Original Research

Prevalence of Peripheral Arterial Disease in Subjects at Moderate Cardiovascular Risk: Greek Results of the PANDORA Study

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Introduction: Peripheral arterial disease (PAD) is a form of atherosclerotic disease that confers a cardiovascular (CV) risk equivalent to that of coronary heart disease. Despite its association with high CV risk, PAD is potentially underdiagnosed. The primary objective of the study was to assess the prevalence of asymptomatic PAD through measurement of the ankle–brachial index (ABI) in subjects at moderate CV risk. Secondary objectives included the assessment of the prevalence of CV risk factors and lifestyle habits in the total population and in subjects with or without PAD, as well as the identification of factors associated with PAD.

Methods: PANDORA (NCT00689377) was a cross-sectional study conducted in 6 European countries. The study required a single visit in which males aged ≥45 or females ≥55 years, with at least 1 additional risk factor, but no overt CV disease or diabetes, underwent ABI measurement. Data on patient demographics, vital signs, CV risk factors, lipid levels and current treatment were recorded.

Results: Eight hundred forty subjects (789 evaluable) were enrolled by 120 office-based physicians across Greece. Age was 62.1 ± 9.1 years and body-mass index 29.6 ± 4.3 kg/m^2; 61.2% of the subjects were male, 47% were smokers, and 73.5% hypertensive. The prevalence of asymptomatic PAD, defined as ABI≤0.90, was 28.0% (95% CI: 24.88-31.14). In logistic regression analysis, hypertension (OR: 2.48, 95% CI: 1.58-3.89, $p<0.0001$), low high-density lipoprotein cholesterol (OR: 2.27, 95% CI: 1.55-3.32, $p<0.0001$), and divorced marital status (OR: 2.63, 95% CI: 1.14-6.07, $p=0.023$), were found to be strong determinants for PAD.

Conclusions: Asymptomatic PAD was highly prevalent in subjects with moderate CV risk treated by office-based physicians in Greece. ABI measurement is a significant tool for identifying subjects at higher risk who may require earlier and possibly more aggressive intervention.

Peripheral arterial disease (PAD), coronary heart disease (CHD) and cerebrovascular disease are atherosclerotic diseases. PAD occurs when plaque builds up in the arteries that supply visceral organs and/or the limbs. The most common symptom of PAD is pain in leg muscles when walking or climbing stairs that resolves with rest, a condition known as intermittent claudication.[1,2]

PAD is associated with increased morbidity and mortality.[3-7] In subjects with PAD, one-year rates of cardiovascular (CV) death and amputation (2.51% and 1.63%, respectively) have been found to be higher than in patients with CHD (1.93% and 0.25%, respectively).[3] In a *post hoc* analysis of the CHARISMA study, which compared dual antiplatelet therapy with aspirin alone in patients with either established atherothrombotic disease or multiple risk factors, the overall rate of CV death, myocardial infarction or stroke was 8.2% in subjects with PAD compared to

6.8% in subjects without PAD.[5] Furthermore, the impact of PAD on health-related quality of life has been reported to be equal to or worse than that in patients with the other forms of cardiovascular disease (CVD), i.e. CHD and cerebrovascular disease.[8]

Despite its association with severe health risk, PAD remains underdiagnosed by physicians and under-recognized by the public. This may partly be due to the mistaken belief that this condition is benign (and thus frequently under-reported) and also due to the fact that about 50% of individuals with PAD are asymptomatic.[2,7] The ankle–brachial index (ABI) has become the gold standard for the detection of PAD, because of its simplicity, reproducibility and cost effectiveness.[9,10] An ABI measurement ≤0.90 identifies subjects with PAD.[1,11]

Although there are several reports on the prevalence of PAD,[12-15] information is lacking concerning "non-high" CV risk subjects. For this reason, the PANDORA (Prevalence of peripheral Arterial disease in subjects with a moderate CVD risk, with No overt vascular Diseases OR diAbetes mellitus) European study was designed to assess the prevalence of asymptomatic PAD in subjects with moderate risk for CVD.[16] Herein the Greek results of the PANDORA study are presented. The prevalence of PAD in subjects with moderate CV risk in Greece is not known, as available reports focus on specific study populations, the first on hospitalized patients[17] and the second on the prevalence of symptomatic PAD.[18]

Methods

Study design

The PANDORA study (NCT00689377) was a non-interventional, cross-sectional, multi-center study conducted in 6 countries (Italy, Belgium, France, the Netherlands, Switzerland and Greece).[16,19] In Greece, data were collected from 120 office-based physicians all over the country. Patients were consecutively recruited from those attending scheduled visits at the participating physicians' offices. Each physician enrolled 7 subjects, for a total of 840 subjects. Data for each subject were obtained in a single visit and included: completion of a 14-item questionnaire on awareness of CV risk factors, knowledge and awareness of PAD, CV risk perception and treatment, as well as frequency of medical consultation; completion by the investigator of a case report form (CRF) with data relevant to patient demographics, vital signs, CV risk factors, lifestyle patterns, lipid levels, and current treatment; measurement of the ABI; and a physician questionnaire assessing his/her knowledge and behavior regarding CVD diagnosis and management, quantity of CVD cases experienced, and general attitudes towards guidelines and goals, treatment and treatment review. The results from the patient and physician questionnaires are not the subject of this report, pending publication of the respective results of the global PANDORA study.

The study population comprised subjects with moderate CV risk, according to the 4th Joint European and National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines,[20,21] with no overt CVD, symptomatic PAD or diabetes mellitus. More specifically, study subjects were males ≥45 or females ≥55 years of age who consented in writing to participation in the study and had at least one additional CV risk factor among: 1) smoking (any tobacco consumption within the last month); 2) hypertension (arterial blood pressure ≥140/90 mmHg or current antihypertensive treatment); 3) low high-density lipoprotein cholesterol (HDL-C<40 mg/dL) or high low-density lipoprotein cholesterol (LDL-C ≥130 mg/dL) within 3 months of study entry; 4) family history of premature CHD, i.e. clinical CHD or sudden death in father or other first-degree male relative <55 years of age, or in mother or other first-degree female relative <65 years of age; or 5) elevated waist circumference (≥102 cm for males, ≥88 cm for females). The main criteria for exclusion included the presence of symptoms of PAD, presence of type 1 or 2 diabetes mellitus, established CHD, other CHD risk-equivalents, or no lipid data collected within the previous 12 months. The rationale and design of PANDORA have been previously published in detail.[16]

This study was performed in accordance with ethical principles based on the Declaration of Helsinki and applicable regulatory requirements.

Clinical evaluation

All data collection took place during the single study visit. Each investigator received theoretical and practical training on the measurement of ABI according to American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of subjects with PAD, along with specific guidance on the ABI test procedure.[1,10] Right and left ABI measurements were performed by measuring the systolic blood pressure (SBP) from both brachial arteries and from both the *dorsalis pedis* and posterior tibial arteries, after each subject had been at rest in the supine position for 10 minutes and remained at rest. Measurements were taken with blood pressure cuffs appropriately sized to the subject's lower calf (immediately above the ankle). The Doppler ultrasonography instrument Elite 100R, Nicolet Vascular Inc. (Golden, Colorado, USA), was chosen for the measurement of the ABI, for comparability with other published studies on PAD prevalence.[15,22] The instrument was equipped with an 8 MHz vascular probe that provided greater sensitivity and reliability than a 5 MHz probe in detecting both superficial and deep arteries. Left and right ABI values (single values for each patient) were calculated in accordance with the ACC/AHA guidelines,[1] as the ratio of the higher of the SBP measurements obtained from the *dorsalis pedis* and posterior tibial arteries of the left and right ankle, respectively, to the higher of the SBP measurements obtained from the two brachial arteries.

Other variables recorded included cigarette smoking habits (habitual smoker, ex-smoker, non-smoker), alcohol intake (no intake; moderate, i.e. up to 2 glasses of wine per day; or high, more than 2 glasses of wine per day), marital status (single; married or living together; widowed, divorced or separated), physical activity (a physically active patient was defined as an individual performing at least 30 minutes of continuous or intermittent moderate intensity exercise 5 days/week), dyslipidemia, family history of premature CHD, arterial hypertension, low HDL-C and high LDL-C, as defined in the eligibility criteria.

CHD risk was assessed according to the Framingham Risk Score (FRS)[23,24] and the risk of CV death was assessed according to the Systematic Coronary Risk Evaluation (SCORE) risk chart.[25] Specifically, the SCORE chart for low risk countries was used for Greece, according to the 2003 European Society of Cardiology guidelines.[26]

Study objectives

The primary objective of the study was to estimate the prevalence of asymptomatic PAD (defined as an ABI measurement of ≤0.90) in the study population. Secondary objectives included the assessment of: 1) prevalence of CV risk factors and lifestyle habits in the total population and subjects with or without PAD; 2) the treatment for CV risk factors; 3) the CHD risk according to the Framingham Point scores risk chart[23,24] and the CVD death risk according to the SCORE chart,[26] in the total population and in subjects with and without asymptomatic PAD; and 4) patients' determinants (i.e. characteristics) for PAD, defined as the detection of an ABI ≤0.9 in a patient never diagnosed with PAD.

Statistical analysis

Statistical analysis was performed using the appropriate methodology required for the specific type of data. For continuous data, the mean, standard deviation, median, minimum, maximum and interquartile ranges were calculated. For categorical data the actual numbers and percentage frequencies in subjects with and without PAD were calculated.

For the primary endpoint (prevalence of asymptomatic PAD) the percentage frequency and the 95% confidence interval (CI) of pathological ABI were calculated. In order to assess the association between pathological ABI and lifestyle habits or CV risk factors, the odds ratio (OR) and 95% CI of lifestyle habits and frequency of risk factors in subjects with ABI ≤0.90 and ABI>0.90 were calculated, and the chi-square test was used for testing the general association.

In addition, the association between PAD and subject and investigator determinants was assessed by a logistic regression analysis with calculation of OR and 95% CI. Subject determinants were identified among the following variables: demographics, marital status, smoking status, alcohol intake, physical activity, family history of premature CHD, hypertension, dyslipidemia, waist circumference, high LDL-C, low HDL-C, and treatment with statins.

The primary analysis was performed on evaluable subjects (all enrolled subjects with signed informed consent, no protocol violations, ABI measurement, and >80% of data collected in CRFs. Statistical significance was set at $p<0.05$. All statistical analyses were performed with SAS version 8.2 (SAS Institute Inc., Cary, NC, USA).

Results

Results presented here are specific to the study population from Greece. As the current work is the Greek sub-group analysis of the PANDORA study, statistical analysis and results are presented according to the paper presenting the global PANDORA results.[19] The results of the global PANDORA study have been presented elsewhere.[19] In Greece, a total of 840 subjects were enrolled into the study between May 2007 and March 2008. Among the enrolled subjects, 789 were considered evaluable. The main reasons for exclusion were: total cholesterol, HDL-C, triglycerides not collected within the previous 12 months (n=27); ABI not measurable (n=9); failure to meet age requirements or age information missing (n=7); presence of diabetes mellitus (n=3); presence of CHD (n=1); and informed consent not signed (n=1).

The demographic characteristics and the physical examination/laboratory variables, respectively, of the total evaluable population and for subjects with PAD (ABI≤0.90) or without PAD (ABI>0.90) are summarized in Tables 1 and 2.

The prevalence of PAD in the evaluable subjects was 28.0% (95% CI: 24.88-31.14). The frequency distribution of ABI ranges in the study population is illustrated in Figure 1.

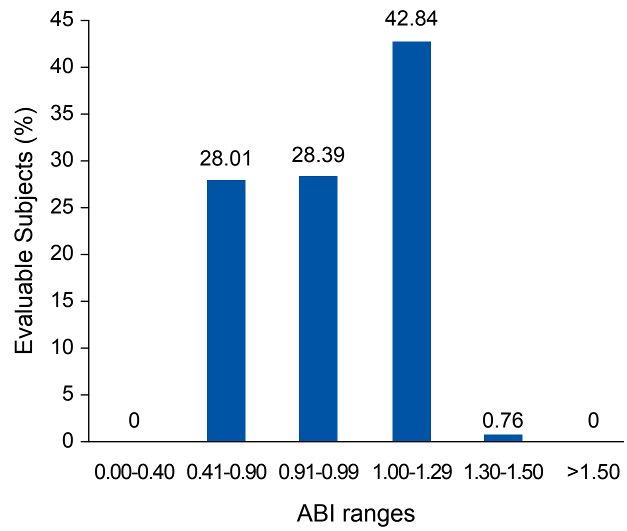

Figure 1. Frequency of ankle–brachial index (ABI) ranges in the Greek population.

Table 1. Demographic characteristics of the total Greek population and of subjects with or without peripheral artery disease, based on ankle–brachial index (ABI).

Demographic characteristic		Total (n=789)	ABI≤0.90 (n=221)	ABI>0.90 (n=568)
Age (years)	Mean ± SD	62.1 ± 9.1	62.3 ± 9.4	62.0 ± 9.0
	Median	61	62	61
	Min-max	45-98	45-98	45-90
Gender (%)	Male	61.22	68.78	58.27
Marital Status (%)	Single	4.94	5.43	4.75
	Married or living together	78.33	76.47	79.05
	Widowed	12.42	11.76	12.68
	Divorced or separated	4.06	5.88	3.35
	Other	0.25	0.45	0.18

Table 2. Physical examination and laboratory variables in the total Greek population and in subjects with or without peripheral artery disease, based on ankle–brachial index (ABI).

	Total (n=789)	ABI≤0.90 (n=221)	ABI>0.90 (n=568)
Physical examination variables (mean ± SD):			
Weight (kg)	85.33 ± 14.68	86.96 ± 13.68	84.70 ± 15.02
Waist circumference (cm)	100.76 ± 13.24	102.80 ± 13.33	99.96 ± 13.13
BMI (kg/m^2)	29.57 ± 4.30	30.01 ± 4.18	29.40 ± 4.33
SBP (mmHg)	137.86 ± 16.00	141.75 ± 15.58	136.35 ± 15.92
DBP (mmHg)	84.48 ± 9.30	86.59 ± 9.32	83.66 ± 9.17
Heart rate (beats/min)	75.97 ± 9.07	78.07 ± 10.39	75.16 ± 8.38
Laboratory variables (mean ± SD):			
TC (mg/dL)	220.97 ± 40.74	222.70 ± 42.72	220.29 ± 39.96
HDL-C (mg/dL)	51.46 ± 22.94	45.68 ± 16.99	53.72 ± 24.51
LDL-C (mg/dL)	138.05 ± 44.23	145.64 ± 43.33	135.21 ± 44.27
Triglycerides (mg/dL)	156.63 ± 67.24	166.90 ± 75.02	152.98 ± 63.94

BMI – body-mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; TC – total cholesterol; HDL-C – high-density lipoprotein-cholesterol; LDL-C – low-density lipoprotein-cholesterol.

Table 3. Frequency distribution of lifestyle habits and cardiovascular risk factors in the total Greek population and in subjects with or without peripheral artery disease, based on ankle–brachial index (ABI).

Variable			Total (n=789)	ABI≤0.90 (n=221)	ABI>0.90 (n=568)	p-value[1]
Smoking:	Habitual smoker (%)		47.02	48.42	46.48	NS
	Ex-smoker (%)		21.17	23.53	20.25	
	Non-smoker (%)		31.81	28.05	33.27	
Hypertension (%)			73.51	85.52	68.84	<0.0001
Family history of premature CHD (%)			32.45	35.75	31.16	NS
Elevated waist circumference (%)			69.17	73.76	67.38	NS
Dyslipidemia (%)			75.92	79.19	74.65	NS
Low HDL-C (%)			27.60	42.53	21.83	<0.0001
Physical inactivity (%)			72.12	79.19	69.37	0.006
Alcohol intake:		Moderate[2] (%)	41.95	45.70	40.49	NS
		High (%)	4.56	5.88	4.05	

[1]Associations between pathological ABI and lifestyle habits or risk factors were evaluated by the chi-square test. [2]Up to 2 glasses/day.
CHD – coronary heart disease: HDL-C – high-density lipoprotein cholesterol; NS – not significant

Among the 221 subjects with PAD, 134 (60.6%) had abnormal measurements on both sides, while 43 (19.4%) and 44 (19.9%) subjects had abnormal measurements only on the right or only on the left side, respectively.

The percentage frequency distribution of lifestyle habits and CV risk factors is presented in Table 3. Most subjects were either smokers or ex-smokers (68.2%), had an elevated waist circumference (69.2%), presented with dyslipidemia (75.9%), and were physically inactive (72.1%). Hypertension, low HDL-C, and physical inactivity were more likely to be present among patients with PAD than in patients without PAD ($p<0.0001$, $p<0.0001$, and $p=0.006$, respectively).

In terms of medications used to treat CV risk factors, 85.5% of patients with PAD were taking at least one CV medication, as compared to 75.5% of patients without PAD. The absence of CV treatment was less likely in PAD patients (OR 0.523, 95%CI: 0.343-0.796, $p=0.002$). Antihypertensive medications were being taken by 54.8% of PAD patients compared to 47.4% of those without PAD. Lipid-lowering treatment with statins only was reported in 56.1% of patients with PAD vs. 53.2% without PAD, statins in combination with other lipid-lowering agents were reported in 3.0% vs. 1.4%, fibrates in 4.0% vs. 8.0%, and other lipid-modifying agents in 8.0% vs. 3.4%, respectively. Only 6.97% of patients (11.3% with vs. 5.3% without PAD) were receiving antiplatelet therapy at the time of the study visit.

The risk factor burden (total number of CV risk factors in addition to age) in the study population and in patients with or without PAD is shown in Table 4. There appeared to be an increased risk of PAD for subjects presenting with a higher number of risk factors, as depicted in Figure 2. More specifically, patients with 3 or 4 additional risk factors appeared to have an almost 3-fold increase in the possibility of having asymptomatic PAD compared to those with 1 additional risk factor (OR 2.91, 95% CI 1.32-6.38 and OR 3.20, 95% CI 1.44-7.09, respectively) and those with 5 additional factors had a 4.5-fold increase in their risk for PAD (OR 4.58, 95% CI 1.85-11.31) as compared with those with only 1 additional CV risk factor.

Table 4. Frequency of risk factors in addition to age in the Greek population and in subjects with or without peripheral artery disease, based on ankle–brachial index (ABI).

Risk factors present	Total (n=789)	ABI≤0.90 (n=221)	ABI>0.90 (n=568)
1	7.98%	3.62%	9.68%
2	22.81%	18.10%	24.65%
3	34.09%	36.20%	33.27%
4	27.50%	31.22%	26.06%
5	7.60%	10.86%	6.34%

The 10-year CHD risk calculated according to the FRS, as well as the 10-year risk of CVD death according to the SCORE algorithm, in the total population and in subjects with and without PAD, are reported in Table 5. The mean 10-year CHD FRS (19.23%) and the mean SCORE (4.42%) were both higher in

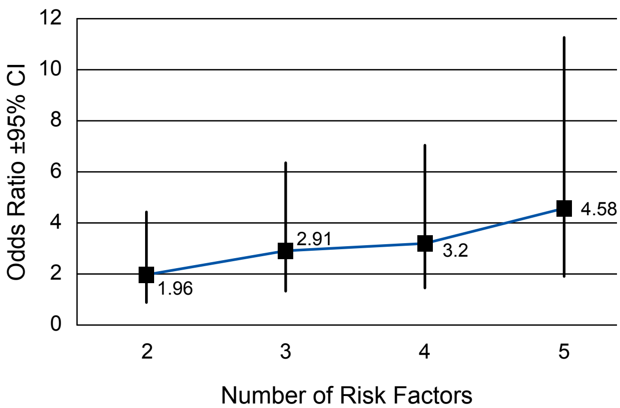

Figure 2. Association of cardiovascular risk factor burden and prevalence of peripheral artery disease in the Greek PANDORA population. Odds ratio: risk of pathological ankle–brachial index in subjects with the specified number of risk factors versus the risk in subjects with only one risk factor (in addition to age).

subjects with PAD than in subjects with non-pathological ABI measurements (15.50% and 3.37%, respectively).

Furthermore, in high-risk subjects as defined by an FRS>20%, pathological ABI presented with higher frequency than non-pathological ABI (43.89% vs. 27.46%), whereas the opposite trend (18.1% vs. 30.63%) was revealed in low-risk subjects (FRS<10%) (Figure 3). Similarly, high-risk subjects as defined according to SCORE (>5%) showed a higher frequency of pathological ABI than non-pathological ABI, with the opposite trend appearing for low-risk subjects (SCORE<1%) (Figure 4).

Logistic regression analysis of the association between PAD and subject characteristics, laboratory values, lifestyle habits and CV risk factors showed that, of all factors examined, hypertension (OR 2.48, 95% CI 1.58-3.89, p<0.0001), low HDL-C (OR 2.27, 95% CI 1.55-3.32, p<0.0001) and divorced marital status (divorced vs. married, OR 2.63, 95% CI 1.14-6.07, p=0.023) were strong determinants of PAD (Figure 5). Physical inactivity revealed a weaker association with PAD, being marginally statistically insignificant (OR 1.49, 95% CI 0.99-2.24, p=0.051).

Discussion

Our study showed that asymptomatic PAD was highly prevalent (28.0%) in subjects at moderate CV risk treated by office-based physicians in Greece. In fact, Greece had the highest prevalence of PAD among the 6 countries that participated in the PANDORA study, with Italy having the second highest (22.9%). The mean prevalence of asymptomatic PAD in the overall PANDORA population was 17.8%.[19]

To our knowledge, this is the first report on the prevalence of asymptomatic PAD in a Greek population at moderate CV risk according to the NCEP ATP III guidelines,[20,21] without diabetes or overt CVD. Comparison of our study with existing studies estimating the prevalence of PAD is difficult given the different study populations. For example, a large study conducted in hypertensive subjects >60 years of age identified a PAD prevalence of 25.5% by measurement of the ABI. The study population was comprised of elderly and hypertensive patients, with approximately 15% and 10% of them having CVD and diabetes, respectively.[27] Another large study conducted in France identified a PAD prevalence of 27.8% in a mixed population of patients >55 years old, with symptoms suggestive of PAD, or established atherothrombotic disease, or 2 or more CV risk factors.[14] Nevertheless, in a sub-group analysis of 2077 patients with 2 or more CV risk factors (including diabetes) the prevalence of PAD was found to be 10.4%, i.e.

Table 5. Summary statistics of the 10-year risk of coronary heart disease (CHD) according to the Framingham algorithm and the 10-year cardiovascular (CVD) death risk score, in the total Greek population and in subjects with and without peripheral artery disease, based on ankle–brachial index (ABI).

		Total (n=789)	ABI ≤0.90 (n=221)	ABI>0.90 (n=568)
10-year CHD risk score (Framingham), %	Mean ± SD	16.54 ± 9.33	19.23 ± 9.29	15.50 ± 9.14
	Median	16	20	14
	Interquartile range	8-25	11-30	8-25
10-year CVD death risk score (SCORE), %	Mean ± SD	3.66 ± 3.39	4.42 ± 4.02	3.37 ± 3.06
	Median	3	3	2
	Interquartile range	1-5	2-6	1-5

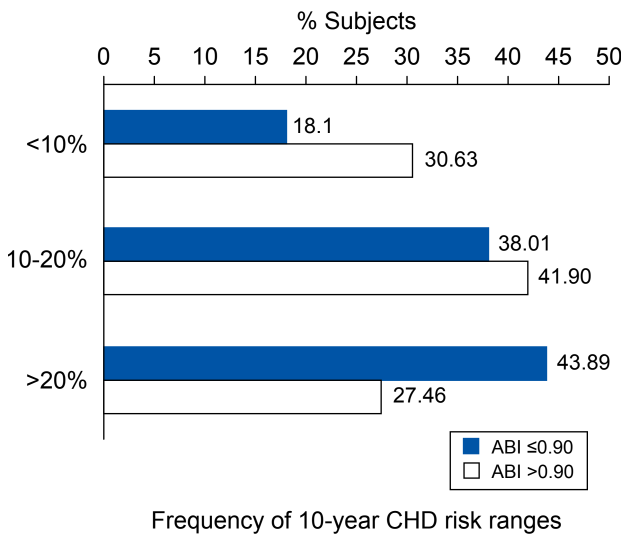

Figure 3. Frequency of Framingham 10-year risk ranges for coronary heart disease (CHD) in Greek subjects with ankle–brachial index (ABI)≤0.90 and ABI>0.90.

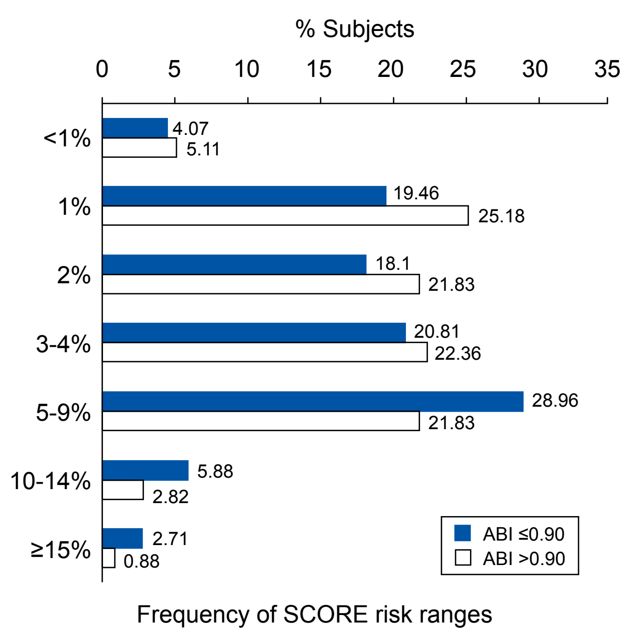

Figure 4. Frequency of the 10-year risk ranges for death from cardiovascular disease in Greek subjects with ankle-brachial index (ABI)≤0.90 and ABI>0.90.

considerably lower than the Greek PANDORA population but similar to that of the French PANDORA population.[14,18] Furthermore, the PARTNERS study, conducted in the United States, identified a PAD prevalence of 29% in subjects who were either aged >70 years or aged 50-69 years but with a history of smoking or diabetes.[15] A subgroup analysis of the

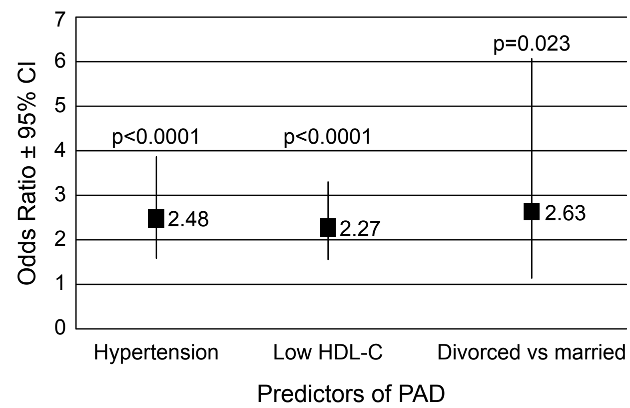

Figure 5. Strong predictors of peripheral artery disease (PAD) based on a logistic regression analysis of evaluable subjects in Greece. HDL-C – high-density lipoprotein cholesterol.

study by Cacoub et al, which included a population somewhat similar to ours, showed a PAD prevalence much lower than in our study.[14]

As far as Greek reports are concerned, in a single-center study conducted in hospitalized patients >50 years old, asymptomatic PAD prevalence using ABI measurements was estimated to be 36%. In this study, 28% of patients had diabetes and 12% CHD.[17] Moreover ABI was measured manually, without a Doppler device, and for the calculation of ABI the lowest arterial ankle pressure was used, whereas ABI measurements in the present study were performed by Doppler ultrasound and the higher of the left and right SBP measurements of the ankle and of the arm were used. Given these differences, it is difficult to make a reliable comparison between this previous study and the present one.

In another Greek multicenter, cross-sectional study (the METS-GREECE study) assessing the prevalence of vascular diseases in patients with or without metabolic syndrome and with or without diabetes, symptomatic PAD prevalence was estimated at 2.3% in the overall study population (23.7% of whom had metabolic syndrome).[18] The fact that the authors considered only symptomatic PAD (established by physical examination and the presence of intermittent claudication) as opposed to asymptomatic PAD in our study makes any comparison between PANDORA and the METS-GREECE study difficult to interpret.

One of the secondary objectives of this study was the measurement of the frequencies of standard CV risk factors and lifestyle habits, such as physical inactivity and alcohol consumption. Study results revealed a high frequency of all CV risk factors (smoking, overweight/obesity, hypertension, dyslipidemia, family history of premature CHD), as well as physical inactivity and moderate alcohol consumption in the study population. This is in agreement with the results of other reports that have demonstrated the high frequency of CV risk factors such as smoking, hypertension, dyslipidemia and overweight/obesity among Greeks.[28,29] In fact, CVD is the leading cause of death among Greek men and women.[30] The high incidence of CVD risk factors in the Greek population may be a cause of the high prevalence of PAD in our study.

It is also worth noting that, although the frequencies of all risk factors examined were higher among patients with asymptomatic PAD compared to patients without PAD, the logistic regression analysis demonstrated that asymptomatic PAD was statistically significantly associated with hypertension, low HDL-C, and divorced marital status. Hypertension and low HDL-C are known risk factors for atherosclerotic diseases, such as PAD, and were highly prevalent in those with asymptomatic PAD (with frequencies of 85.52% and 42.53%, respectively). The association between marital status and CVD along with its risk factors has been reported previously.[31-34] A study of the relationship between marital status and CV risk factors in Greek healthy subjects enrolled in the ATTICA study showed that eating patterns may mediate the association between marital status and certain CV risk factors.[35] This finding (poorer dietary habits) may potentially explain in part the higher PAD prevalence observed in the divorced vs. the married subjects in our population. The lack of an association between PAD and smoking status is unexpected, as a wealth of evidence has suggested their strong association.[36,37] However, this finding may have been due to the fact that smoking was self-reported and thus may have been underestimated. In addition, evidence for an association between asymptomatic PAD and smoking is limited to a report of an association with heavy smoking,[38] whereas in the present study the smoking factor encompassed any smoking, whether light, moderate or heavy.

Multiple reports correlate low ABI measurements with an increased risk of CVD, CV mortality, all-cause mortality, stroke and transient ischemic attack,[4,27,39-43] and a decreased quality of life.[44] The present study examined the total CV risk using both the FRS[23] and the European SCORE[25] in the entire study population, which was considered to be at moderate (non-high) CV risk upon study enrolment. A considerable proportion of patients were eventually found to be at high CV risk according to their FRS and SCORE (FRS>20%, SCORE>5%). This shows the importance of the standard total CV risk calculation tools in identifying subjects at higher risk who may require more intensive treatment.

Moreover, a notable percentage of patients classified as moderate or low risk by FRS and SCORE were found to have an ABI value consistent with asymptomatic PAD, and therefore should have been reclassified as at high CV risk. This finding underscores the usefulness of the ABI as a tool for identifying subjects who otherwise would have been classified as being at non-high risk and, as such, would not have been considered candidates for more intensive treatment. This is supported by findings from a large-scale study (6262 participants) in which, among those 35-74 years of age and free of CVD, 6.1% were classified as being at moderate to high 10-year CHD risk by the FRS, but this proportion increased to 8.7% with, measurement of the ABI.[45] The advantage of using the ABI was shown to be higher for women than for men, with another study reporting that inclusion of ABI with the FRS would reclassify 36% of women and 19% of men from their FRS risk category.[46]

Although the present study yielded interesting insight into "real life" clinical routine, it has some limitations. Firstly, due to its design (cross-sectional single visit), the study does not provide patient follow up regarding their CV outcomes, so any association between ABI and risk factors should be interpreted with caution. Another potential limitation is that a single method was used for the measurement of ABI, while it has been demonstrated that the calculated prevalence of asymptomatic PAD varies significantly according to the ABI measurement method.[47-49] Consequently, additional research is warranted to determine the most accurate method of determining ABI.[49] Another potential limitation may be related to the lack of experience of office-based physicians in determining ABI, despite their training in the technique, which could lead to misclassification of subjects with regard to their ABI status. Lastly, while this study assessed and identified several factors among the patients' sociodemographic and clinical characteristics associated with the diagnosis of asymptomatic PAD, it would be of interest for future studies to evaluate a possible association of PAD diagnosis with other sociodemographic factors, such as educational level and socioeconomic status. It would also be of interest to calculate the CVD risk for the Greek PANDORA population with the nationally calibrated version of SCORE (the HellenicSCORE[50]), since the current study analysis did not include locally calibrated risk charts.

Conclusions

In conclusion, the present study has demonstrated that the prevalence of asymptomatic PAD is alarmingly high in a Greek population with more than 2 CV risk factors, but without diabetes or overt CVD. Furthermore, it has demonstrated that ABI measurement in primary care may be a significant tool for identifying asymptomatic subjects at higher risk of CVD who may require earlier and possibly more aggressive intervention. It is imperative that primary care physicians are properly trained and provided with an increased awareness of the importance of ABI measurement for the detection of PAD. Prompt detection of PAD and its effective management through the management of total CV risk, along with increased public awareness of PAD and its risk factors, will likely reduce the high rates of myocardial infarction, stroke, hospitalization and death from CVD.

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