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Coronary artery disease prediction in hypertensive patients using peripheral arteries ultrasound

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Abstract

Cardiovascular disease is one of the main causes of mortality worldwide, with multifactorial etiology and a high impact on the healthcare system due to the complexity of optimal management. The first two major risk factors are arterial hypertension and atherosclerosis and they both frequently coexist and have a bidirectional causality. A current focus is the prevention and early detection of cardiovascular disease using cost-efficient investigations; however, the prediction of coronary atherosclerosis using non-invasive methods is a goal yet to be achieved. Current vascular ultrasound parameters do not show sufficient sensitivity and specificity for predicting coronary lesions and the intima-media thickness index is now a class III indication in cardiovascular risk assessment. Two new parameters appear to have greater accuracy in predicting CAD: atherosclerosis burden score (ABS) and carotid plaque score (PS). We sought to evaluate the predictive capacity for significant coronary artery disease (>50% luminal stenosis) of the aforementioned parameters. We performed a post-hoc analysis on a cohort of 51 consecutive hypertensive patients admitted for typical chest pain. All patients underwent coronary angiography and were divided into two groups: Group 1 with significant CAD (>50% luminal stenosis on any of the left anterior descending, right coronary artery and/or circumflex artery) and Group 2 with coronary stenosis <50% (non-significant CAD). Atherosclerosis burden score (ABS) and carotid plaque score (PS) were calculated as previously defined based on carotid and femoral ultrasound examination. In our cohort, both ABS and PS independently predicted the existence of coronary lesions after adjusting for age, sex, smoking status, dyslipidemia, diabetes and body mass index (BMI) value. Additionally, ROC-curve analysis demonstrated incremental value for predicting significant coronary artery disease for ABS, which exhibited higher AUC values compared to PS.

Keywords: hypertension, coronary artery disease, vascular ultrasound, atherosclerosis burden score, carotid plaque score, cardiovascular disease.

Introduction

Cardiovascular disease is one of the main causes of mortality worldwide, with multifactorial etiology and a high impact on the healthcare system due to the complexity of optimal management. The first two major risk factors are arterial hypertension

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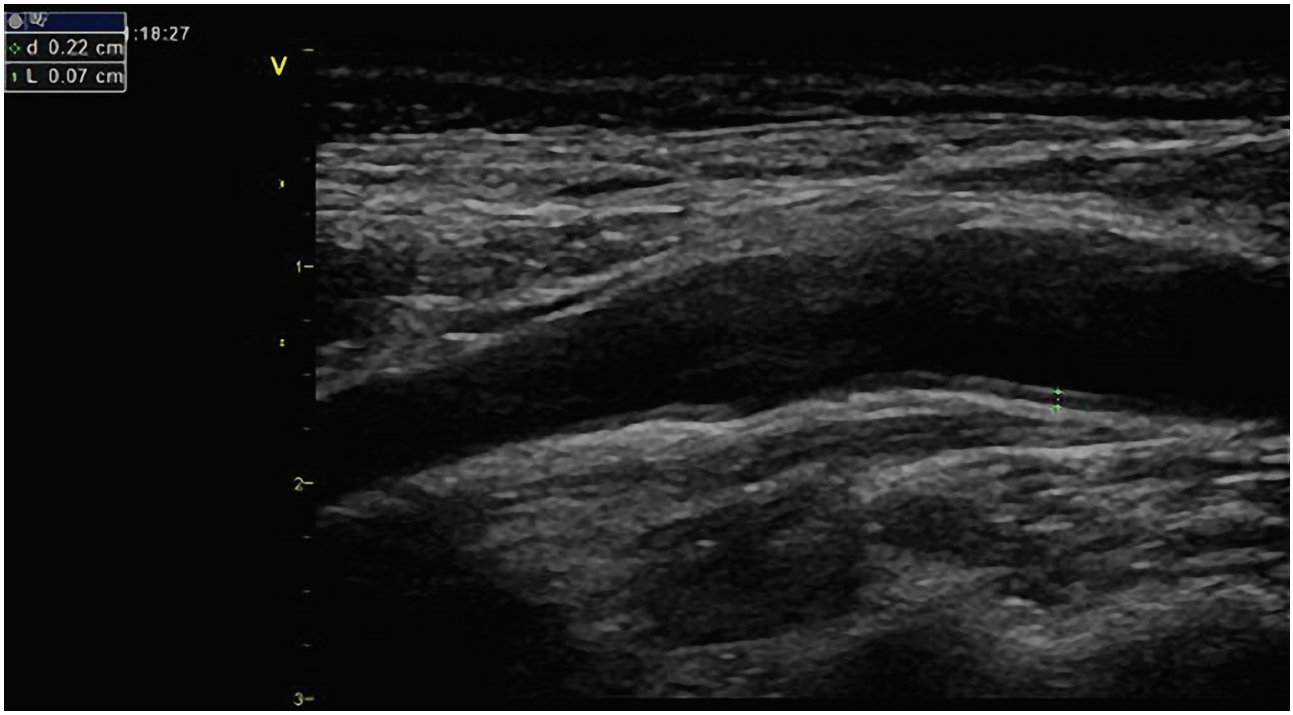

Figure 1. Common carotid artery bifurcation; intima=0.7 mm.

and atherosclerosis; both frequently coexist and are strongly interrelated. Along with diabetes mellitus, smoking and obesity, they are the main causal and modifiable factors of coronary artery disease (CAD). The early detection and control of any risk factor represent an ideal standard to be reached.

As the incidence of cardiovascular disease is continuously increasing worldwide, prevention and early detection with cost-efficient investigations are the current focus [1]. The prediction of coronary atherosclerosis by non-invasive methods is a goal that has yet to achieve. Easily accessible for examination,

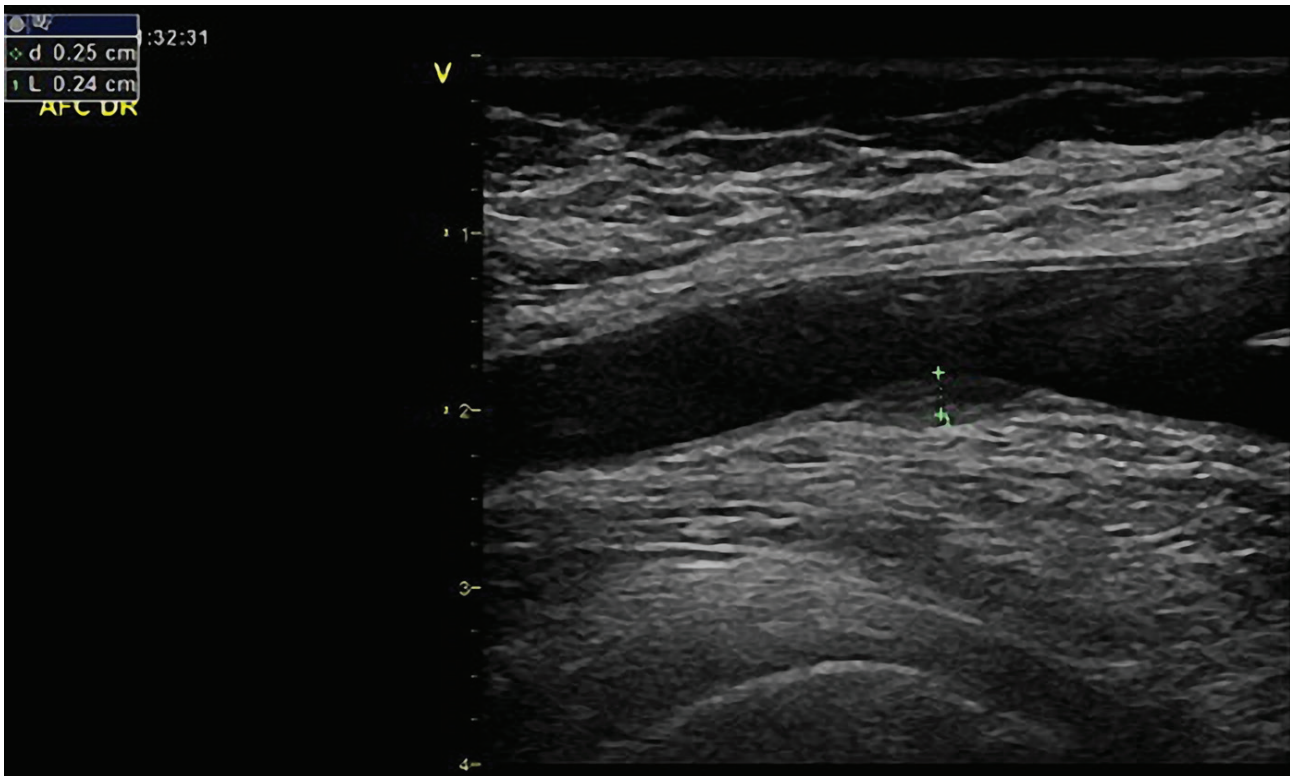

Figure 2. Ultrasound of the common femoral artery and the bifurcation – atherosclerotic plaque with 2.4 mm height.

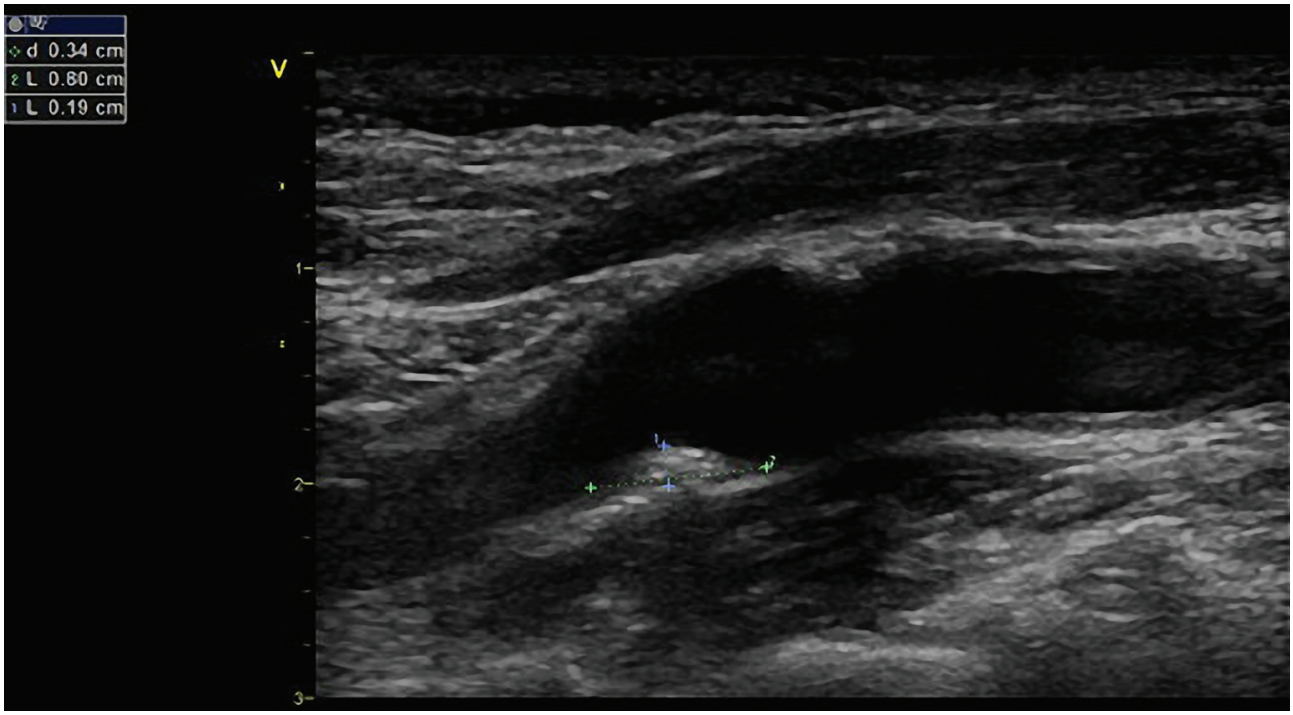

Figure 3. Longitudinal view: ultrasound of common carotid artery bifurcation and an atherosclerotic calcific plaque at the origin of internal carotid artery (width 8 mm, height 3.4 mm).

the peripheral arteries are and can be considered a surrogate marker for coronary atherosclerosis, considering atherosclerosis affects the entire arterial system. Current ultrasound parameters evaluating the carotid and lower limb arteries do not show sufficient sensitivity and specificity for predicting coronary lesions. The traditional parameters used in carotid ultrasound such as the intima-media thickness index (IMT), are not correlated with the presence of coronary lesions. However, there are two parameters that could be appropriate predictors of CAD: atherosclerosis burden score (ABS) and carotid plaque score (PS), that according to more recent studies, appear to have greater accuracy [2].

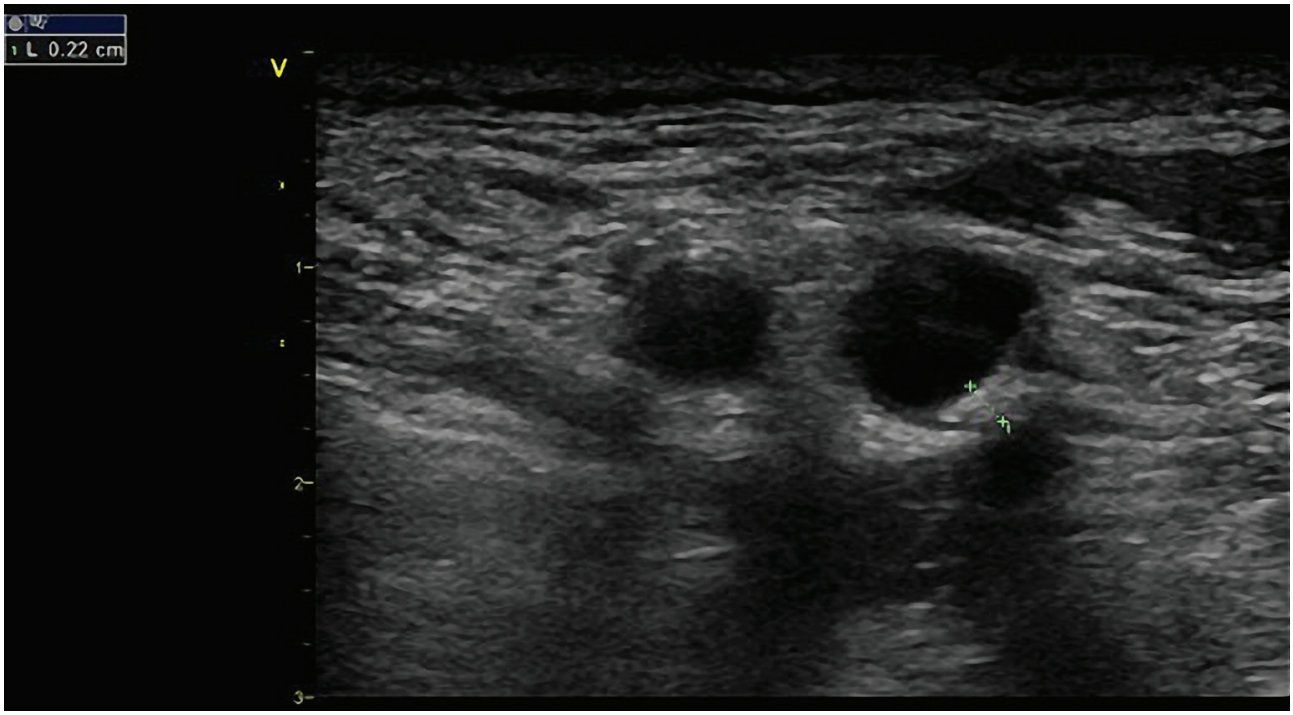

Figure 4. Transversal view: atherosclerotic calcific plaque at the origin of internal carotid artery (2.2 mm height).

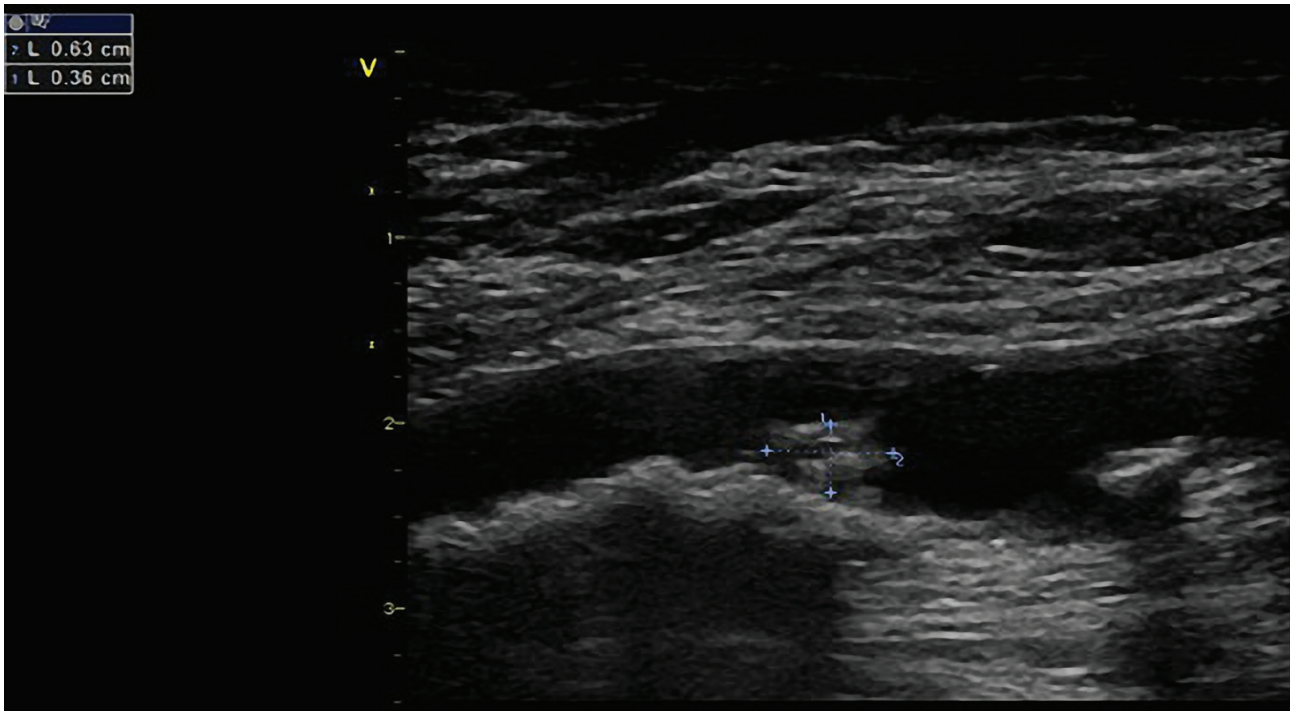

Figure 5. Longitudinal view: common femoral artery bifurcation showing a calcific atherosclerotic plaque, 6.3 mm width and 3.6 mm height.

Material and methods

We enrolled 51 consecutive hypertensive patients admitted to the cardiology ward for typical chest pain who underwent coronary angiography during their hospital admission. According to the current guidelines, arterial hypertension was defined as BP>140–159/90–99 mmHg [3]. The 51 patients were divided into two groups according to coronary

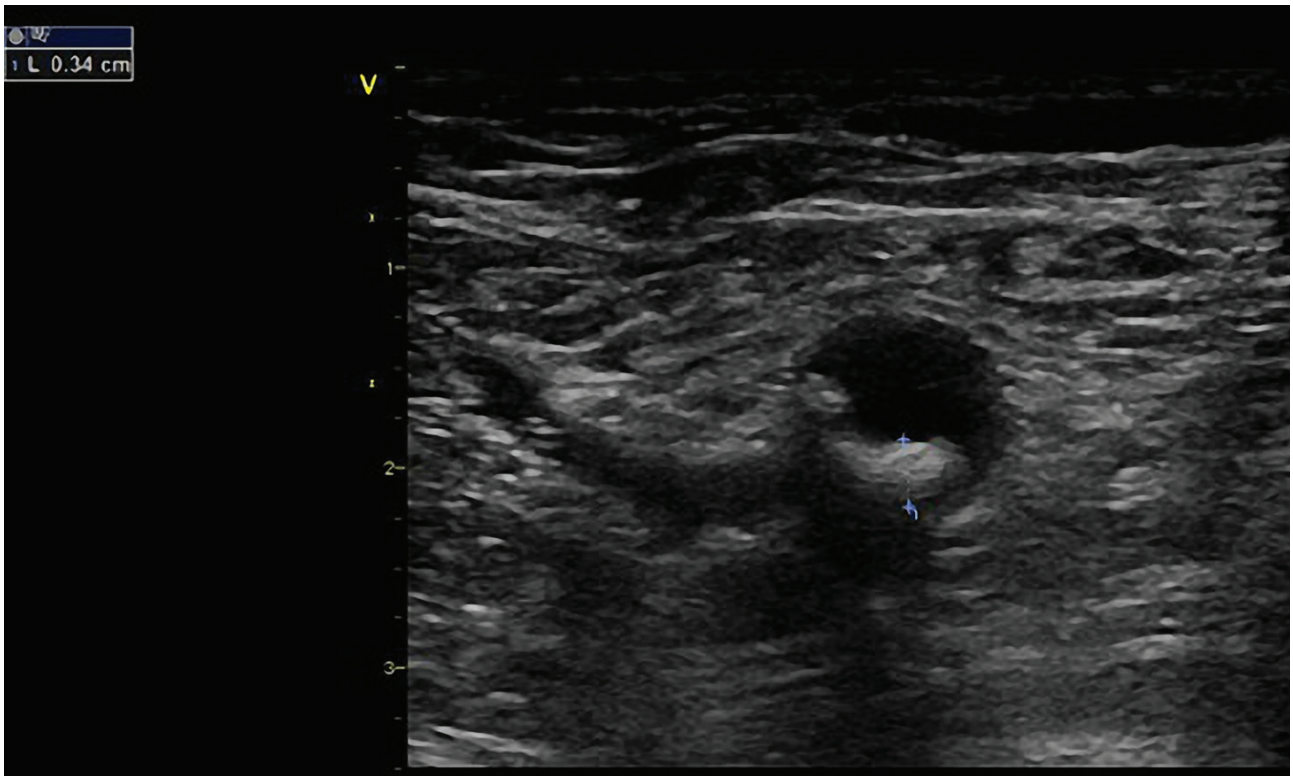

Figure 6. Transversal view: common femoral artery proximal to bifurcation showing a 3.4 mm height atherosclerotic plaque.

Table 1. Baseline characteristics of the study population.

Variable	Group 1 (CAD)	Group 2 (NsCAD)	P-value
Age (years)	60.46±12.17	59.57±9.27	0.806
Sex (male)	7 (50%)	28 (75.7%)	0.099
Sex (female)	7 (50%)	9 (24.3%)	0.099
Active smoking	27 (73%)	3 (21.4%)	0.001
Dyslipidemia	32 (86.5%)	8 (57.1%)	0.051
Bmi (kg/m^2)	28.53±4	27.07±3.65	0.318
Diabetes mellitus, type 2	10 (27%)	4 (28.6%)	1.000

angiography findings: Group 1 had coronary atherosclerotic disease (CAD), and Group 2 had no significant coronary atherosclerotic disease (NsCAD). Significant coronary stenosis was defined as more than 50% of the vascular lumen. Carotid and femoral ultrasound were performed on each patient and atherosclerosis burden score (ABS) and carotid plaque score (PS) were documented (Figures 1–6).

The atherosclerotic plaque was defined as the presence of a focal wall thickening that is ≥50% greater than the surrounding vessel wall or as a focal region with an IMT measurement of ≥1.5 mm that protrudes into the lumen [1, 4].

ABS is a score that sums the number of femoral and carotid bifurcations with atherosclerotic plaques, ranging from 0 to 4. ABS had a better predictive value in the detection of coronary artery disease in comparison to intima-media thickness (IMT) in a cohort of patients that underwent coronary angiography (18). The PS score was calculated by summing the maximum thickness of each identified carotid plaque. A total PS was obtained by adding the scores on each side, measured in millimeters.

Statistic analysis was performed using SPSS software version 23 (IBM Corp., Armonk, NY, USA) and Prism 9 software (GraphPad Software, LLC, San Diego, CA, USA). Continuous data were expressed as mean±standard deviation (SD) for normally distributed data and median (IQR 25–75%) for non-normally distributed data. Categorical data were expressed as count (percentage). Categorical variables were compared using Fisher's exact test/chi-square test and continuos data were compared by Student t-test if normally distributed or non-parametric tests (Mann Whitney U Test). Logistic regression was used to assess the predictive capacity of ABS and PS after adjustment of typical risk factors for coronary artery disease (age, sex, active smoking, dyslipidemia, body mass index, type 2 diabetes mellitus).

Results

The baseline characteristics of our study population are summarized in Table 1. The mean age in Group 1 was 60.46±12.17 years, while in Group 2 was 59.57±9.27, p=0.806. In group 1, there were more dyslipidemic patients [86.5% (n=32) *vs.* 57.1% (n=8)] than in group 2. There were no significant differences between the characteristics of the two groups, thus inferring that they are homogeneous. However, the only statistically significant difference was active smoking which was significantly more frequent in Group 1 [73% (n=23) *vs.* 21.4% (n=3), p=0.001].

ABS and PS values – comparison between the two groups, after adjustment for age, sex, BMI, dyslipidemia and active smoking (Table 2, Figures 7 and 8): Group 1 (patients with significant CAD) had significantly higher values of both ABS (2.00±1.43 *vs.* 0.28±0.61, p<0.001) and PS (2.59±2.73 *vs.* 0.40±1.12, p<0.001) compared to Group 2.

The proposed model shows that both factors, ABS and PS, are independent predictors for the existence of coronary lesions after adjusting for age,

Table 2. ABS and PS values – comparison between the two groups, after adjustment for age, sex, BMI, dyslipidemia and active smoking.

Variables	Univariate analysis		Multivariate analysis*	
	OR (95% CI)	p	OR (95% CI)	p
ABS	4.212 (1.649–10.759)	0.003	4.748 (1.374–16.406)	0.014
PS	1.802 (1.078–3.012)	0.025	2.448 (1.014–5.912)	0.047

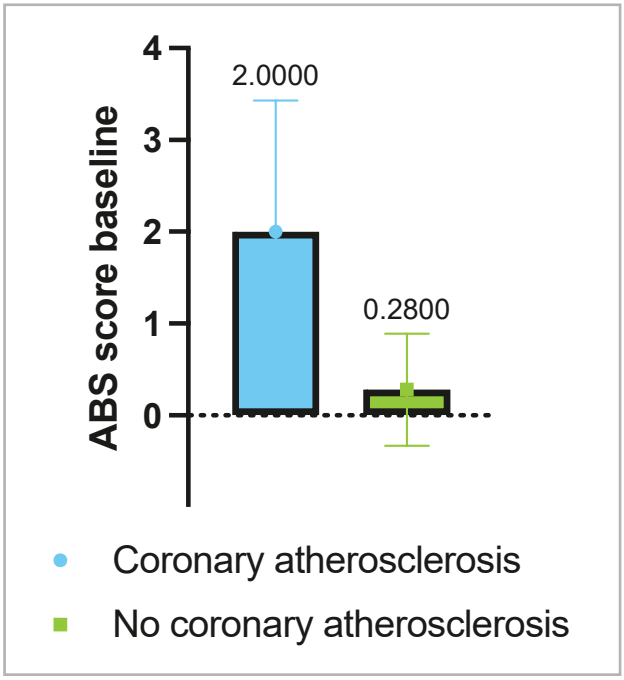

Figure 7. ABS values – comparison between the two groups, after adjustment for age, sex, BMI, dyslipidemia and active smoking.

sex, smoking status, dyslipidemia, diabetes and BMI value (Figure 9).

ROC curve analysis (Table 3, Figure 10) demonstrated good predictive value of ABS for the existence of coronary lesions (AUC 0.851, p<0.001) while PS showed only fair predictive value (AUC 0.737, p=0.010).

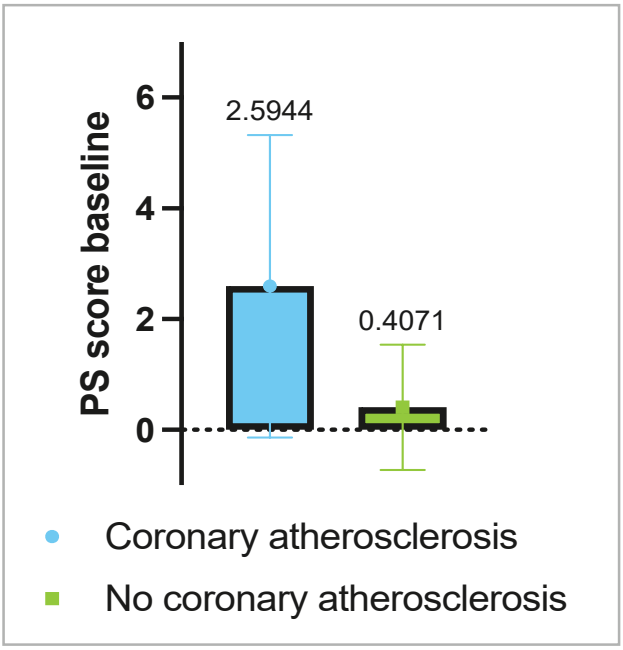

Figure 8. PS values – comparison between the two groups, after adjustment for age, sex, BMI, dyslipidemia and active smoking.

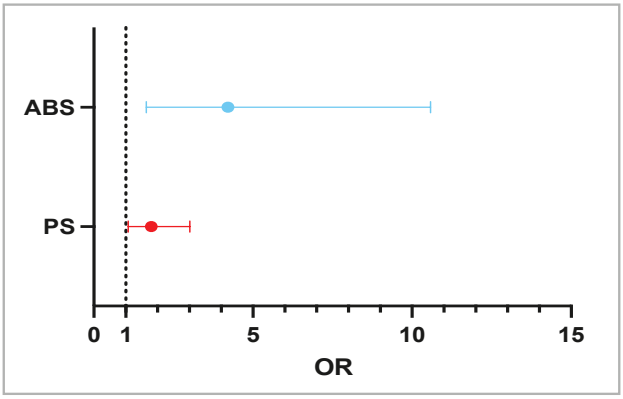

Figure 9. Multivariable logistic regression model for CAD prediction for ABS and PS after adjustment for age, sex, BMI, dyslipidemia and active smoking.

Discussions

The bidirectional causality between arterial hypertension and atherosclerotic plaque development was analyzed in multiple studies. The most frequently described mechanism of atherogenesis in hypertensive patients is the hemodynamic force which causes endothelial dysfunction [5]. The increased shear stress induced by blood pressure is crucial in both atherosclerosis onset and progression [6, 7]. Upon endothelial dysfunction, low-density lipoprotein accumulates and modifies in the intima [8, 9], allowing the fatty streak formation and, in time, the fibrous plaque development followed by plaque calcification constitute the hallmarks of advanced atherosclerosis [10]. However, atherosclerosis is not solely caused by hypertension.

Currently, the classic cardiovascular risk assessment parameters have undergone a reclassification so that IMT, a widely used ultrasound parameter, has become a class III indication [1].

Since atherosclerosis in the peripheral carotid and femoral arteries can be easily evaluated by fast and non-invasive ultrasound methods, it is desired to define new imaging parameters with a much better role in predicting significant coronary atherosclerotic disease. This desired new predictive model for the characterization of atherosclerosis is still in development [11]. According to Koulouri *et al.*, the atherosclerosis burden score can be a useful non-invasive method in detecting high-risk patients who could benefit from a more thorough cardiovascular

Table 3. ROC curve analysis.

Variable	Area under the curve	p
ABS	0.851	<0.001
PS	0.737	0.010

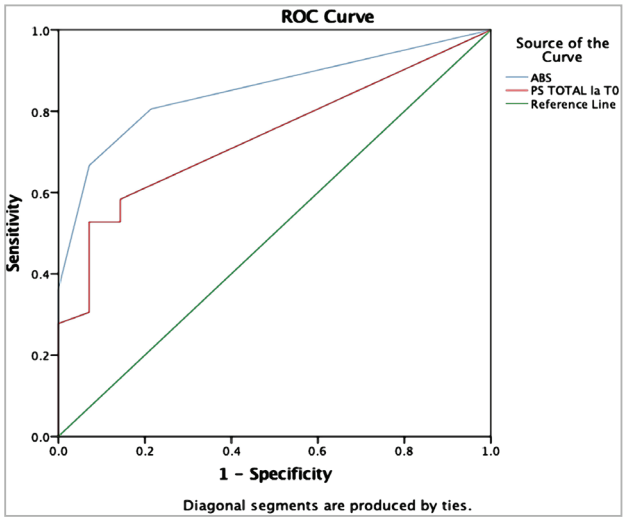

Figure 10. ROC curve analysis.

disease prevention. This ultrasonographic score predicted CAD more accurately than other non-invasive investigations (coronary artery calcium score, carotid intima-media thickness, ankle-brachial index) and had a similar performance to coronary artery calcium score in patients at intermediate risk of coronary heart disease [12].

In our study, ABS provided incremental value for predicting the existence of coronary lesions in symptomatic CAD and hypertensive patients, compared to PS, with results that were similar to the ones in the current literature. Moreover, CAD was evaluated by coronary angiography.

In studies carried out so far, the 2 plaque scores PS and ABS, are pertinent to use in the general population, both in the adult population and in the elderly.

Conclusions

Based on ROC curve analysis, ABS provided incremental value for predicting the existence of coronary lesions compared to PS in hypertensive patients. ROC curve analysis demonstrated a good predictive value of ABS for the existence of coronary lesions in hypertensive patients (AUC 0.851, p<0.001), while PS showed only a fair predictive value (AUC 0.737, p=0.010). Active smoking was significantly more frequent in the significant coronary artery disease group (Group 1).

Conflict of interest

The authors declare no conflict of interest.

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