Psychiatria Danubina, 2019; Vol. 31, Suppl. 5, pp S814-S820
Medicina Academica Mostariensia, 2019; Vol. 7, No. 1-2, pp 92-98 *Original paper*

IS 64-ROW MULTI-DETECTOR COMPUTED TOMOGRAPHY ANGIOGRAPHY EQUAL TO DIGITAL SUBTRACTION ANGIOGRAPHY IN TREATMENT PLANNING IN CRITICAL LIMB ISCHEMIA?

Vesna Đurović Sarajlić[1], Dragan Totić[2], Amina Bičo Osmanagić[3], Refet Gojak[4] & Lidija Lincender[5]
[1]*Clinic for Radiology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina*
[2]*Clinic for Cardiovascular Surgery, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina*
[3]*Clinic for Heart, Vascular Diseases and Rheumatology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina*
[4]*Clinic for Infectious Diseases, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina*
[5]*Policlinic Sunce Agram, Sarajevo, Bosnia and Herzegovina*

received: 5.7.2019 revised: 7.9.2019 accepted: 28.11.2019

SUMMARY

Background: *Critical limb ischemia (CLI) represents the end stage of peripheral arterial disease (PAD). It is defined as a chronic ischemic rest pain, ulcers or gangrene, attributable to proven arterial occlusive disease. Intra-arterial digital subtraction angiography (IA DSA) still represents the gold standard for the evaluation of steno-occlusive lesions, but it has greatly been replaced with non-invasive multi-detector computed tomography angiography (MDCTA). The purpose of this prospective study was to compare diagnostic performance of MDCTA versus DSA in treatment planning in patients with CLI according to TransAtlantic Inter-Society Consensus Document on Management of Peripheral Arterial disease (TASC II).*

Subjects and methods: *The study was designed as prospective; it was conducted from March 2014 to August 2016, and included 60 patients with symptoms of CLI, Fontaine stage III and IV. MDCTA of the peripheral arteries was performed first, followed by DSA. The lesions of aorto-iliac, femoro-popliteal and infra-popliteal regions were classified according to the TASC II guidelines, and inter-modality agreement between MDCTA and DSA was determined by using Kendall's tau-b statistics.*

Results: *Inter-modality agreement was statistically significant in all three vascular beds, with excellent agreement >0.81 in aortoiliac and femoropopliteal regions, and a very good agreement >0.61 in infrapopliteal region. Treatment recommendations based on MDCTA findings and DSA findings were identical in 54 (90%) patients. In one patient (1.7%), CTA was not interpretable. In five patients (8.3%), CTA findings disagreed with DSA findings in regard to the preferable treatment option.*

Conclusion: *64-row MDCT angiography is highly competitive to DSA in evaluation of steno-occlusive disease and treatment planning in patients with critical limb ischemia.*

Key words: *multi-detector computed tomography angiography - digital subtraction angiography - peripheral arterial disease - critical limb ischemia*

* * * * *

INTRODUCTION

Critical limb ischemia (CLI) represents the end stage of peripheral arterial disease (PAD). It is defined as chronic ischemic rest pain, ulcers or gangrene, attributable to proven arterial occlusive disease (Hiatt et al. 2008, Varu et al. 2010). It is a result of chronic insufficiency of blood supply to the extremities, and should not be mixed with acute limb ischemia. CLI represents 1% of the total number of patients with PAD (Norgren et al. 2007). Figure 1.

The treatment of patients with CLI includes conservative therapy, endovascular or surgical revascularization, and amputation (Dohmen et al. 2012). Diagnostic angiographies have a crucial role in characterization of the lesions, staging of the PAD and treatment planning.

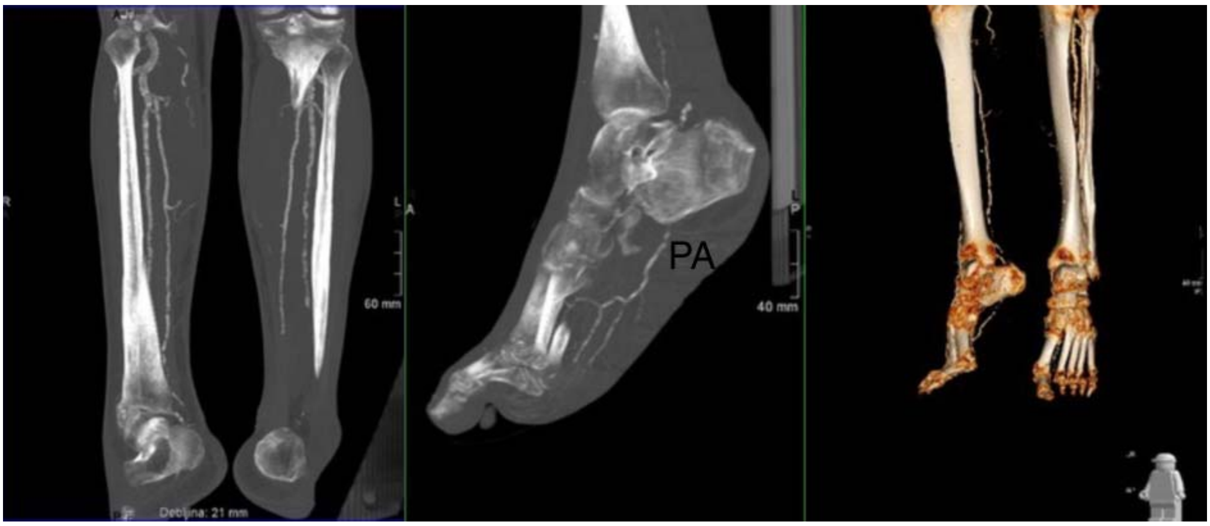
Intra-arterial digital subtraction angiography (in further text DSA) still represents the gold standard for the evaluation of steno-occlusive lesions, but it has greatly been replaced with non-invasive diagnostic modalities - magnetic resonance angiography (MRA) and multi-detector computed tomography angiography (MDCTA) (Krishnan 2016, Cowell et al. 2012, Amy et al. 2012).

The studies conducted up to date prove excellent diagnostic performance of MDCTA and MRA in evaluation of steno-occlusive disease of peripheral arteries in comparison to DSA, including manly patients with symptoms of intermittent claudication, and less patients with symptoms of critical limb ischemia (Napoli et al. 2011, Cernic et al. 2009, Sharegi et al. 2010, Jens et al. 2013). Only few studies compared diagnostic performance of MDCTA and DSA exclusively in patients with CLI (Schernthaner et al. 2009, Fotiadis et al. 2011).

In CLI the most affected vascular bed is in infrapopliteal region, with usually heavily calcified walls of the crural arteries, which are anyhow of small diameter. Diffuse wall calcifications represent the main obstacle in analysis of the circulating lumen in CTA (Ouwendijk et al. 2006, Fleichman et al. 2006) (Figure 2).

a. **b.**

Figure 1. Lower extremity Buerger's disease. (a, b) Maximum intensity projection (MIP) and Volume rendering (VR) 3D images in a patient with critical limb ischemia due to Buerger's disease, show occlusion of the right fibular and distal part of the right posterior tibial artery, and occlusion of the left posterior tibial artery and distal part of the left fibular artery



a. **b.** **c.**

Figure 2. Peripheral CTA of a 65-year-old man with critical limb ischemia due to diabetes mellitus. (a, b) Maximum intensity projection (MIP) reconstruction images of the lower leg and foot show multiple short stenotic lesions and wall calcifications of the crural arteries and lateral branch of the plantar artery. (c) Volume rendering (VR) image of the same patient. Wall calcifications are hyperdense in comparison to the circulating lumen

This problem is avoided in DSA, as it is essentially lumenography, with better spatial resolution, and less beaming artifacts than CTA (Sze 2002). The purpose of this study was to prove that CTA is highly comparable to DSA, and sufficient imaging modality in detection of the viable recipient artery for the endovascular treatment or the surgical by-pass in majority of patients with CLI.

SUBJECTS AND METHODS

Study design and data collection

The study was designed as prospective; it was conducted from March 2014 to August 2016. The Ethical Committee of the Clinical Center University of Sarajevo approved the study, the reference number 0207-33300. It was performed in accordance with the World Health Organization Declaration of Helsinki on ethical principles for medical research involving human subjects, revised document from 2008. The study included 60 patients with symptoms of critical limb ischemia, stages III and IV of Fontaine's clinical classification of peripheral arterial disease, and all patients signed the informed consent for participation.

Specialists of internal medicine or vascular surgery from the Clinical Center University of Sarajevo referred the patients for diagnostic angiography.

Population characteristics

For each patient the following data was obtained: gender, age, smoking status, hypertension, hyperlipidemia, diabetes mellitus, obesity, history of angina pectoris, history of myocardial and cerebrovascular infarction, ischemic rest pain in the foot, and presence of ulcers or gangrene (Fontaine stage III and IV) (Table 1).

Table 1. Fontaine's classification of peripheral arterial disease (PAD)

Stage of disease	Symptoms
I	Walking distance unlimited
II a	Walking distance > 200 m
II b	Walking distance < 200 m
III	Ischemic rest pain
IV	Trophic changes (ulcers, gangrene)

Values of urea and creatinine were checked in all patients before contrast application, and they were within the reference interval. Values of INR and APTT were checked before the DSA was performed.

MDCTA of the peripheral arteries was performed first, followed by DSA within the next 30 days.

Two radiologists, each with more than seven years' experience in vascular radiology, separately evaluated CTA and DSA images.

MDCT Angiography

MDCT angiography was performed on 64-row MDCT, Light Speed VCT 64, General Electric, according to the CTA Run-off 0,625 protocol, which implies slice thickness of 0.625 mm. To each patient, 120–140 ml of a nonionic iodinated contrast medium Iopamiro 300 (300 mg I/ ml) was applied through the cubital vein by the automated injector, at a flow rate of 4 ml/s, and pressure 250-300 psi. The scanning conditions were 360 mA and 120 kV. The SmartPrep was used for starting the contrast injection, after the enhancement of the abdominal aorta exceeded concentration of 200 H.U. The scanning time was 25 seconds, covering the area from the diaphragm to the toes (Fleischmann 2009). The images were analyzed on a dedicated work - station MultiSync LCD 1990 sxi, axial scans, as well as 2D and 3D reconstructions – multiplanar reformation (MPR), maximum intensity projection (MIP) and volume rendering (VR) reconstructions.

Digital Subtraction Angiography

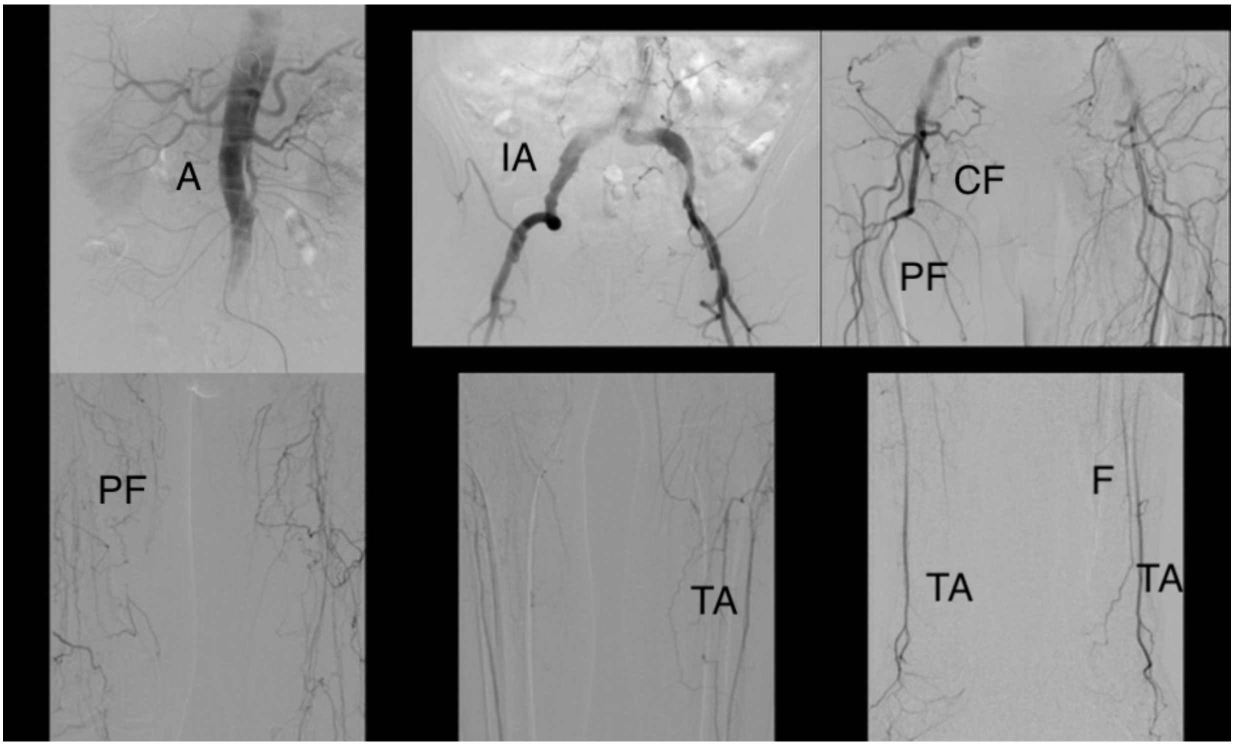
DSA was performed on floor-mounted C–arm AXIOM ARTIS SIEMENS (2007). The vascular access was through the common femoral artery. We used 5F introducers and pig-tail flush catheters, through which a nonionic iodinated contrast medium (Iopamiro 300) was administered. A first field covered abdominal aorta with a catheter tip positioned at the level of Th12 vertebral body, and subsequent fields covered pelvic, upper leg, lower leg and feet arteries, with a catheter tip withdrawn to the level of L3 vertebra. For each field, 25-30 ml of contrast medium was administered, at a flow rate 15 ml/s, pressure 900 psi, and 2 frames/s (Damiano 2002). The obtained angiograms were evaluated on a dedicated AXIOM ARTIS work - station. Figure 3.

TASC classification

According to TASC II classifications, vascular bed was divided into three regions: aortoiliac (infrarenal aorta, common, external and internal iliac arteries), femoropopliteal (common, superficial and deep femoral arteries, and popliteal arteries), and infrapopliteal region (anterior and posterior tibial arteries, fibular artery, posterior tibial truncus, dorsal and plantar pedal arteries).

Detected lesions in each vascular segment were categorized according to the degree, number and length, as lesions type TASC A, B, C or D. According to the TASC II guidelines and its supplement for the below-the-knee arteries the preferable type of treatment was provisionally recommended to each patient, both on the basis of CTA and DSA, and the results were compared (Jens et al. 2013). In patients with no detectable recipient run-off arteries for surgical by-pass or endovascular treatment, conservative treatment or the amputation were taken into consideration.

a. b. c.



d. e. f.

Figure 3. Digital subtraction angiography (DSA) of the lower extremities in a 57-year-old man with critical limb ischemia with rest pain of the right foot. (a, b, c) Images show circulating lumen of the abdominal aorta, iliac arteries and common femoral arteries. (d, e, f) Images show bilateral absence of the superficial femoral arteries and popliteal arteries in the upper leg and knee, with the reconstruction of fibular arteries below the knee via collateral muscular branches of the deep femoral artery

Statistical analysis

For statistical analysis we used program package SPSS for Windows and Microsoft Excel; data were tabulated for continuous variables as mean and standard deviation, and for categorical variables as absolute and relative frequencies. Statistical significance was p≤0.05.

Inter-modality agreement between MDCTA and DSA was determined by using Kendall's tau-b statistics, where a Kendall's tau-b value of less than 0.20 indicated a poor agreement, a value of 0.21-0.40 indicated a slight agreement, and value of 0.41-0.60 a moderate agreement. Kendall's tau-b values of 0.61-0.80, and 0.81-1.00 indicated respectively a very good and excellent agreement.

RESULTS

Sixty patients were included in the study. The majority of them was male: 45 (75%), with the mean age of 65.9±11.14. Fifteen patients (25%) were female (25%), with the mean age of 72.80±10.47. The age difference between males and females was statistically significant (p=0.04). Patients characteristics, risk factors and comorbidities are given in table 2.

Table 2. Patient's characteristics, risk factors and comorbidities

Gender	Male	45 (75%)
	Female	15 (25%)
Age	Male	65.9±11.3
	Female	72.8±10.5
Smoking status	Yes	34 (56.7%)
Hypertension	Yes	10 (16.7%)
Diabetes mellitus	Yes	25 (41.7%)
Hyperlipidemia	Yes	35 (58.3%)
Obesity	Yes	20 (33.3%)
Angina pectoris	Yes	6 (10.0%)
Transitory ischemic attack	Yes	1 (1.7%)
Cerebrovascular infarction	Yes	9 (15%)
Myocardial infarction	Yes	9 (15%)
Ischemic rest pain (IRP)	Yes	25 (41.7%)
Trophic changes (ulcers/gangrene)	Yes	43 (71.7%)
IRP and trophic changes	Yes	13 (21.6%)

The Kendall's tau-b value of inter-modality agreement between MDCTA and DSA in aortoiliac segment was 0.806, which was statistically significant, p=0.0001.

The Kendall's tau-b value was 0.811 for the right femoropopliteal segment, and 0.865 for the left femoropopliteal segment. Both values were statistically significant, p=0.0001.

In infrapopliteal region, inter-modality agreement was calculated separately for each crural artery.

Kendall's tau-b values for the right anterior tibial artery, right posterior tibial artery, and right fibular artery were 0.745, 0.684, and 0.749 respectively; all statistically relevant with p=0.0001.

Kendall's tau-b values for the left anterior tibial artery, left posterior tibial artery, and left fibular artery were 0.723, 0.604 and 0.704 respectively; all statistically relevant with p=0.0001.

In aortoiliac and femoropopliteal region, 30 lesions were classified as type TASC A and TASC B according to CTA, and 72 lesions as type TASC C and TASC D.

In the same vascular regions, 22 lesions were classified as TASC A and B according to DSA, and 66 lesions as TASC C and TASC D.

In infrapopliteal region, 135 lesions were classified as TASC C and TASC D according to CTA, while according to DSA 124 lesions were classified as type TASC C and TASC D lesions.

Treatment recommendations based on MDCTA findings and DSA findings were identical in 54 (90%) patients. In one patient (1.7%), CTA was not interpretable.

In five patients (8,3%), CTA findings disagreed with DSA findings in regard to the preferable treatment option.

In two of these five patients (3,3%), the CTA findings suggested that amputation might be needed, but after DSA was performed, patients underwent a surgical by-pass. In the remaining three patients (5%), either conservative or surgical treatment was recommended on the basis of the CTA, while DSA findings suggested that amputation might be needed. After clinical evaluation of the patients and the local status of the limb, amputation was performed in one patient only, while other two patients were treated conservatively.

DISCUSSION

Our study is one of the few studies comparing clinical utility of the CTA versus DSA in evaluation and treatment planning exclusively in patients with CLI. We used TASC II classification for PAD lesions in aortoiliac and femoropopliteal vascular regions, and its supplement for the classification of the infrapopliteal disease (Jaff et al. 2015). We have not found other studies referring to the use of the TASC classification supplement for the infrapopliteal region, its practicability and acceptance among the clinicians.

Inter-modality agreement was statistically significant in all three vascular regions, and, by the Kendall's tau-b test, it showed "excellent level of agreement" in aortoiliac and femoropopliteal regions. The calculated inter-modality agreement in infrapopliteal region showed a slightly lower value, categorized as "a very - good agreement".

In 54 (90%) patients, the same treatment approach was suggested on the grounds of both CTA and DSA.

Surgical revascularization was recommended to majority of the patients in our study, as the lesions were more complex and diffuse, extending to more than one vascular bed.

In one patient, CTA was non-interpretable, while in five patients CTA and DSA led to opposite recommendations. In two of these patients, DSA was more accurate in evaluation of vascular status. These two patients had circumferential wall calcifications in all three crural arteries, and CTA overestimated a degree of stenosis due to the blooming artifacts. Even with the window adjustment we were not able to reliably evaluate the circulating lumen. This kind of wall calcification distribution is most common in patients with chronic renal disease. In our study, a longtime smoking, male gender, advanced age and diabetes mellitus were predisposing risk factors for this kind of lesions in infrapopliteal arteries.

In the remaining three patients, both CTA and DSA classified infrapopliteal lesions as TASC C and TASC D. For all three patents conservative treatment was recommended upon the CTA finding, while DSA suggested that amputation might be needed. In these three patients, DSA imaging was suboptimal due to the poor opacification of the infrapopliteal arteries. It is a known fail of DSA in patients with cardiac insufficiency, due to the slow circulation and contrast dilution. Our patients were two male and one female patient, with symptoms of chronic cardiac insufficiency. Two of them were treated conservatively, while in one patient amputation was performed after the clinical evaluation of the limb.

The decisions on treatment option in these five patients, in who CTA or DSA findings did not match, were made considering the patients' overall health status, hemodynamic condition and the local status of the affected limb (Leiner et al. 2009).

Studies, which have so far, compared CTA and DSA performance in patients with PAD, have generally included patients with different stages of disease, patients with IK and CLI. These studies proved that 64-MDCT angiography is almost equal to DSA in detection and treatment planning in PAD, with accuracy >0.98 (Napoli et al. 2011, Cernic et al. 2009, Sharegi et al. 2010).

Napoli et al. evaluated diagnostic performance and effect on treatment planning of 64-row MDCT with DSA in 212 patients with PAD, out of which 34 patients had symptoms of CLI. Therapy recommendations according to CTA findings and TASC II classification were same in all but one patient (Napoli et al. 2011).

In 2009, Schernthaner et al. published a study evaluating value of MDCTA in developing treatment planning exclusively in patients with CLI. Their study included 28 patients with CLI, and CTA suggested that endovascular and surgical treatment was needed in 14 patients, and that was confirmed by successfully completed procedures. Conservative treatment was recommended in eight patients, and above-the-knee amputation in only one. DSA was performed in only five patients, but it did not give additional information in comparison to CTA (Schernthaner et al 2009).

The results of our study are comparable to the results of these studies. It is relevant for clinical practice as it implicates that MDCTA is reliable for diagnosing and treatment planning in patients with CLI.

DSA as a diagnostic tool in patients with the CLI has been almost completely replaced with the MDCTA, and it may be indicated only in sporadic patients according to our experience.

Regarding the TASC classification for the infrapopliteal lesions, we found it a time consuming, and the clinicians as well as radiologist in our working environment are not yet familiar with it.

Future investigations may be directed in evaluation of MDCT angiographies performed on 128 or more sliced CT machines, or with application of contrast media with higher iodine concentrations (370 or 400 mg I/ml), and its potential to improve imaging and evaluation of heavily calcified infrapopliteal run-off arteries.

CONCLUSION

Our study proves that 64-row MDCT angiography is almost equal to DSA in evaluation of steno-occlusive disease and treatment planning in patients with critical limb ischemia. In ambiguous cases the wright clinical decision on treatment option can only be made considering the overall status of the patient and affected limb.

TASC guidelines for the classification of infrapopliteal peripheral arterial disease is yet to be accepted and recognized by radiologists and clinicians.

Contribution of individual authors:

Drafting the article: Vesna Đurović Sarajlić.

Acquisition, analysis and interpretation of data: Vesna Đurović Sarajlić, Dragan Totić, Amina Bičo Osmanagić & Refet Gojak.

Revising it critically for intellectual content: Lidija Lincender.

Acknowledgements:

I thank Clinic for Radiology and Clinical Centre University of Sarajevo for their support. I remain grateful to Mirjana Evtov for language editing.

Conflict of interest : None to declare.

References

1. *Amy W. Pollak, Patrick Norton, Christopher M. Kramer: Multimodality Imaging of Lower Extremity Peripheral Arterial Disease: Current Role and Future Directions. Circ Cardiovasc Imaging. November 2012; 5:797-807*
2. *Cernic S, Pozzi Mucelli F, Pellegrin A, Pizzolato R, Cova MA: Comparison between 64-row CT angiography in the study of lower extremities: personal experience. Radiol Med (Torino) 2009; 114:1115-1129*
3. *Cowell GW, Reid AW, Roditi GH: Changing trends in a decade of vascular radiology – the impact of technical developments of non-invasive techniques on vascular imaging. Insights Imaging 2012; 3:495-504*
4. *Damiano MM: Injection Rates and Image-Acquisition Programs. In Kandarpa K, Aruny JE, ed. Handbook of Interventional Radiologic Procedures, Lippincott Williams &Wilkins 2002; pg 580-584*
5. *Dohmen A, Eder S, Euringer W, Zeller T, Beyersdorf F: Chronic critical limb ischemia. Dtsch Arztebl Int 2012; 109:95–101*
6. *Fleischmann D, Hallet RL, Rubin GD: CT Angiography of Peripheral Arterial Disease. J vasc Interv Radiolo 2006; 17:3-26*
7. *Fleischmann D: Contrast Medium Administration in Computed Tomographic Angiography. In Rubin GD, Rofsky NM, ed. CT and MR Angiography, Comprehensive vascular Assesment, Wolters Kluwer/Lippincott Williams &Wilkims 2009; pg 149-152*
8. *Fotiadis N, Kyriakides C, Bent C, Vorvolakos T, Matson M: 64-section CTA in patients with critical limb ischemia and severe claudication: comparison with digital subtraction angiography. Clin Radiol 2011; 66:945-952*
9. *Hiatt WR, Goldstone J, Smith SC, McDermott M, Moneta G, Oka R, Newman AB, Pearce WH: American Heart Association Writing Group 1. Atherosclerotic Peripheral Vascular Disease Symposium II: Nomenclature for vascular diseases. Circulation 2008; 118:2826-2829*
10. *Jaff MR, White CJ, Hiatt WR, Fowkes GR, Dormandy J, Razavi M, Reekers J, Norgren L: An Update on Methods for Revascularization and Expansion of the TASC Lesion Classification to Include Below-the-Knee Arteries: A Supplement to the Inter- Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Vascular Medicine 2015; 20:465-478*
11. *Jens S, Koelemay MJ, Reekers JA, Bipat S: Diagnostic performance of computed tomography angiography and CE MRA in patients with critical limb ischemia and intermittent claudication: systemic review and meta-analysis. Eur Radiol 2013; 23:3104-3114*
12. *Krishnan MN: Peripheral angiography: View and technique. Journal of Indian College of Cardiology 2016; 6:114-117*

13. *Leiner T, Fleischmann D, Rofsky NM: Lower Extremities Vasculature. In: CT and MR Angiography, Comprehensive Vascular Assesment. Goeffry Rubin, Neil M. Rofsky, ed. Wolters Kluwer/Lippincott Williams&Wilkins 2009; pg. 924-983*
14. *Napoli A, Anzidei M, Zaccagna F, Cavallo Marincola B, Zini C, Brachetti G, Cartocci G, Fanelli F, Catalano C, Passariello R: Peripheral Arterial Occlusive Disease: Diagnostic Performance and Effect on Therapeutic Management of 64-Section CT Angiography. Radiology 2011; 261*
15. *Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG: Inter- society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg 2007; suppl S:S5–S67*
16. *Ouwendijk R, Kock MC, van Dijk LC, van Sambeek MR, Stijnen T, Hunink MG: Vessel wall calcifications at multidetector row CT angiography in patients with peripheral arterial disease: effect on clinical utility and clinical predictors. Radiology 2006; 241:603-608*
17. *Schernthaner R, Fleischmann D, Stadler A, Schernthaner M, Lammer J, Loewe C: Value of MDCT Angiography in Developing Treatment Strategies for Critical Limb Ischemia. American Journal of Roentgenology 2009; 192:1416-1424*
18. *Sharegi S, Gopal A, Gul K, Matchinson JC, Wong CB, Weinberg N, Lensky M, Budoff MJ, Shavelle DM: Diagnostic accuracy of 64 multidetector computed tomographic angiography in peripheral vascular disease. Catheter Cardiovasc Interv 2010; 75:23-31*
19. *Sze DY: Conventional Angiography in the Noninvasive Era. In: Rubin GD, Rofsky NM, ed. CT and MR Angiography, Comprehensive Vascular Assesment, Wolters Kluwer/Lippincott Williams & Wilkins 2002; pg 88-89*
20. *Varu VN, Hogg ME, Kibbe MR: Critical limb ischemia. J Vasc Surg 2010; 51:230-41*

Correspondence:
Vesna Đurović Sarajlić, MD
Department for Vascular and Interventional Radiology,
Clinic for Radiology, Clinical Center University of Sarajevo
Bolnička 25, 71 000 Sarajevo, Bosnia and Herzegovina
E-mail: vesnasarajlic8@gmail.com