Diagnostic Importance of Pulse Oximetry in the Determination of the Stage of Chronic Arterial Insufficiency of Lower Extremities

Nebojša Ignjatović¹, Marina Vasiljević², Dragan Milić¹, Jelena Stefanović³, Miroslav Stojanović¹, Aleksandar Karanikolić¹, Aleksandar Zlatić¹, Goran Djordjević¹, Saša Živić¹, Ljiljana Jeremić¹, Ivona Djordjević⁴, Radmilo Janković¹

¹Surgical Clinic, Clinical Centre, Niš, Serbia;

²Department for Anaesthesiology and Reanimation, Ophthalmology Clinic, Clinical Centre, Niš, Serbia; ³Faculty of Medicine, University of Niš, Niš, Serbia;

⁴Clinic of Paediatric Surgery, Clinical Centre, Niš, Serbia

SUMMARY

Introduction Chronic arterial insufficiency (CAI) of lower extremities is important socio-economical and healthcare problem, due to its high incidence of morbidity, disability and mortality.

Objective The aim of our work was to determine the diagnostic importance of pulse oximetry in the early detection of stage of lower extremities CAI based on peripheral arterial oxygen saturation of haemoglobin (SpO₂).

Methods Prospectively, we analyzed a group of 50 patients, admitted at the Vascular Department of Surgical Clinic in Niš during the period from September 2006 to October 2007, with evident symptoms and signs of different stages of lower extremities CAI verified by ultrasonography. In patients with lower extremity disorder of tissue arterial capillaries, SpO₂ was determined by pulse oximetry.

Results Using pulse oximetry, depending on the of stage of lower extremities CAI, we revealed a considerable difference in the stages of functional ischemia SpO₂: Fontaine I – 95.33±1.41%, Fontaine IIa – 92.14±2.27% and Fontaine IIb – 79.67±2.73%; in stage critical ischemia SpO₂: Fontaine III – 62.54±4.39% and Fontaine IV – 47.67±6.16%. In 3 patients with gangrenous foot and fingers SpO₂ was immeasurable and progressive decrease in SpO₂ of arterial capillaries (p<0.01 between stages).

Conclusion Due to the reliability and simplicity of pulse oximetry it can be a routinely used diagnostic device for patients with early determined stage of lower extremities CAI.

Keywords: pulse oximetry; haemoglobin oxygen saturation; chronic arterial insufficiency of lower extremities.

INTRODUCTION

The frequency of arterial degeneration diseases, especially atherosclerosis, is constantly increasing due to a currently worldwide aging human population. Atherosclerosis is a disease which causes gradual thickening and elasticity loss of the arterial wall, and simultaneous stenosis and/ or occlusion of luminar [1].

Chronic arterial insufficiency (CAI) results in stenotic-occlusive disease of tissues and organs of vascularized arterial disorders. CAI of the lower extremities represents a significant medical and socio-economic problem due to a high incidence of morbidity (intermittent claudication, pain at rest, muscular atrophy, ulcerations and gangrene), invalidity (limitations of active movement and amputation of the devitalized part of the extremity) and mortality.

Depending on the localization of stenoticocclusive lesion and the possibility of the establishment of collateral circulation results in complex haemodynamic disorders. Such lesions determine the rapidity of progression and the degree of CAI severity leasing to hypoxemia and resultant disorders aerobic cell metabolism of limb tissues, due to the reduction in the supply of arteries with oxygen [2].

By the end of the 20th century it became obvious that empirical means have not given valid results in lower extremity perfusion, because of the loss of their sensitivity and specifics. The necessary improvement in the research of instruments and techniques resulted in the discovery of numerous and different objective methods which could be applied in the diagnostics of peripheral vascular diseases [3]. Among the tested invasive methods, beside electronic oscillometry with oscillography, plehyismography, capillaroscopy, thermometry with thermography, Doppler echosonography and its modality (CW Doppler, duplex scanning-B mode and triplex scanning colour Doppler), in numerous worldwide conducted clinical studies pulse oximetry has shown to be invaluable in the determination of the stage of peripheral ischemia [4, 5].

Historical sources of pulse oximetry go as far as the period when colour spectrum and Isaac Newton's sunlight were disclosed in 1666, with the first description of haemoglobin in 1860. In 1874 Karl von Vierordt tried to measure blood oxygen saturation of the human hand [6].

Correspondence to:

Nebojša IGNJATOVIĆ Surgical Clinic, Clinical Centre Bul. dr Zorana Djindjića 48 18000 Niš, Serbia **n.ignjat@gmail.com** Quantitative oximetry started with Krogh after the First World War in 1930 in Copenhagen [7]. In 1935 Matthes constructed the first appliance for continuous measuring of the human blood oxygen saturation using the two light sheaves of different wavelengths, red-sensitive to oxygenation changes and green-insensitive, so as to compensate for the changes in tissue thickness, haemoglobin type and light intensity [8].

The first pulse oximeter was constructed by the Japanese physiologist and bioengineer Takuo Aoyagi in 1973. He concluded that the variation of tissue arterial blood volume may be useful for obtaining a signal depending only on pulse characteristics of arterial blood, which can be used for measuring arterial oxygen saturation [9]. Further development of pulse oximetry in this country occurred in early 1980 conducted by Biox (Ohmeda) and Nellcor companies by the application of microprocessor technologies which improved the performance of oximetry [10]. Recent dated oximetry use light emitting diodes (LED) which emit red and infrared light in the sensor for the ear and finger. Since then, a few more companies have entered the field of investigating pulse oximetry, thus, large achievements were accomplished to make the signal of the oximeter exceptionally resistant to the surrounding influence [11].

The principle of measuring haemoglobin oxygen saturation (SpO₂) by pulse oximetry is based on spectrophotometry principles according to the Beer-Lambert law from 1851, which linked a concentration solution substance with light transmitted intensity through solution. Pulse oximetry non-invasively measures arterial blood oxygen saturation and pulse frequency of pulse with the confidence interval of ± 2 -3 for SpO₂ values from 70-100%, and ± 3 for SpO₂ values from 50-70%, indicating the desaturation of oxihaemoglobin prior to the colour of the patient's skin becomes evident [12].

OBJECTIVE

The aim of the study was to examine and evaluate the following: 1. gender and age of the patient in the stages of functional (Fontaine stage IIa and IIb) and critical ischemia (Fontaine stage III and IV) of CAI of lower extremities; 2. diagnostic values of pulse oximetry in early detection and determination of the stage of CAI of the lower extremities; and 3. reliability of stage diagnostics of pulse oximetry in relation to colour Doppler duplex scan echosonography in patients with CAI of the lower extremities.

METHODS

The prospective clinical study involved a group of 50 patients, admitted at the Vascular Department of Surgical Clinic in Niš from September 2006 to October 2007, who manifested signs and symptoms of the different stages of CAI of lower extremities verified by ultrasonography.

Depending on the evolution stage of the disease the patients were classified into 2 subgroups: the subgroup of

301

I, IIa and IIb) and the subgroup of 25 patients in the stage of critical ischemia (Fontaine stage III and IV). CAI of the lower extremity was determined on the basis of clinical findings and colour Doppler duplex scan echosonography results. The colour Doppler duplex scan echosonography imaging of the lower extremity arteries was performed using the apparatus SIEMENS Sienna Sonoline (Diagnostic Ultrasound System, Siemens mead System, Inc., Issaquah, WA 988029-7002, USA) with a probe LINEAR ARREY 7.5 MHz L 40. Using the conventional method (single-gate) and

colour Doppler duplex scan (multi-gate), the presence and localization of stenosis, the segmental predominance (with multisegmental forms) and the degree of progression of stenotic-occlusive lesions were verified. The control group consisted of 50 patients treated at the Surgical Clinic due to other surgical diseases without

the Surgical Clinic due to other surgical diseases, without clinically manifested signs and symptoms of CAI of lower extremities. There were 25 male and 25 female (ratio of 1:1). The average age of patients was 55.5±4.8 years.

The colour Doppler duplex scan ultrasonography was used to determine the localization of stenotic-occlusive lesion in the study group of patients in the stage of functional ischemia and showed that the most frequent involvement was the femoropopliteal segment disclosed in 12 patients (48%), multisegmental localization was revealed in 7 patients (28%), the aorto-iliac segment in 5 patients (20%) and the tibio-peroneal segment was seen in one patient (4%). In the studied group of patients in the stage of critical ischemia colour Doppler duplex scan echosonography imaging showed that the most frequent involvement was the femoropopliteal segment shown in 13 (52%), the aorto-iliac segment in 6 (24%), multisegment localization in 7 (28%) and the tibio-peroneal segment in 2 patients (8%).

The determination of SpO₂ was performed in all patients using pulse oximetry as a part of monitoring (DATEX the ACE/3[™] Nellcor[®] Compatible Saturation Module M-NSAT, Anaesthesia Monitor), applied after the patients were acclimatized to temperature from 22-23°C. The sensor Datex SpO₂ FingerSat Nellcor[®] OXISENSOR, Sensor SAS-F4, (DATEX, Division of Instrumentarium Corp. Finland, 1995.) was used on the patient's toe at rest in supine position (Figure 1).

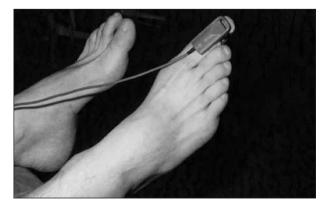


Figure 1. Application of digital sensors (Datex SpO₂ FingerSat Nellcor[®] OXISENSOR, Sensor SAS-F4) of the patient's toe nail of the lower extremity

Pulse oximetry measurements of SpO₂ rating 95% ± 2 and higher were taken to be the normal value for toe nail capillaries in patients with the lower extremity disease; while the lower values of SpO₂ indirectly marked the degree of compromised major arterial blood flow in patients with stenotic-occlusive specific lesion stage of CAI of the lower extremities.

The statistical analysis of data was carried out by analitical and descriptive methods, while the data were classified and graphically presented (Microsoft Word 2003). Using the comparative method the analyzed investigation results of the study and control groups underwent analysis. Significance of the data was tested using the Student t-test.

RESULTS

The study group with functional ischemia (Fontaine stage I, IIa and IIb stage) consisted of 25 patients: 15 men (60%) with an average age of 61.4 ± 7.3 years and 10 women (40%) with an average age of 58.6 ± 5.2 years (p<0.1); with the man to female ratio of 1.5:1 (Graph 1).

The study group with critical ischemia (Fontaine stage III and IV) consisted of 25 patients: 17 men (68%), average age of 64.8 ± 5.2 years, and 8 women (32%), average age 59.5 ± 4.8 years (p<0.05); with man to female ratio of 2.12:1 (p<0.05) (Graph 2).

In the study group Fontaine stage I with critical ischemia, SpO_2 of the toe nail capillaries of the involved lower extremity rated $95.33\pm1.41\%$, while in those with Fontaine stage IIa it was $92.14\pm2.27\%$ and Fontaine stage IIb it was $79.67\pm2.73\%$; in the study group Fontaine stage III with critical ischemia

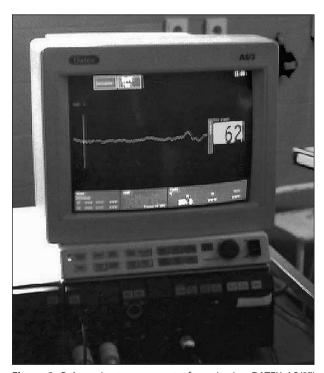
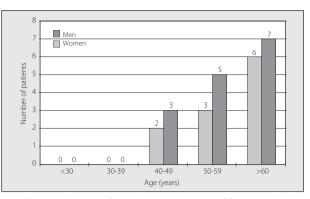
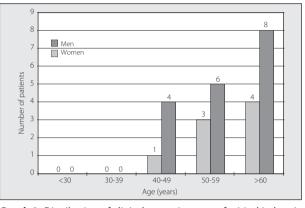


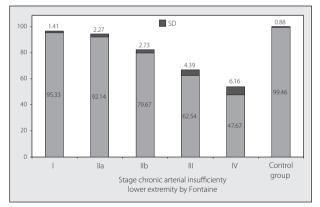
Figure 2. Pulse oximetry as a part of monitoring DATEX AS/ 3^{TM} Nellcor* Compatible Saturation Module M-NSAT, Anaesthesia Monitor (DATEX, Division of Instrumentarium Corp. Finland, 1995.) showing the patient's SpO₂ saturation of 62% in Fontaine stage III of critical ischemia



Graph 1. Distribution of clinical group in stage of functional ischemia by age



Graph 2. Distribution of clinical group in stage of critical ischemia by age



Graph 3. Review of SpO_2 percentage of foe capillaries according to Fontaine stage of functional and critical ischemia in patients and control group

 SpO_2 was 62.54±4.39% (Figure 2), stage Fontaine IV it was 47.67±6.16%, while in 3 patients with gangrenous foot and fingers SpO_2 was not possible to be measured (Graph 3). In the control group patients SpO_2 was 99.44±0.88%.

Measuring of SpO₂ of toe nail capillaries using pulse oximetry is significantly different depending on the stage of CAI of the lower extremities. In all groups we determined statistically a significant progressive decrease of SpO₂ values in correlation with the severity of the disease (p<0.01, between stages). At the same time, the patients with the lightest form of the disease (stage I of functional ischemia) had considerably lower SpO₂ value in relation to the control group (p<0.01).

DISCUSSION

CAI of lower extremities is clinically manifested by certain clinical features of functional and critical ischemia, which dependents on the localization of stenotic-occlusive lesions of the arteries, their size, extent of involvement and the development of collateral arterial network.

In 1945 the French surgeon René Fontaine made a classification of stages of CAI of lower extremities according to the severity of lower extremity CAI [13]. The original classification according to the progression or regression of the disease was based on illness history data and it is still in use up-to-date. First stage is marked by uncharacteristic initial problems involving the lower limbs (coldness, numbness, fatigue), second stage is characterized by intermittent claudication symptoms (intensive spasm in sporadic muscle groups of legs) with the passed claudication distance of over 100 meters in stage IIa and shorter than 100 meters in stage IIb. Third stage is presented by pains during night and at rest. Fourth stage presents with ulcerations and gangrene of feet and lower extremities below knees.

In 1995 the European Committee for Consensus Document on Critical Limb Ischemia proposed and modified Fontaine's Classification by including into each illness stage, beside clinical evaluation, the evaluation of pathophysiological onset mechanism and the findings of blood flow obtained by ultrasonographic and plethysmographic methods, the findings of metabolic oxygen concentration in tissues by oximetry with the determination of perfusion pressure by Doppler [12].

Modern epidemiological studies have shown that general population has 5% of men and 2.5% of women over the average ages of 60 years with the initial development of the symptoms of lower extremity CAI. The prevalence of intermittent claudication and functional ischemia symptoms in men younger than 60 years is about 1-2%, while it is higher in men older than 60 years (5%) [13]. Our group confirms the higher frequency of clinical manifestations of CAI of lower extremities in the 7th decade of life and in older age population with a gradual decrease in the frequency in younger age groups, as well as a mild predomination of men in both study subgroups (in stages of functional ischemia, with man to female ratio of 1.5:1, and in stages of critical ischemia, with man to female ratio of 2.12:1. In patients older than 70 years the frequency of CAI of the lower extremities is almost identical in men and women [14]. In the study group there were no patients younger than 40 years, which also confirms the study of Criqui et al. on the incidence of clinical manifestion of CAI of lower extremities [15].

The use of pulse oximetry as a noninvasive method for measuring SpO_2 saturations in the evaluation of peripheral arterial occlusive diseases has begun in the last 15 years. Data obtained by this study has confirmed the reduction of SpO_2 values in tissues which vascularize the arteries inflicted by stenotic-atherosclerosis [16-20]. In a study by Joyce, pulse oximetry investigation of SpO_2 of the foot dorsum and posterior tibial area in patients with peripheral arterial-occlusive disease, intermittent claudication and critical ischemia, indicates that there is a significant correlation between the

decreased SpO_2 and the stage and the level of lower extremity arterial occlusion [21].

Findings of SpO₂ obtained by pulse oximetry are also in considerable correlation with colour Doppler ultrasonography and with Doppler duplex scan imaging results of peripheral vascular disease, indicating the severity of the stage of stenotic process. In a study by Couse et al. similar results were obtained when diagnosis was made in patients with non-critical peripheral vascular insufficiency by experimental provocation of a specific stage of occlusion applying tourniquet pressure at a specific level of the lower extremity; indirect data on the transient major artery of the lower extremity obtained by ultrasonography colour Doppler duplex scan were compared with the findings of pulse oximetry [22]. Our study also confirmed positive correlation of pulse oximetry findings with the results of colour Doppler duplex scan ultrasonography in patients with a stage of functional and critical ischemia.

By the analysis of pulse oximetry investigation performed in our study with patients in a stage of functional and critical ischemia of CAI of lower extremities by determining SpO₂ in toe nail capillaries the following results were reached: in Fontaine stage I of functional ischemia SpO₂ was 95.33 \pm 1.41%, in Fontaine stage IIa was 92.14 \pm 2.27% and in Fontaine stage IIb stage it was 79.67 \pm 2.73%, in Fontaine stage III of critical ischemia oxygen saturation of haemoglobin was 62.54 \pm 4.39%, in Fontaine IV stage it was 47.67 \pm 6.16%, in patients with gangrene of the foot and finger it was not possible to measure SpO₂. In control group patients SpO₂ was 99.44 \pm 0.88%. Previously mentioned lowered pulse oximetry values had a significant positive correlation with the stage of CAI of lower extremities, which confirms the positive diagnostic value in the evaluation of patients.

The method of pulse oximetry is not only simple and rapid to use, but it is also a noninvasive method, which does not require calibration and is highly precise. Recent technical solutions of the device enable easy transport and application under all conditions. Later technical development of pulse oximetry involves the solution of the problem with respect to modifications of the skin sensor of pulse oximetry which will extend the spectre of its application and the precision of measurements by reducing sensitivity of the signal to movements and improvement of the sensitivity in patients with darker pigmentation and dishaemoglobinemia [23].

In future, pulse oximetry will have diagnostic value in the determination of stages of functional and critical ischemia of CAI of lower extremities, because of the high level of precision and simplicity in the use of the instrument. SpO₂ values of lower extremity distal tissues can be applied for estimating the outcomes of planned surgical reconstructive procedures and determining the safe level of the amputation of extremities in patients with critical ischemia and developed tissue necrosis and gangrene [24].

CONCLUSION

Using non-invasive SpO₂ measurement by applying pulse oximetry has shown the reduction of oxygen values in tissues

that vascularize arteries with stenotic-occlusive process. It confirms its diagnostic value in the determination of the stage of CAI of lower extremities. By SpO₂ values, pulse oximetry

REFERENCES

- Stoffers HE, Rinkens PE, Kaster AD, Kaiser V, Knottnerus JA. The prevalence of asymptomatic and unrecognized peripheral arterial occlusive disease. Int J Epidemiol. 1996; 25(2):282-90.
- Creager MA, Dzau VJ. Vascular diseases of the extremities. In: Isselbacher KL, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harisson's Principles of Internal Medicine. New York, St. Luis, San Francisco: Mc Graw Hill; 1999. p.1140-1142.
- Weitz JI, Byrne J, Clagett GP, Farkouh ME, Porter JM, Sackett DL, et al. Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review. Circulation. 1996; 94(11):3026-49.
- Green RM, Ouriel K. Peripheral arterial disease. In: Schwartz SI, Shires GT, Spencer FC. Principles of Surgery. New York, St. Luis, San Francisco: McGraw-Hill; 1994. p.925-77.
- Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA. 2001; 286:1317-24.
- Bowes WA 3rd, Corke BC, Hulka J. Pulse oximetry: A review of the theory, accuracy, and clinical applications. Obstet Gynecol. 1989; 74(3 Pt 2):541-6.
- Severinghaus JW. Some personal reflections on International Symposium on Innovations and Applications of Pulse Oximetry. Anesth Analg. 2002; 94:15.
- 8. Jubran A. Pulse oximetry. In: Tobin MJ, et al, editors. Principles and Practice of Intensive Care Monitoring. New York, St. Luis, San Francisco: McGraw; 1998. p.261-88.
- Aoyagi T, Miyasaka K. Pulse oximetry: its invention, contribution to medicine, and future tasks. Anesth Analg. 2002; 94(1 Suppl):S1-3.
- 10. Severinghaus JW. History, status and future of pulse oximetry. Adv Exp Med Biol. 1987; 220:3-8.
- Ahrens T. Pulse oximetry. Crit Care Nurs Clin North Am. 1999; 11:87-97.
- Fontaine R, Kim M, Kieny R. Die chirurgische Behandlung der peripheren Durch-blutungsstörungen. Helv Chirur Acta. 1954; 5/6:499-533.

- reflects the stage and severity of CAI and has shown diagnostic precision in comparison with colour Doppler duplex scan ultrasonography in patients with CAI of lower extremities.
- 13. Golledge J. Lower-limb arterial disease. Lancet. 1997; 350:1459-65.
- Dormandy J, Mahir M, Ascady G, Balsano F, De Leeuw P, Blombery P, et al. Fate of the patient with chronic leg ischaemia: a review article. J Cardiovasc Surg (Torino). 1989; 30:50-7.
- Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, Gabriel S, Goodman D. The prevalence of peripheral arterial disease in a defined population. Circulation. 1985; 71:510-5.
- Parameswaran GI, Brand K, Dolan J. Pulse oximetry as a potential screening tool for lower extremity arterial disease in asymptomatic patients with diabetes mellitus. Arch Intern Med. 2005; 165(4):442-6.
- Portig I, Maisch B. Noninvasive methods in the diagnosis of macro- and microangiopathy of peripherial and carotid arteries. Herz. 2004; 29(1):17-25.
- Shelley KH, Murray WB, Chang D. Arterial-pulse oximetry loops: a new method of monitoring vascular tone. J Clin Monit. 1997; 13(4):223-8.
- Johansson KE, Marklund BR, Fowelin JH. Evaluation of a new screening method for detecting peripheral arterial disease in a primary health care population of patients with diabetes mellitus. Diabet Med. 2002; 19(4):307-10.
- Mannheimer PD, O'Neil MP, Konecny E. The influence of larger subcutaneous blood vessels on pulse oximetry. J Clin Monit Comput. 2004; 18(3):179-88.
- Joyce WP, Walsh K, Gough DB, Gorey TF, Fitzpatrick JM. Pulse oximetry: a new non-invasive assessment of peripheral arterial occlusive disease. Br J Surg. 1990; 77(10):1115-7.
- Jawahar D, Rachamalla HR, Rafalowski A, Ilkhani R, Bharathan T, Anandarao N. Pulse oximetry in the evaluation of peripheral vascular disease. Angiology. 1997; 48(8):721-4.
- Couse NF, Delaney CP, Horgan PG, O'Keeffe J, Joyce WP, Gorey TF, et al. Pulse oximetry in the diagnosis of non-critical peripheral vascular insufficiency. J R Soc Med. 1994; 87(9):511-2.
- 24. Weininger S. Designing a pulse oximeter safety standard. Anesth Analg. 2002; 94:S4-7.

Дијагностичка вредност пулсне оксиметрије у одређивању стадијума хроничне артеријске инсуфицијенције доњих екстремитета

Небојша Игњатовић¹, Марина Васиљевић², Драган Милић¹, Јелена Стефановић³, Мирослав Стојановић¹, Александар Караниколић¹, Александар Златић¹, Горан Ђорђевић¹, Саша Живић¹, Љиљана Јеремић¹, Ивона Ђорђевић⁴, Радмило Јанковић¹

¹Хируршка клиника, Клинички центар, Ниш, Србија;

²Одељење анестезије и реанимације, Клиника за очне болести, Клинички центар, Ниш, Србија;

³Медицински факултет, Универзитет у Нишу, Ниш, Србија; ⁴Клиника за дечју хирургију, Клинички центар, Ниш, Србија

КРАТАК САДРЖАЈ

Увод Хронична артеријска инсуфицијенција (ХАИ) доњих екстремитета је значајан медицински и социоекономски проблем због развоја високог морбидитета, инвалидитета и морталитета оболеле особе.

Циљ рада Циљ рада је био да се утврде дијагностичка вредност и значај пулсне оксиметрије у раном одређивању стадијума ХАИ доњих екстремитета на основу ткивне засићености (сатурације) артеријског хемоглобина кисеоником (*SpO*₂).

Методе рада Проспективно је испитано 50 болесника лечених на васкуларном одељењу Хируршке клинике у Нишу од септембра 2006. до октобра 2007. године с израженим симптомима и знацима различитих стадијума ехосонографски потврђене ХАИ доњих екстремитета. Пулсним оксиметром је одређиван *SpO*2 ткивних артеријских капилара оболелих доњих екстремитета испитаника.

Резултати Пулсном оксиметријом су, у зависности од стадијума ХАИ доњих екстремитета, утврђени значајна разлика (у стадијумима функционалне исхемије *SpO*₂: Фонтан *I* – 95,33±1,41%, Фонтан *IIa* – 92,14±2,27% и Фонтан *IIb* – 79,67±2,73%; у стадијумима критичне исхемије *SpO*₂: Фонтан *III* – 62,54±4,39% и Фонтан *IV* – 47,67±6,16%; код три болесника са гангреном стопала и прстију *SpO*₂ се није могао измерити) и прогресивно смањење вредности *SpO*₂ артеријских капилара (*p*<0,01, између стадијума). Закључак Због поузданости и једноставности примене, пулсна оксиметрија се може сматрати рутинском дијагностичком методом у раном одређивању стадијума ХАИ доњих екстремитета. Кључне речи: пулсна оксиметрија; засићеност хемоглобина кисеоником; хронична артеријска инсуфицијенција доњих екстремитета