

# Relationship Between Sociodemographic, Anthropometric and Biochemical Characteristics and Degree of Peripheral Arterial Disease

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## SUMMARY

**Introduction** Peripheral arterial disease (PAD) is a severe atherosclerotic condition. The relationship between various risk factors and severity of PAD, measured by Ankle Brachial Index (ABI), has been the subject of a relatively small number of studies.

**Objective** The aim of the present study was to investigate whether there was any relationship between severity of PAD, expressed as ABI, and anthropometric, clinical and biochemical characteristics of patients, including inflammatory markers.

**Methods** The cross-sectional study, involving 388 consecutive patients with verified PAD, was performed at the Dedinje Vascular Surgery Clinic in Belgrade. The diagnosis of PAD was defined by Doppler sonography as ABI<0.9, and by symptoms. Data on cardiovascular risk factors, anthropometric parameters, clinical and biochemical characteristics were collected for all participants. In the analysis,  $\chi^2$  test, t-test and multivariate logistic regressions were used.

**Results** According to the results of multivariate analysis (the model of which included age, percentage of body fat, average value of uric acid, high sensitivity C-reactive protein – hsCRP  $\geq 3$  mg/L, fibrinogen  $\geq 4$  g/L, Baecke index of physical activity at work and Baecke index of leisure-time physical activity), the patients with more severe form of peripheral arterial disease (ABI $\leq 0.40$ ) had more frequently increased high sensitivity C-reactive protein ( $p=0.002$ ), lower Baecke index of physical activity at work ( $p=0.050$ ) and lower Baecke index of leisure-time physical activity ( $p=0.024$ ). Average value of body fat was significantly higher in the patients with a less severe form of disease ( $p=0.006$ ).

**Conclusion** According to the results obtained, the increased values of hsCRP and physical inactivity are associated with a more severe form of PAD (ABI $\leq 0.40$ ).

**Keywords:** peripheral arterial disease; cross-sectional study; risk factors; high sensitivity C-reactive protein

## INTRODUCTION

Atherosclerotic diseases are the main cause of death in both developed and developing countries [1]. Atherosclerotic process begins in the early period in life, the inflammation being considered as very important for its development [2].

Peripheral vascular, or peripheral arterial disease (PAD) has been defined as the presence of classic lower extremity pain with exertion (intermittent claudication) or as absent or markedly diminished pulses in physical examination. An abnormal ankle-brachial index (ABI) is used as a broader, but more specific definition of PAD [3].

According to Criqui et al. [4], and Aronow [5], the prevalence of PAD varies from 2% to more than 30% depending on age, sex, and ethnicity. According to another group of authors, the prevalence of PAD ranges from 0.6 to 8.8% [6]. The main risk factors associated with the development of PAD, such as age, sex, cigarette

smoking, hypertension, diabetes, and dyslipidaemia, are similar to those of other types of atherosclerotic disease.

## OBJECTIVE

Since the relationship between various risk factors and severity of PAD has been the subject of a relatively small number of investigations, the aim of the present study was to investigate whether there was any relationship between severity of PAD, expressed as Ankle Brachial Index (ABI), and anthropometric, clinical and biochemical characteristics of patients, including inflammatory markers.

## METHODS

For the present investigation, a cross-sectional study was used. The study involved 388 consecutive patients with verified PAD referred to the

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Dedinje Vascular Surgery Clinic in Belgrade, from April 2006 to November 2007. The diagnosis of PAD was defined by Doppler sonography as ABI<0.9, and by symptoms (claudication, rest pain, and gangrene). Doppler sonography was performed on both lower limbs, and the lowest value was recorded as the ABI. According to ABI, the patients were divided in two groups (ABI≤0.40 and ABI>0.40).

The patients under 18 years of age and the patients with malignant disease or rheumatoid arthritis were excluded from the study.

Anthropometric parameters and data on cardiovascular risk factors were collected for all participants.

For the assessment of body composition and abdominal obesity, body mass index (BMI) and waist circumference were used respectively in the way proposed by the World Health Organization [7]. Body fat was calculated according to the method proposed by Durnin and Womersley [8].

Blood pressure measurements were taken using the auscultatory method recommended by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [9].

For estimating fasting blood glucose (FBG) and lipoproteins, blood samples were obtained after an overnight fast and abstention from liquids. The levels of FBG, total cholesterol (TC), serum triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were estimated using the commercial kits (Abbot, III) on an automated analyser (AEROSET, Abbot). The levels of high-sensitivity C-reactive protein (hsCRP) and fibrinogen were measured using the Immunoturbidimetric fixed time test (Olympus Diagnostics, O'Callagan's Mills Co Clare, Ireland), and the high value of hsCRP was assessed according to the Centers for Disease Control (CDC) recommendation (≥3 mg/L) [10]. Referent values for fibrinogen were 2-4 g/L [11].

Data on smoking and alcohol consumption were collected using a questionnaire prepared for this study. Each participant was classified as a non-smoker, former smoker or current smoker and as a non-drinker, former drinker and current drinker respectively [12]. Alcohol consumption was analysed in 2 ways, (1) by using the alcohol consumption yes/no variable and (2) by calculating the total dose of alcohol consumption for each participant by adding all individual beverages weighted to their alcohol content [12].

Data on physical activity were collected by the use of the questionnaire prepared for this study and by the use of Baecke questionnaire [13].

### Statistical analysis

Continuous variables were described as means and standard deviation, and categorical variables were presented by counts and percentages. In the analysis of data, chi-square test, 2-tailed t-test, and multivariate logistic regression analysis were used. In multivariate logistic regression analysis, there were included variables which were related to PAD (according to chi-square test and t-test) at significance level of p≤0.10.

A level of α=0.05 was used to indicate statistical significance. Data were analysed using Statistical Package for the Social Sciences, version 12 (SPSS Inc., Chicago, IL, USA).

### Ethical approval

The study was approved by the Ethics Committee of the Medical Faculty in Belgrade. All patients gave a written informed consent.

### RESULTS

Out of 388 patients with PAD, 214 (55.2%) had ABI≤0.40, and 174 (44.8%) had ABI>0.40.

The patients with PAD did not significantly differ in their socio-demographic characteristics according to ABI. However, the patients with ABI≤0.40 were older than those with ABI>0.40, and the difference was at borderline significance (p=0.054) (Table 1).

There were no significant differences between the compared groups in the average values of anthropometric, clinical and biochemical parameters with the exception of the value of uric acid which was significantly greater in the patients with more severe form of disease – ABI≤0.40 (p=0.048) (Table 2).

In comparison with the patients whose ABI was >0.40, the patients with a more severe disease (ABI>0.40) had significantly higher average values of hsCRP (p=0.002) and fibrinogen (p=0.012), as well as higher percentage of those with increased values of both hsCRP (p=0.006) and fibrinogen (p=0.018). The patients with ABI>0.40 had higher percent of body fat in comparison with the patients whose ABI was ≤0.40, but this difference was at significance level of p≤0.10 (Table 3).

**Table 1.** Socio-demographic characteristics of patients according to severity of peripheral arterial disease (number of patients)

Variable	Group with ABI≤0.40 (n=214)	Group with ABI>0.40 (n=174)	p*	
Age (years)	62.5±9.1**	60.8±7.9**	0.054	
Sex	Female	42 (19.6%)	42 (24.1%)	0.283
	Male	172 (80.4%)	132 (75.9%)	
Marital status	Married	154 (72.0%)	133 (76.4%)	0.719
	Divorced	20 (9.3%)	13 (7.5%)	
	Widowed	31 (14.5%)	20 (11.5%)	
	Single	9 (4.2%)	8 (4.6%)	
Education	Elementary school	57 (26.6%)	40 (23.0%)	0.120
	Secondary school	109 (50.9%)	89 (51.1%)	
	High school	22 (10.3%)	14 (8.0%)	
	University	26 (12.1%)	31 (17.8%)	
Occupation	Industrial worker	106 (49.5%)	79 (45.4%)	0.251
	Agricultural worker	4 (1.9%)	6 (3.4%)	
	Clerk	91 (42.5%)	84 (48.3%)	
	Housewife	13 (6.1%)	5 (2.9%)	

\* According to chi-square test or t-test

\*\* expressed in mean value (X) with standard deviation (SD)

**Table 2.** Anthropometric, clinical and biochemical characteristics of patients according to severity of peripheral arterial disease ( $\bar{X}\pm SD$ )

Variable	Group with ABI $\leq$ 0.40 (n=214)	Group with ABI>0.40 (n=174)	p*	
Body Mass Index (kg/m <sup>2</sup> )	25.8 $\pm$ 4.0	26.4 $\pm$ 3.6	0.109	
Body fat (%)	28.9 $\pm$ 6.6	30.1 $\pm$ 6.3	0.068	
Waist circumference (cm)	Women	92.7 $\pm$ 14.2	90.6 $\pm$ 9.7	0.431
	Men	97.6 $\pm$ 10.8	99.0 $\pm$ 9.6	0.220
Blood pressure (mm Hg)	Systolic	141.8 $\pm$ 22.4	140.9 $\pm$ 21.2	0.680
	Diastolic	81.9 $\pm$ 10.4	81.9 $\pm$ 10.7	0.937
Triglycerides (mmol/L)	2.2 $\pm$ 1.5	2.1 $\pm$ 1.4	0.657	
Cholesterol (mmol/L)	Total	5.2 $\pm$ 1.3	5.4 $\pm$ 1.3	0.207
	HDL	0.9 $\pm$ 0.2	1.0 $\pm$ 0.2	0.216
	LDL	3.3 $\pm$ 1.0	3.5 $\pm$ 1.2	0.209
Glucose (mmol/L)	5.7 $\pm$ 1.9	5.8 $\pm$ 2.4	0.593	
Uric acid ( $\mu$ mol/L)	364.6 $\pm$ 108.7	343.4 $\pm$ 99.6	0.048	

\* According to t-test

**Table 3.** Inflammatory markers in patients according to severity of peripheral arterial disease ( $\bar{X}\pm SD$  and number of patients)

Variable	Group with ABI $\leq$ 0.40 (n=214)	Group with ABI>0.40 (n=174)	p*	
hsCRP (mg/L)	$\bar{X}\pm SD$	8.9 $\pm$ 14.7	5.0 $\pm$ 8.6	0.002
	<3	93 (43.5%)	100 (57.5%)	0.006
	$\geq$ 3	121 (56.5%)	74 (42.5%)	
Fibrinogen (g/L)	$\bar{X}\pm SD$	3.8 $\pm$ 1.4	3.4 $\pm$ 1.2	0.012
	<4	134 (63.2%)	126 (74.6%)	0.018
	$\geq$ 4	78 (36.8%)	43 (25.4%)	

\* According to chi-square test or t-test  
hsCRP – high sensitivity C-reactive protein**Table 4.** Distribution of smoking, alcohol consumption and physical activity according to severity of peripheral arterial disease (number of patients)

Variable	Group with ABI $\leq$ 0.40 (n=214)	Group with ABI>0.40 (n=174)	p*	
Smoking status	Non-smoker	22 (10.3%)	16 (9.2%)	0.565
	Current smoker	129 (60.3%)	98 (56.3%)	
	Former smoker	63 (29.4%)	60 (34.5%)	
Alcohol consumption	No	105 (49.1%)	90 (51.7%)	0.680
	Yes – current	51 (23.8%)	35 (20.1%)	
	Yes – former	58 (27.1%)	49 (28.2%)	
Daily alcohol consumption (dL)	$\bar{X}\pm SD$	3.5 $\pm$ 5.9	3.0 $\pm$ 5.9	0.299
	Median	0	0	
	Min	0	0	
	Max	52.5	48.0	
Physical activity** (times per month)	0-4	198 (92.5%)	152 (87.4%)	0.158
	5-8	14 (6.5%)	21 (12.1%)	
	$\geq$ 9	2 (0.9%)	1 (0.6%)	
Baecke index of physical activity ( $\bar{X}\pm SD$ )	Work	2.9 $\pm$ 0.6	2.9 $\pm$ 0.7	0.073
	Sports	1.9 $\pm$ 0.4	2.0 $\pm$ 0.4	0.197
	Leisure time	2.2 $\pm$ 0.5	2.3 $\pm$ 0.7	0.005

\* According to chi-square test or t-test

\*\* at least 30 minutes a day

**Table 5.** Factors independently related to severity of peripheral arterial disease – results of multivariate logistic regression analysis

Variable	Odds ratio	95% CI	p
Percent of body fat – average values	0.9	0.9-1.0	0.006
hsCRP $\geq$ 3mg/L	1.9	1.3-3.0	0.002
Baecke index of physical activity at work	0.7	0.5-1.0	0.050
Baecke index of leisure time physical activity	0.7	0.5-0.9	0.024

The groups compared did not significantly differ in smoking, alcohol consumption and the frequency of physical activity defined as any type of non-occupational physical exercise lasting more than 30 minutes per day during the previous month. However, when physical activity was assessed by the use of Baecke questionnaire, significant differences were present in leisure-time physical activity. The patients with ABI>0.40 were more physically active in their leisure-time ( $p=0.005$ ). The patients with ABI>0.40 were also more physically active at work in comparison with the patients whose ABI was ABI $\leq$ 0.40, but this difference was at significance level of  $p\leq 0.10$  (Table 4).

In order to find out which of potential risk factors are independently related to ABI, multiple logistic regression analysis was used. In the model of multivariate analysis were included following variables (variables which were according to chi square test or t-test related to ABI at significance level of  $p\leq 0.10$ ): age, percentage of body fat, average value of uric acid, hsCRP $\geq 3$  mg/L, fibrinogen  $\geq 4$  g/L, Baecke index of physical activity at work and Baecke index of leisure-time physical activity. According to the result of multivariate analysis, in comparison with the patients whose ABI was >0.40, the patients with more severe PAD (ABI>0.40) had lower percentage of body fat and lower Baecke index of physical activity at work and Baecke index of leisure-time physical activity, but among them significantly more subjects had increased values of hsCRP ( $\geq 3$  mg/l) (Table 5).

## DISCUSSION

According to the results of this study, in the patients with PAD, higher values of hsCRP and physical inactivity were significantly independently related to a more severe form of disease (ABI  $\leq 0.40$ ), but percentage of body fat was higher in the patients with ABI >0.40.

It is considered that inflammatory process plays the central part in pathogenesis of atherosclerosis and its complications. In many investigations, the association was found between cardiovascular disease and various inflammatory markers among which C-reactive protein has been most frequently studied [14].

C-reactive protein is a very sensible marker of inflammatory process and many investigators associate CRP with atherosclerotic process [15]. At the beginning, it was believed that CRP was only an inflammatory marker, but data have been accumulated suggesting that CRP is directly involved in atherogenesis and that arterial plaques can produce CRP [14, 16].

There are many data showing the association between CRP and PAD [17, 18]. CRP, which is inversely related to ABI [19], is an independent risk factor for the occurrence and severity of PAD [20, 21] and a predictor of other atherosclerotic diseases in subjects with severe form of PAD [22]. The level of CRP was also related to subclinical atherosclerosis including PAD [23, 24]. The investigation conducted on a representative sample of the USA people free of cardiovascular diseases diabetes and hypertension, showed that increased value of CRP was related to PAD independently

of other risk factors [25]. The ratio of total cholesterol and HDL cholesterol and the level of CRP were the strongest independent predictors of PAD development in the study of Ridker et al. [26] and the addition of either CRP or fibrinogen to standard lipid screening significantly improved the predictive value of the computed risk prediction models [26]. C-reactive protein provided additive prognostic information over standard lipid measures [26].

The association between physical inactivity and cardiovascular diseases was the subject of many studies [26-31]. According to the results of the study involving 9, 824 men free of atherosclerotic disease at baseline examination, Crespo et al. [27] concluded that any physical activity, even lower than the recommended one, was better than a sedentary type of life. In comparison with physically inactive subjects, those physically active had significantly more frequently adequate BMI and significantly lower mortality not only from atherosclerotic diseases but also from other diseases [27]. In a study which comprised 9,193 patients with hypertension and with hypertrophy of left ventricle and followed for 4.8 years, Fossum et al. [28] found that regular physical activity (30 minutes two or three times per week) significantly decreased the risk of any atherosclerotic disease and of type 2 diabetes. Lee et al. [29], who also found that physical activity decreased the risk of atherosclerotic diseases, suggested that instead of following general recommendations for physical activity, every person should have his/her own programme of physical activity that would depend on the age and presence of other cardiovascular risk factors or diseases.

In the above-mentioned studies, the effect of leisure-time physical activity was investigated. The effect of physical activity at work was studied only in few investigations [30]. The majority of these investigations showed that physical activity at work was an important component of healthy life [30] and that physical activity at work decreased mortality from cardiovascular diseases [31]. There are no literature data about the effect of physical inactivity, measured by Baecke questionnaire, on severity of PAD. On the basis of this cross-sectional study, we cannot tell whether the patients with  $ABI \leq 0.40$  were less physically active (at least when sports and leisure-time physical activities are concerned) because of severity of disease, or physical inactivity influenced the progression of disease.

According to the results of many studies, obesity has an adverse effect on health, especially on cardiovascular morbidity and mortality [32, 33]. Obesity is considered as the risk factor for atherosclerotic diseases. However, the data

on the relationship between obesity and PAD are not consistent. In Planes et al. study [34], PAD was related to abdominal fat distribution expressed as waist-hip ratio, but it was not related to BMI. In old people ( $\geq 60$  years), BMI might not be a proper indicator of obesity [35, 36]. In spite of increasing adiposity, BMI can remain the same or can even decrease because of substantial loss of lean body mass. There are no literature data about the association between percentage of body fat and PAD. Also, we have no explanation for significantly greater percentage of body fat in the patients with  $ABI > 0.40$ , not in those with a more severe form of disease.

The present study has some limitations. One of them is its cross-sectional design, which makes it difficult to judge causal relations. Another limitation is that the study participants had a clinical manifestation of PAD and there is a possibility that the analysed variables might be changed after the events. The study participants were taken from a single hospital and they did not represent all patients with PAD. As in other studies based on self reported data, in this investigation, there is a problem of reliability of data on smoking, alcohol consumption and physical activity. However, since in the present study all participants were patients, misclassification is most probably not differential but it is equally distributed in the compared groups.

## CONCLUSION

The patients with a severe form of PAD ( $ABI \leq 0.40$ ) had significantly more frequently increased values of hsCRP ( $\geq 3$  mg/L), which is in line with other authors' findings that CRP is an independent risk factor for development and severity of PAD. The study results are also in agreement with the already existing data about the influence of physical inactivity on the development of atherosclerosis. We have no explanation for significantly greater percentage of body fat in the patients with  $ABI > 0.40$  in comparison with those who had a more severe form of disease ( $ABI \leq 0.40$ ).

## NOTE

This paper is a part of the PhD thesis by Dr. Miloš Maksimović titled "Relationship between lifestyle and metabolic syndrome in patients with atherosclerotic disease", which was defended at the Faculty of Medicine in Belgrade, March 2009. The supervisor was Prof. Dr. Jagoda Jorga, and co-supervisor Prof. Dr. Djordje Radak.

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## Веза између социодемографских, антропометријских и биохемијских одлика и степена тежине периферне артеријске болести

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### КРАТАК САДРЖАЈ

**Увод** Периферна артеријска болест (енгл. *peripheral arterial disease – PAD*) је тешко атеросклеротско обољење. Повезаност различитих фактора ризика с тежином овог обољења, израженом као *Ankle Brachial Index (ABI)*, предмет је истраживања малог броја студија.

**Циљ рада** Циљ рада је био да се утврди да ли је степен тежине *PAD* изражен преко *ABI* повезан са социодемографским, антропометријским, клиничким и биохемијским одликама, као и показатељима запаљењског процеса.

**Методе рада** Истраживање је урађено као студија пресека, а изведено је на Институту за кардиоваскуларне болести „Дедиње“ у Београду. Обухватило је 388 болесника са *PAD* која је дијагностикована доплер сонографијом (*ABI* мањи од 0,9) и на основу клиничких симптома обољења. Од свих испитаника су специфичним упитником прикупљени подаци о факторима ризика за кардиоваскуларне болести и урађена антропометријска мерења, клиничка и биохемијска испитивања болесника. У

анализи података коришћени су  $\chi^2$ -тест, Студентов *t*-тест и мултиваријантна логистичка регресија.

**Резултати** Према резултатима мултиваријантне анализе, у чији модел су били укључени старост болесника, проценат телесне масти, просечне вредности мокраћне киселине, ултрасензитивни *C*-реактивни протеин (*hsCRP*  $\geq 3,0$  *g/l*), фибриноген ( $\geq 4$  *g/l*), Бекеов индекс физичке активности на послу и Бекеов индекс рекреативне физичке активности, код испитаника с тежим обликом обољења (*ABI*  $\leq 0,40$ ) биле су значајно чешће повећане вредности *hsCRP* ( $p=0,002$ ) и мање вредности Бекеовог индекса физичке активности на послу ( $p=0,050$ ) и рекреативне физичке активности ( $p=0,024$ ). Просечне вредности процента масног ткива су биле значајно веће код испитаника с лакшим обликом болести ( $p=0,006$ ).

**Закључак** Резултати студије показују да су повишене вредности *hsCRP* и физичка неактивност повезани с тежим обликом *PAD*.

**Кључне речи:** периферна артеријска болест; студија пресека; фактори ризика; ултрасензитивни *C*-реактивни протеин