7.
72. Schanzer A, Conte MS. Critical limb ischemia. Curr Treat Options Cardiovasc Med. 2010;12(3):214-29.
73. Sachs T, Pomposelli F, Hamdan A, Wyers M, Schermerhorn M. Trends in the national outcomes and costs for claudication and limb threatening

ischemia: angioplasty vs bypass graft. J Vasc Surg. 2011;54(4):1021-31.
74. Goodney PP, Beck AW, Nagle J, Welch HG, Zwolak RM. National trends in lower extremity bypass surgery, endovascular interventions, and major amputations. J Vasc Surg. 2009;50(1):54-60.
75. Nowygrod R, Egorova N, Greco G. Trends, complications, and mortality in peripheral vascular surgery. J Vasc Surg. 2006;43:205-16.
76. Rowe VL, Lee W, Weaver FA, Etzioni D. Patterns of treatment for peripheral arterial disease in the United States: 1996-2005. J Vasc Surg. 2009;49(4):910-7.
77. Goodney PP, Tarulli M, Faerber AE, Schanzer A, Zwolak RM. Fifteen-year trends in lower limb amputation, revascularization, and preventive measures among medicare patients. JAMA Surg. 2015;150(1):84-6.
78. Nieves JT, Singh G, Laird J, Pevec W, Humphries M. Endovascular versus open bypass surgery for TASC D femoropopliteal lesions in patients with critical limb ischemia. J Vasc Surg. 2016;64:545-6.
79. Jacobs DL, Motaganahalli RL, Cox DE, Wittgen CM, Peterson GJ. True lumen re-entry devices facilitate subintimal angioplasty and stenting of total chronic occlusions: Initial report. J Vasc Surg. 2006;43(6):1291-6.
80. Shin SH, Baril D, Chaer R, Rhee R, Makaroun M, Marone L. Limitations of the Outback LTD re-entry device in femoropopliteal chronic total occlusions. J Vasc Surg. 2011;53(5):1260-4.
81. Singh KJ, Jaff M, Joye J, Laird J, Ansel G, Schneider P, et al. Major adverse limb events and wound healing following infrapopliteal artery stent implantation in patients with critical limb ischemia: the XCELL trial. Catheter Cardiovasc Interv. 2012;80(6):1042-51.
82. Bosiers M, Scheinert D, Peeters P, Torsello G, Zeller T, Deloose K, et al. Randomized comparison of everolimus-eluting versus bare-metal stents in patients with critical limb ischemia and infrapopliteal arterial occlusive disease. J Vasc Surg. 2012;55(2):390-8.
83. Iida O, Soga Y, Yamauchi Y, Hirano K, Kawasaki D, Tazaki J, et al. Anatomical predictors of major adverse limb events after infrapopliteal angioplasty for patients with critical limb ischaemia due to pure isolated infrapopliteal lesions. Eur J Vasc Endovasc Surg. 2012;44(3):318-24.
84. Conte MS. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) and the (hoped for) dawn of evidence-based treatment for advanced limb ischemia. J Vasc Surg. 2010;51(5):69-75.
85. Bradbury A, Wilmink T, Lee AJ, Bell J, Prescott R, Gillespie I, et al. Bypass versus angioplasty to treat severe limb ischemia: factors that affect treatment preferences of UK surgeons and interventional radiologists. J Vasc Surg. 2004;39(5):1026-32.
86. Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366(9501):1925-34.
87. Menard MT, Farber A, Assmann SF, Choudhry NK, Conte MS, Creager MA, et al. Design and Rationale of the Best Endovascular Versus Best Surgical Therapy for Patients With Critical Limb Ischemia (BEST-CLI) Trial. J Am Heart Assoc. 2016;5(7):3219.
88. Kumar A, Brooks SS, Cavanaugh K, Zuckerman B. FDA perspective on objective performance goals and clinical trial design for evaluating catheter-based treatment of critical limb ischemia. J Vasc Surg. 2009;50(6):1474-6.
89. Conte MS, Geraghty PJ, Bradbury AW, Hevelone ND, Lipsitz SR, Moneta GL, et al. Suggested objective performance goals and clinical trial design for evaluating catheter-based treatment of critical limb ischemia. J Vasc Surg. 2009;50(6):1462-73.
90. León LR, Dieter RS, Gadd CL, Ranellone E, Mills JL, Baker MF, et al. Preliminary results of the initial United States experience with the Supera woven nitinol stent in the popliteal artery. J Vasc Surg. 2013;57(4):1014-22.
91. Bosanquet DC, Glasbey JC, Williams IM, Twine CP. Systematic review and meta-analysis of direct versus indirect angiosomal revascularisation of infrapopliteal arteries. Eur J Vasc Endovasc Surg. 2014;48(1):88-97.
92. Biancari F, Juvonen T. Angiosome-targeted lower limb revascularization for ischemic foot wounds: systematic review and meta-analysis. Eur J Vasc Endovasc Surg. 2014;47(5):517-22.
93. Manzi M, Palena LM. Treating calf and pedal vessel disease: the extremes of intervention. Semin Intervent Radiol. 2014;31(4):313-9.
94. Jung HW, Ko YG, Hong SJ, Ahn CM, Kim JS, Kim BK, et al. Impact of Endovascular Pedal Artery Revascularisation on Wound Healing in Patients With Critical Limb Ischaemia. Eur J Vasc Endovasc Surg. 2019;58(6):854-63.
95. Teymen B, Aktürk S. Comparison of drug eluting balloon angioplasty to infrapopliteal artery critical lesions with or without additional pedal artery angioplasty in patients with diabetes mellitus and critical limb ischemia. J Interv Cardiol. 2018;31(3):400-6.
96. Nakama T, Watanabe N, Haraguchi T, Sakamoto H, Kamoi D, Tsubakimoto Y, et al. Clinical Outcomes of Pedal Artery Angioplasty for Patients With Ischemic Wounds: Results From the Multicenter RENDEZVOUS Registry. JACC Cardiovasc Interv. 2017;10(1):79-90.
97. Kawarada O, Fujihara M, Higashimori A, Yokoi Y, Honda Y, Fitzgerald PJ. Predictors of adverse clinical outcomes after successful infrapopliteal intervention. Catheter Cardiovasc Interv. 2012;80(5):861-71.
98. Wei LM, Zhu YQ, Zhao JG, Wang J, Lu HT, Zhang PL. Retrograde transplantar arch angioplasty of below-the-knee arterial occlusions: outcomes

compared to anterograde recanalization. Acad Radiol. 2014;21(11):1475-82.
99. Dua A, Rothenberg KA, Lee JJ, Gologorsky R, Desai SS. Six-Month Freedom From Amputation Rates and Quality of Life Following Tibial and Pedal Endovascular Revascularization for Critical Limb Ischemia. Vasc Endovascular Surg. 2019;53(3):212-5.

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