

Peripheral artery disease - contemporary approach through case report

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Abstract

Introduction. Peripheral arterial disease (PAD) of the lower extremities is an atherosclerotic disease of the arteries of the legs. Due to the frequent overlap of PAD and ischemic heart disease, cardiologists are in a unique position to screen, diagnose, and treat PAD. The aim of the paper is to present the initial results of the Department of Invasive Cardiology of Health center Zaječar in the diagnosis and treatment of patients with PAD of the lower extremities.

We present the initial results of the Department of Invasive Cardiology, including screening, non-invasive and invasive (angiographic) diagnosis of PAD of the lower extremities. Starting from March 2020, the Department of Invasive Cardiology is performing diagnostic invasive peripheral angiography in patients selected by non-invasive diagnostics from the territory of Eastern Serbia. In 2020 there were 3 and in 2021 5 more invasive peripheral angiographies performed. The number of these procedures is gradually increasing and during the first 10 months of 2022, 10 peripheral angiographies were performed. A total of 6 percutaneous angioplasties were performed as part of the endovascular treatment of PAD of the lower extremities, two of them within the Department of Invasive Cardiology Health center Zaječar symposium - ZASINK 2021. A complex patient with numerous comorbidities who was successfully treated with percutaneous angioplasty in our center is also presented.

Case report. A 67-year-old female patient with intermittent claudication at a distance of less than 10 meters after a physical examination was referred to ABI, which indicated a hemodynamically significant disease of the left leg (1.02 right; 0.68 left). Peripheral angiography was performed, which showed short segment stenosis of the left common iliac artery of about 80% and endovascular treatment was planned for the second act. During the following angiography, the mentioned segment was occluded. Percutaneous angioplasty was performed with the implantation of two balloon-expandable bare metal stents, with an excellent immediate angiographic result. After the procedure, the patient had significant symptomatic improvement. Dual antiplatelet therapy was continued for 6 months. During the follow-up period of 8 months, there were no clinically significant events in the patient. **Conclusion.** In a health center with experience in the treatment of various forms of coronary artery disease, the diagnosis and treatment of patients with PAD of the lower extremities can be successfully done with low procedural risk, as shown by our experience with 17 peripheral angiographies and 6 peripheral angioplasties performed, with a tendency to further increase the number and complexity of procedures performed.

Key words peripheral artery disease; PAD; ABI, angioplasty; peripheral angiography

Introduction

Peripheral arterial disease (PAD) of the lower extremities is an atherosclerotic disease of the arteries of the legs¹. As a manifestation of systemic atherosclerosis, PAD is associated with significantly increased cardiovascular morbidity, mortality and reduced quality of life. Due to the frequent overlap of PAD and ischemic heart disease, cardiologists are in a unique position to screen, diagnose, and treat PAD. Clinical evi-

dence is not as robust in patients with PAD compared to patients with coronary artery disease. However, the treatment goals in both groups are the same: to prevent ischemic cardiovascular events by changing lifestyle, medical therapy management and weighing the risks and benefits of revascularization procedures².

The aim of this study is to present of the initial results of the work of the Department of Invasive Cardiology Health center Zaječar in the diagnosis and treatment of patients with PAD of the lower extremities.



Figure 1.



Figure 2.

We present the initial results of the Department of Invasive Cardiology, including screening, non-invasive and invasive (angiographic) diagnosis of PAD of the lower extremities. Starting from March 2020, the Department of Invasive Cardiology is performing diagnostic invasive peripheral angiographies in patients selected by non-invasive workup from the territory of Eastern Serbia. In 2020, there were 3 and in 2021 five more invasive peripheral angiographies performed. The number of these procedures is gradually increasing and during the first 10 months of 2022, 10 peripheral angiographies were performed. A total of 6 percutaneous angioplasties were performed as part of the endovascular treatment of PAD of the lower extremities, two of them within the Department of Invasive Cardiology Health center Zaječar symposium - ZASINK 2021. A complex patient with numerous comorbidities who was successfully treated with percutaneous angioplasty in our center is also presented.

Case presentation

A 67-year-old patient was referred to the Council of the Department of Invasive Cardiology due to intermittent claudication at a distance of less than 10 meters. In the medical history review she had a colour duplex scan examination of the major arteries, and an occlusion of the left anterior tibial artery was found. After that, she was referred to a vascular surgeon at a tertiary health care level, where she was prescribed pentoxifylline and later cilostazol. In addition medical history is remarkable for arterial hypertension, chronic obstructive pulmonary disease and essential thrombocythemia, on cytoreductive therapy with hydroxyurea. After a physical examination with pulse palpation, the ankle brachial index (ABI) was performed: 1.02 on the right and 0.68 on the left. Acetylsalicylic acid and a high dose statin were prescribed to the patient and peripheral angiography was indicated. An angiographically significant lesion of the left common iliac artery of an estimated 80% diameter narrowing was appreciated (Figure 1). An endovascular treatment was

indicated. In the second act dated 9/4/2022. during the planned PTA procedure performed through the right radial artery, there is an ostial occlusion of the left common iliac artery (Figures 2 and 3). Terumo straight stiff type wire 0.035 260cm passes through the lesion. Predilatation of the lesion was performed with Allunga PTA 5x40mm balloons at 4 atm and with the same type of 6x10mm balloon at 6 atm. Bare metal stents Omnilink Elite 7x59mm and Omnilink 8x59mm were implanted. Stent overlap was optimized with a balloon stent carrier and an excellent final angiographic finding was obtained (Figure 4). Dual antiplatelet therapy was continued for 6 months, after which clopidogrel was discontinued. After percutaneous angioplasty, there is no more claudication and walking is limited only partially by osteomuscular disease.

Discussion

Despite the fact that PAD of the lower extremities affects about 230 million people worldwide², a recent survey found that 61% of general practitioners screen patients for PAD and only 6% are familiar with evidence-based therapy guidelines³. After detailed history, every examination of a patient with suspicion of PAD should be supplemented with a targeted physical examination, because certain clinical findings have prognostic significance: the difference in arterial blood pressure in the arms over 15 mmHg is a marker of vascular disease and mortality⁴; murmur over the femoral artery is an independent prognostic marker of future ischemic coronary events⁵. Following that in the non-invasive diagnostic algorithm comes ABI (ankle brachial index). The limited availability of this method is considered one of the reasons for the underdiagnosis of PAD, even in countries such as the United States of America⁶. ABI of one side of the body represents the highest systolic pressure measured by inflating the cuff over the ankle with the Doppler blood flow signal registered over a. dorsalis pedis and a. tibialis posterior and then divided by the highest systolic pressure obtained over the ipsilateral brachial artery by



Figure 3.



Figure 3.

inflating the cuff on the upper arm. It is determined individually for each side of the body. Values below 0.9 are suggestive of PAD of the lower extremities; 0.9-1.4 are considered normal; values over 1.40 indicate stiff/non compressible arteries and are caused by medial calcinosis, occurring more often in the elderly and patients with chronic kidney disease. In unclear cases, ABI can be performed after Treadmill exercise, increasing the sensitivity of the test². The sensitivity and specificity of ABI in the detection of stenosis over 50% compared to imaging diagnostics as the gold standard is 61-73% and 83-96% respectively¹. ABI is slightly lower in women, on average 0.017, which is not clinically significant⁷. This test shows lower reliability (proportion of true positive plus true negative patients out of the total population tested) in diabetics - 66%, compared to 81% in non-diabetic individuals. In diabetics, a better indicator, as well as in a population where greater arterial stiffness is expected, a better diagnostic indicator is TBI (toe-brachial index), because the small arteries of the fingers are very rarely affected by medial calcinosis (8). In the case of borderline ABI 0.9-1 and typical PAB symptoms in the lower extremities, exercise ABI is proposed, preferably on a treadmill. A drop in ABI below 0.9 or more than 20% of the pretest value or a drop in leg systolic pressure greater than 30 mmHg are considered diagnostic⁹.

A color duplex scan can be used in non-invasive diagnostics. This method is non-invasive, there is no radiation exposure but is largely operator dependent. With this method, the femoropopliteal segments can generally be adequately examined, while the aortoiliac segments are less accessible due to intestinal gas and body habitus, especially in obese individuals¹.

MDCT angiography of the aorta and lower extremity arteries considered the "gold standard" in the definitive non-invasive diagnosis of PAD in order to assess the anatomical complexity of the disease and decide on revascularization modality. The sensitivity of the method in comparison with conventional angiography is about 90%. The advantage is a short acquisition time of only a few seconds, as well as the avoidance of vascular access site

complications during diagnostic procedures, while the disadvantage is ionizing radiation exposure and the interference of calcified lesions with the findings obtained^{1,10}. MR angiography has excellent sensitivity in the diagnosis of PAD - 90-100%¹¹. The advantages of MR angiography over CT angiography are the absence of ionizing radiation and no interference with calcium in the diagnostic study. The disadvantage is the considerably longer time required for examination¹. There is also a risk of nephritogenic systemic fibrosis in patients with significantly reduced renal function. Studies with newer paramagnetic contrast agents indicate that this risk is virtually non-existent¹¹. Despite all the advantages, MR angiography is a less available diagnostic method in our country and worldwide.

In Health center Zaječar, after the targeted anamnestic data collection and physical examination of the patient with pulse palpation and auscultation of possible murmurs over the peripheral arteries, determination of ABI is carried out. For these purposes, an automated ABI (MESI ABPI MD) device is used, which simultaneously determines the systolic pressure in all four extremities, and the acquisition period is about one minute. The system uses an automated Doppler signal delivered via pre-positioned cuffs on the upper arms and above the ankles and has a measurement error detection system. Patients with an index below 0.9 on one or both sides of the body are referred for peripheral invasive angiography.

Invasive peripheral angiography has long been considered the gold standard in the diagnosis of PAD, but nowadays is mainly used in the planning of endovascular procedures in patients with already performed anatomical non-invasive diagnostics¹². Due to the local specifics of the health care system (unavailability of CT and MR angiography) and availability of trained medical personnel working in the field of interventional cardiology in Health center Zaječar after positive ABI finding is appreciated, peripheral invasive angiography is indicated for patients as a diagnostic and, depending on the findings, therapeutic procedure in the same or subsequent act.

Invasive peripheral angiography is based on the acquisition of angiographic images after the injection of an

iodinated contrast agent, usually diluted with normal saline because of the local irritation it produces. Since the image of blood vessels in the environment of bones and large surrounding muscle mass is obtained, the method of subtraction (digital subtraction angiography - DSA) of the surrounding structures is used to obtain angiographic images of blood vessels of the legs with excellent resolution. Usually, the common femoral artery is used as a vascular access with the placement of a 5 or 6F vascular introducer. Then, the blood vessels of the ipsilateral leg are visualized by contrast injection through the vascular sheath and then a crossover is performed with a diagnostic catheter to the contralateral common iliac artery to visualize the blood vessels of the other leg¹³. In our center, the first angiograms were performed using a transfemoral approach. In the later course, diagnostic procedures are carried out by cannulation of the radial or ulnar artery, at first using a pigtail catheter, and then the JR4 5F 125 cm catheter (longer than the standard catheter for cannulation of the right coronary artery) becomes the standard in diagnosis, which can be used to reach the bifurcation of the aorta in most people with a standard stature. The first angiographic record is usually with the tip of the catheter before the aortic bifurcation to visualize the distal aorta and common iliac arteries and then the left and right common iliac arteries are selectively cannulated. A system of manual injection of diluted iodine contrast agent is used. When obtaining angiographic images of the infrapopliteal arterial segments, slight angulation of the C arch laterally up to 10 degrees and internal rotation of the patient's hip joint is used to avoid superposition of the lower leg bones. The total amount of applied contrast agent usually does not exceed 150-200ml and so far there have been no cases of contrast-induced nephropathy. Due to the transition to transradial vascular access, local vascular complications of the puncture site have been avoided so far.

Revascularization of PAD of the lower extremities is recommended in case of failure of medical therapy and supervised physical training and when symptoms of PAD significantly impair the patient's daily living activities¹⁴. The presented patient had a claudication distance of less than 10 m, so it was decided to plan revascularization along with the introduction of drug therapy. Isolated iliac lesions (stenoses or occlusions) shorter than 5 cm have excellent long term outcome with endovascular treatment, with a five-year patency >90% with a low risk of complications¹⁵. The first peripheral angiography showed a short iliac stenosis in our patient, which corresponds to a TASC II type A lesion in which the recommended treatment is endovascular, so percutaneous transluminal angioplasty is indicated in the second act, for technical reasons. The subsequent peripheral angiography performed three months later, in which endovascular treatment was intended, revealed occlusion of the diseased segment of the artery. This corresponds to a TASC II type B lesion in which endovascular treatment is also recommended¹⁶, so percutaneous angioplasty was performed using right radial and left femoral access simultaneously. Balloon-expanding bare metal stents were used, the main advantages of which are greater radial strength and more predictable positioning compared to self-expanding stents, and they are preferred in ostial and calcified lesions. In a

study with the treatment of 222 lesions, the Omnilink stent showed excellent results with 93.1% of lesions successfully treated (less than 30% residual stenosis) with a total of 5.4% major adverse events in the 9-month follow-up period and 91% of lesions without clinically guided target lesion revascularization in a 3 years follow-up period (only 9% of clinically detected in-stent restenosis)¹⁷. After successful endovascular revascularization, at least one month of dual antiplatelet therapy is recommended, regardless of the type of stent used¹⁴, although in some trials, dual antiplatelet therapy was used for 2 months¹⁸ or one year¹⁹. However, the aforementioned studies were performed with drug-eluting stents or drug-coated balloons, which were not used in our procedure. Our patient has chronic myeloproliferative disease - essential thrombocythemia in which there is an increased risk of both ischemic and hemorrhagic complications²⁰⁻²², so the question of the optimal duration of dual antiplatelet therapy arose. Given that the patient is on cytoreductive therapy with hydroxyurea and the platelet count is well controlled, it was estimated that the ischemic risk outweighed the hemorrhagic one, so she was treated with dual antiplatelet therapy for 6 months, after which she was switched to monotherapy with aspirin.

Conclusion

In a center with experience in the treatment of various forms of coronary artery disease, the diagnosis and treatment of patients with peripheral arterial disease of the lower extremities can be successfully done with low procedural risk, as shown by our experience with 17 peripheral angiographies and 6 peripheral angioplasties performed, with a tendency to further increase the number and complexity of procedures performed.

References

1. Gerhard-Herman MD, Gornik HL, Barrett C, *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. *Circulation* 2017;135:726-779.
2. Tran B. Assessment and management of peripheral arterial disease: what every cardiologist should know. *Heart* 2021; 107:1835-1843.
3. Bridgwood BM, Nickinson AT, Houghton JS, *et al.* Knowledge of peripheral artery disease: what do the public, healthcare practitioners, and trainees know? *Vasc Med* 2020; 25:263-273.
4. Clark CE, Taylor RS, Shore AC, *et al.* Association of a difference in systolic blood pressure between arms with vascular disease and mortality: a systematic review and meta-analysis. *Lancet* 2012;379:905-914.
5. Cournot M, Taraszkiwicz D, Cambou JP, *et al.* Additional prognostic value of physical examination, exercise testing, and arterial ultrasonography for coronary risk assessment in primary prevention. *Am Heart J* 2009;158:845-851.
6. Pradhan AD, Aday AW, Beckman JA. The Big MAC attack on peripheral artery disease. *Circulation* 2020; 141:1211-1213.
7. Aboyans V, Criqui MH, McClelland RL, *et al.* Intrinsic contribution of gender and ethnicity to normal ankle-brachial index values: the Multi-Ethnic Study of Atherosclerosis (MESA). *J Vasc Surg.* 2007;45:319-327.
8. AbuRahma AF, Adams E, AbuRahma J, *et al.* Critical analysis and limitations of resting ankle-brachial index in the diagnosis of symptomatic peripheral arterial disease patients and the role of

- diabetes mellitus and chronic kidney disease. *J Vasc Surg* 2020; 71:937–945.
9. Aboyans V, Criqui MH, Abraham P, et al.; on behalf of the American Heart Association Council on Peripheral Vascular Disease; Council on Epidemiology and Prevention; Council on Clinical Cardiology; Council on Cardiovascular Nursing; Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. *Circulation* 2012; 126:2890–2909.
 10. Takahashi EA, Kinsman KA, Neidert NB, et al. Guiding peripheral arterial disease management with magnetic resonance imaging. *Vasa* 2019; 48:217–222.
 11. Woolen SA, Shankar PR, Gagnier JJ, et al. Risk of nephrogenic systemic fibrosis in patients with stage 4 or 5 chronic kidney disease receiving a group II gadolinium-based contrast agent: a systematic review and meta-analysis.
 12. Sun Z. Digital Variance Angiography: A promising alternative technology to traditional angiography for improvement of image quality with reduction of radiation and contrast medium doses. *Cardiovasc Interv Radiol* 2021; 44:460–461.
 13. Posa, A.; Tanzilli, A.; Barbieri, et al. Digital subtraction angiography (DSA) technical and diagnostic aspects in the study of lower limb arteries. *Radiation* 2022; 2:376–386.
 14. Aboyans V, Ricco JB, Marie-Louise EL, et al. ESC Scientific Document Group, 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 arteries. Endorsed by the European Stroke 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.
 15. Indes JE, Pfaff MJ, Farrokhhyar F, et al. Clinical outcomes of 5358 patients undergoing direct open bypass or endovascular treatment for aortoiliac occlusive disease: a systematic review and meta-analysis. *J Endovasc Ther* 2013; 20:443–455.
 16. Hardman RL, Jazaeri O, Yi J, et al. Overview of classification systems in peripheral artery disease. *Semin Intervent Radiol* 2014; 31(4):378–388.
 17. Aggarwal V, Waldo SW, Armstrong EJ. Endovascular revascularization for aortoiliac atherosclerotic disease. *Vasc Health Risk Manag* 2016; 12:117–127.
 18. Dake MD, Ansel GM, Jaff MR, et al. Durable clinical effectiveness with paclitaxel-eluting stents in the femoropopliteal artery: 5-year results of the Zilver PTX randomized trial. *Circulation* 2016; 133:1472–1483.
 19. Laird JR, Schneider PA, Tepe G, et al. Durability of treatment effect using a drug-coated balloon for femoropopliteal lesions: 24-month results of IN.PACT SFA. *J Am Coll Cardiol* 2015; 66:2329–2338.
 20. Fenaux F, Simon M, CAulier MT, et al. Clinical course of essential thrombocythemia in 147 cases. *Cancer* 1990; 66(3):549–556.
 21. Pósfai É, Marton I, Borbényi Z, et al. Myocardial infarction as a thrombotic complication of essential thrombocythemia and polycythemia vera. *Anatol J Cardiol* 2016; 16(6):397–402.
 22. Palandri F, Polverelli N, Ottaviani E, et al. Long-term follow-up of essential thrombocythemia in young adults: treatment strategies, major thrombotic complications and pregnancy outcomes. A study of 76 patients. *Haematologica*. 2010; 95(6):1038–1040.

Sažetak

Periferna arterijska bolest – savremen pristup kroz prikaz slučaja

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Uvod. Periferna arterijska bolest (PAB) donjih ekstremiteta je aterosklerotsko oboljenje arterija nogu. Zbog čestog preklapanja PAB i ishemijske bolesti srca kardiolozi su u jedinstvenoj prilici da sprovedu skring, dijagnostiku i lečenje PAB. Cilj rada je prikaz početnih rezultata rada Odeljenja invazivne kardiologije ZC Zaječar u dijagnostici i lečenju bolesnika sa PAB donjih ekstremiteta.

Metode. U radu su prikazani početni rezultati rada Odeljenja invazivne kardiologije, uključujući skring, neinvazivnu i invazivnu (angiografsku) dijagnostiku PAB donjih ekstremiteta. Počev od marta 2020. godine na Odeljenju invazivne kardiologije sprovode se dijagnostičke invazivne periferni angiografije kod pacijanata selektovanih neinvazivnom dijagnostikom sa teritorije istočne Srbije. U 2020. godini urađeno je 3 i u sledećoj 2021. još 5 invazivnih perifernih angiografija. Postepeno dolazi do povećanja broja ovih procedura i tokom prvih 10 meseci 2022. godine urađeno je 10 perifernih angiografija. Ukupno je urađeno 6 perkutanih angioplastika u sklopu lečenja PAB donjih ekstremiteta, od toga dve u okviru simpozijuma Odeljenja invazivne kardiologije ZC Zaječar - ZASINK 2021. godine. Prikazana je i kompleksna bolesnica sa brojnim komorbiditetima koja je uspešno lečena perkutanom angioplastikom u našem centru.

Prikaz slučaja. Bolesnica starosti 67 godina sa intermitentnim kludikacijama pri distanci kraćoj od 10 metara nakon fizikalnog pregleda upućena je na ABI koji je ukazao na hemodinamski značajnu bolest leve noge (1.02 desno; 0.68 levo). Urađena je periferna angiografija na kojoj je viđena stenoza leve zajedničke ilijačne arterije oko 80% u kraćem segmentu i za drugi akt planirano endovaskularno lečenje. Pri narednoj angiografiji navedeni segment je okludiran. Urađena je perkutana angioplastika sa implantacijom balon oslobađajuća 2 bare metal stenta, uz odličan neposredni angiografski rezultat. Nakon procedure pacijentkinja ima značajno simptomatsko poboljšanje. Sprovedena je dvojna antirombocitna terapija u trajanju od 6 meseci. U periodu praćenja od 8 meseci nije bilo kliničkih događaja od značaj kod bolesnice.

Zaključak. U centru sa iskustvom u lečenju različitih oblika prezentacije koronarne arterijske bolesti može se uspešno organizovati dijagnostika i lečenje bolesnika sa perifernom arterijskom bolešću donjih ekstremiteta uz nizak proceduralni rizik što pokazuju naša iskustva sa 17 urađenih perifernih angiografija i 6 perifernih angioplastika, sa tendencijom daljeg povećanja broja i kompleksnosti izvedenih procedura.

Ključne reči: periferna arterijska bolest donjih ekstremiteta; PAB; angioplastika, ABI, periferna angiografija