Indian Heart Journal 70 (2018) 808–815

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Prevalence of peripheral artery disease and risk factors in the elderly: A community based cross-sectional study from northern Kerala, India

Mangalath Narayanan Krishnan[a,*,1], Zachariah Geevar[b], Padinhare Purayil Mohanan[c], Krishnannair Venugopal[d], Shanmughasundaram Devika[e]

[a] Govt. Medical College, Kozhikode, Kerala, India
[b] Mother Hospital, Thrissur, Kerala, India
[c] Westfort High-tech Hospital, Thrissur, Kerala, India
[d] Pushpagiri Hospital, Tiruvalla, Kottayam, Kerala, India
[e] ICMR National Institute of Environmental Health, Bhopal, Madhya Pradesh, India

ARTICLE INFO

Article history:
Received 9 August 2017
Accepted 2 November 2017
Available online 4 November 2017

Keywords:
Prevalence
Peripheral artery disease
Risk factors

ABSTRACT

Background and objective: There are no data on the prevalence of peripheral artery disease (PAD) and risk factors in Indians. This study was aimed at studying the prevalence of PAD and risk factors in elderly population of northern parts of Kerala, South India.

Methods: In a prospective observational survey we evaluated men and women of age between 60 and 79 years from Kerala. Anthropometric measurements, biochemical investigations and electrocardiogram were done. The diagnosis of PAD was made by ABI < 0.9. Assessment of coronary artery disease CAD was performed using historical, angina questionnaire and electrocardiographic criteria.

Results: Of the total sample of 1330, we could evaluate 1148 respondents (86.3%). Overall mean (SD) ABI was 0.97 (0.19). Age-adjusted prevalence of PAD was 26.7% (95% CI (24.3, 29.4)) with no difference between urban and rural population. Prevalence of symptomatic PAD was low. Diabetes, hypertension, high cholesterol, low high-density lipoprotein cholesterol, sedentary life style and smoking was observed in 25.5%, 62.9%, 61.6%, 35.9% 38.1% and 30.7%, respectively. On multivariate analysis age, smoking and physical inactivity were strong predictors of PAD. There was independent association of PAD with definite CAD.

Conclusions: There was high prevalence of PAD in Kerala, driven by high prevalence of risk factors. The prevalence was equal in rural and urban population. Intermittent claudication was uncommon. Age, female gender, smoking, physical inactivity, diabetes were independent predictors for presence of PAD.

1. Introduction

Peripheral artery disease (PAD) refers to obstructive disease of major arteries below the aortic bifurcation. Vast majority of PAD is caused by atherosclerosis. It is a major cause of lower limb symptoms, disability and limb loss. With the rise in aging population, the prevalence of PAD is also on the increase. Most cases of PAD are asymptomatic; approximately a quarter of patients with PAD present with intermittent claudication (IC) and progress to critical limb ischemia with rest pain and gangrene leading to significant disability and limb loss.[1] Several studies have demonstrated that patients with asymptomatic as well as symptomatic PAD are at an increased risk of cardiovascular morbidity and mortality compared with subjects without PAD.[2–4] There have been large epidemiological studies on the prevalence and associations of PAD from the developed Western societies.[5–7] Surveys have also been published from India on the prevalence of PAD among non-insulin dependent diabetes mellitus (DM) and other high-risk population.[8,9] However, there has been no large study on the prevalence of PAD from India among unselected elderly population. We sought to estimate the prevalence of PAD on the basis of ankle-brachial index (ABI), and risk factors of PAD among a population of men and women between the ages of 60 and 79 years, who were participants of the Cardiological Society of India Kerala Coronary Artery Disease and Its Risk Factors Prevalence Study (CSI Kerala CRP study).

Abbreviations: PAD, peripheral artery disease; CAD, coronary artery disease; ABI, ankle brachial index.

* Corresponding author at: Govt. Medical College, Kozhikode, Kerala, 673008 India.
E-mail address: kedaram@gmail.com (M.N. Krishnan).
[1] Present address: Ahalia Hospital, Hamdan, Abu Dhabi, United Arab Emirates.

https://doi.org/10.1016/j.ihj.2017.11.001

2. Patients and methods

A detailed description of the design, sample, and methods of CSI Kerala CRP study and the data on prevalence of coronary artery disease (CAD) and risk factors among the participants have already been published.[10,11] Briefly, this was a cross-sectional community-based survey during the period from January to June 2011. The main objective of CSI Kerala CRP study was to determine the prevalence of CAD and its risk factors in rural and urban areas from three geographical regions of the state of Kerala, India, among men and women between the age 20 and 79 years. There were 5167 subjects in the main study. A sub-sample of elderly men and women from urban and rural regions of Kozhikode district (north) and Thrissur (central) district of the state constituted subjects for the present study. All men and women at or above the age of 60 years from all the listed households of these regions were included in the study. The sample selection procedure is shown in Fig. 1.

We collected data using the standard interview method and responses recorded on a questionnaire. Information on basic socio-economic and demographic details, smoking, physical activity, dietary habits, and personal history of hypertension, dyslipidemia, diabetes mellitus and CAD were collected. Rose Questionnaire (RQ) was used to draw data for intermittent claudication and angina.[12] History of documented prior myocardial infarction, unstable angina, coronary artery bypass grafting (CABG) surgery, noninvasive investigations for CAD, coronary angiography, coronary angioplasty, documented use of drugs for CAD, hospital admission for CAD, family history of ischemic heart disease, stroke and coronary risk factors was also recorded.

2.1. Ankle brachial index

Trained doctors obtained ankle-brachial systolic blood pressure measurements. Subjects were asked to lie supine for at least 5 min before blood pressure measurement. Arm and ankle blood pressure was taken using standard mercury sphygmomanometer. For leg blood pressure, cuffs were applied to the calf with the midpoint of the bladder over the posterior tibial artery (PTA), two inches above the medial malleolus. Both ankle and brachial systolic blood pressure was taken with an 8 MHz Doppler pen probe (Dopplex D900 – Non-directional Doppler, Huntleigh Technologies, Cardiff, UK). Single measurement of both brachial and ankle pressures were recorded. For each limb the cuff was inflated quickly to the maximal inflation level and deflated at a rate of 2 mm Hg per second until audible sound appeared. The first appearance of sound was recorded as the systolic pressure. If the posterior tibial pulse could not be located by palpation or with the Doppler probe, measurement was taken from the dorsalis pedis artery (DPA).

2.2. Definitions

The ankle-brachial systolic blood pressure index (ABI) was defined as the ratio of the lower of the systolic blood pressures at either ankle (PTA) to the higher of the systolic blood pressures in the brachial arteries. If only one PTA pressure was available, that was taken for leg systolic pressure. If both PTA pressures were missing, lower or available DPA pressure was taken as the leg systolic pressure. The ABI values were corrected to 2 decimal points. We considered PAD to be present if the ABI is <0.9, as defined by Fowkes et al and Meijer et al.[5,6] Those with ABI >1.5 were excluded from analysis as this ABI reflects severe arterial rigidity and spurious ankle pressures. We evaluated IC according to Rose Questionnaire. Symptomatic PAD was defined as subjects with PAD by ABI associated with IC.

We defined coronary artery disease as: (a) Definite CAD based on *any of*: documented evidence of prior acute coronary syndrome (ACS) or treatment for CAD, documented history of undergoing coronary angioplasty or CABG, more than 50% epicardial coronary stenosis by invasive coronary angiography, ECG showing pathological Q waves (any of Minnesota code 1-1-1 to 1-1-7or 1–2-1 to 1–2-5 or 1–2-7), imaging evidence of a region of loss of viable myocardium that is thinned and has a motion abnormality, in the absence of a non-ischemic cause,[13] Rose Angina Questionnaire (RAQ) angina *plus* ECG changes (any of Minnesota codes 4-1-1, 4-1-2, 4-2 or 5-l, 5-2), or RAQ angina *plus* positive treadmill ECG (exercise-induced horizontal or down-sloping ST depression of >1 mm at 80 ms from J point), or inducible ischemia on stress imaging;(b) Probable CAD based on *any of* (in *the absence of any of the definite criteria*):RAQ angina without significant ECG changes, ECG changes (any of Minnesota Code 4-1-1,4-1-2, 4-2 *or* 5-1, 5-2) without RAQ angina, or positive treadmill ECG without RAQ angina. Any CAD was defined as those who have satisfied either definite or probable CAD criteria.

We defined DM as fasting blood glucose value of ≥7 mmol/L and/or if there was current use of medications for diabetes,[14]

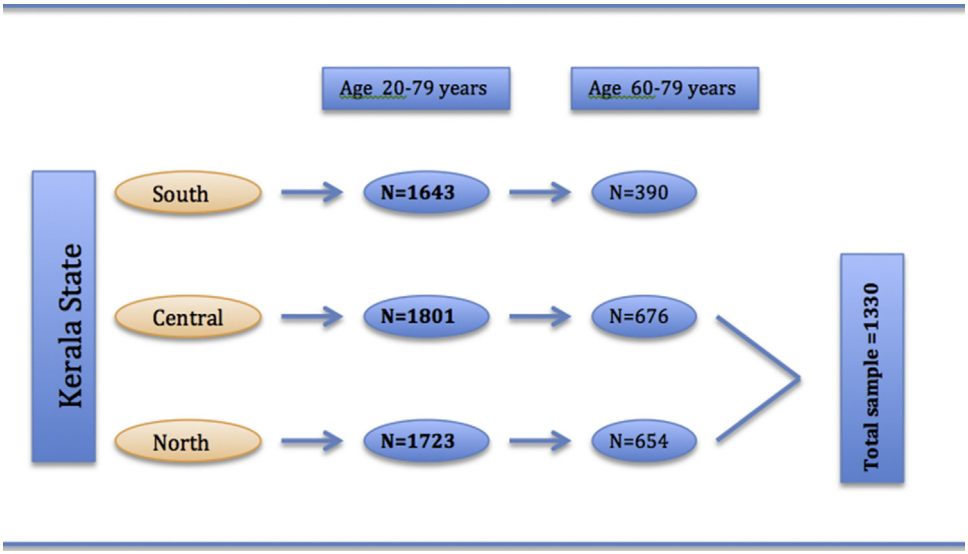

Fig. 1. Sampling procedure for the study.

hypertension as blood pressure ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic and/or currently on drugs for high blood pressure,[15] and dyslipidemia as any of: serum total cholesterol ≥200 mg/dL, serum LDL cholesterol ≥ 130 mg/dL, serum HDL cholesterol <40 mg/dL, in men or <50 mg/dL in women, or serum triglycerides ≥150 mg/dL.[16] We categorized body mass index (BMI) as normal (18.0-22.9 kg/m^2), overweight (23.0-24.9 kg/m^2), or obesity (≥25 kg/m^2). Abdominal obesity was defined as a waist circumference of ≥90 cm in men or ≥80 cm in women.[17] Physical activity level was classified into sedentary and non-sedentary. All subjects doing activity involving physical effort for at least 30 min a day for a minimum of 5 days a week (household activities involving physical effort, walking to and from work involving at least 30 min, manual workers, those performing leisure-time physical activities) were considered non-sedentary. All others were classified as sedentary.

2.3. Ethical clearance

The present study was in compliance with the Helsinki Declaration. The Ethics Committee of Cardiological Society of India, Kerala Chapter, approved the study. Informed written consent was obtained from all participants.

2.4. Statistical analysis

We estimated the sample size based on an anticipated prevalence of 9% of PAD in the Edinburgh Artery Study[5]in a sample of men and women aged between 55 and 74 years. The total sample size (n) was estimated using the formula, $n = Z^2 P (1- P)/e^2$ where Z was the level of confidence (95%), P was the anticipated prevalence (9%) and e was the level of precision (2%). A design effect of 1.5 was considered for sample size. The estimated total sample size was 1180.

We entered data into CS Pro software (the US Census Bureau) version 4.0 for Windows. Data cleaning and statistical analysis were performed using Stata (Stata Corp, Texas, USA) version 13.0 for Windows. Frequency distribution was done for categorical variables and descriptive statistic for continuous variables. Comparisons of prevalence or mean between different categories were done using two-tailed proportion test or independent sample test depending upon the distribution of data. The differences in prevalence or mean with 95% confidence interval (CI) were provided. Risk factor analysis was done using log binomial model to obtain prevalence ratio (PR) and its 95% CI as the prevalence of PAD was over10%. Most recent epidemiologic models prefer PR to odds ratio (OR) to assess the degree of association, as using OR may lead to overestimation.[18] All the risk factors studied in univariate analysis were considered for multivariate model. We also provided age-adjusted prevalence of PAD using World Health Organization population data. P value <0·05 defined the level of statistical significance.

3. Results

Of the 1330 men and women at or above 60 years of age enlisted for the study, 1172 responded. Of this, ABI values were not available in 24 participants leaving 1148 subjects available for analysis (Men43.2%); the overall response was 86.3%. The response rate in men and women was similar (84.6% vs. 87.5%; p = 0.5539). Missing data for diabetes, hypertension, serum cholesterol, and HDL were 3,4,7,and 7 subjects respectively. The baseline characteristics of the sample are depicted in Table 1. Prevalence of diabetes and hypertension was similar in men and women. Women were more often obese, with higher prevalence of abdominal obesity, high cholesterol and low HDL levels. Men had better education, higher prevalence of definite CAD and more often sedentary. Smoking was prevalent only in men.

3.1. Distribution of ABI

The overall mean (SD) ABI among 1148 participants was 0.97 (0.19). Fig. 2 depicts gender-wise distribution of ABI. Over two-third of the ABI occurred in the range of 0. 9 to 1.2. There was no difference in mean ABI between urban and rural sample (Fig. 3). Mean ABI was significantly lower in women [0.95 (0.17) vs 0.99

Table 1
Baseline charecteristics of the sample.

Variables	Total (n = 1148)	Men (n = 496)	Women (n = 652)	P value
Age, years (Mean; SD)	66.66 (5.40)	66.69 (5.51)	66.64 (5.31)	0.8929
BMI (Mean; SD)	22.86 (4.31)	22.04 (3.82)	23.48 (4.55)	<0.001
Educational status				
No formal education	126 (10.98)	23 (4.64)	103 (15.80)	<0.001
1–4 years	261 (22.74)	91 (18.35)	170 (26.07)	
5–10 years	665 (57.93)	322 (64.92)	343 (52.61)	
>10 years	96 (8.36)	60 (12.10)	36 (5.52)	
FBS mg/dL Mean (SD)	98.58 (28.04)	99.64 (29.94)	97.78 (26.50)	0.2724
SBP mmHg, Mean (SD)	139.21 (23.40)	140.16 (23.23)	138.48 (23.52)	0.2285
DBP mm Hg, Mean (SD)	76.05 (11.91)	76.95 (11.91)	75.38 (11.87)	0.0273
Total Cholesterol mg/dL, Mean (SD)	214.13 (45.34)	199.26 (40.14)	225.45 (45.83)	<0.001
Serum HDL mg/dL, Mean (SD)	50.02 (12.35)	47.75 (12.32)	51.75 (12.10)	<0.001
Diabetes (%)	292 (25.50)	130 (26.26)	162 (24.92)	0.6064
Hypertension (%)	720 (62.94)	300 (60.85)	420 (64.52)	0.2038
High cholesterol (%)	703 (61.61)	239 (48.48)	464 (71.60)	<0.001
Low HDL (%)	410 (35.93)	118 (23.94)	292 (45.06)	<0.001
Smoking (%)		152 (30.65)		
Sedentary (%)	437 (38.07)	210 (42.34)	227 (34.82)	0.0093
BMI (%)				
Low	129 (11.26)	64 (12.90)	65 (10.00)	<0.001
Normal	494 (43.11)	241 (48.59)	253 (38.92)	
Overweight	190 (16.58)	93 (18.75)	97 (14.92)	
Obese	333 (29.06)	98 (19.76)	235 (36.15)	
Abdominal Obesity (%)	604 (52.80)	177 (35.76)	427 (65.79)	<0.001
Any CAD (%)	334 (29.09)	134 (27.02)	200 (30.67)	0.1764
Definite CAD (%)	150 (13.07)	77 (15.52)	73 (11.20)	0.0311

BMI-body mass index; FBS- Fasting blood sugar; SBP- Systolic blood pressure; DBP- diastolic blood pressure; HDL- high density lipoprotein; CAD- coronary artery disease.

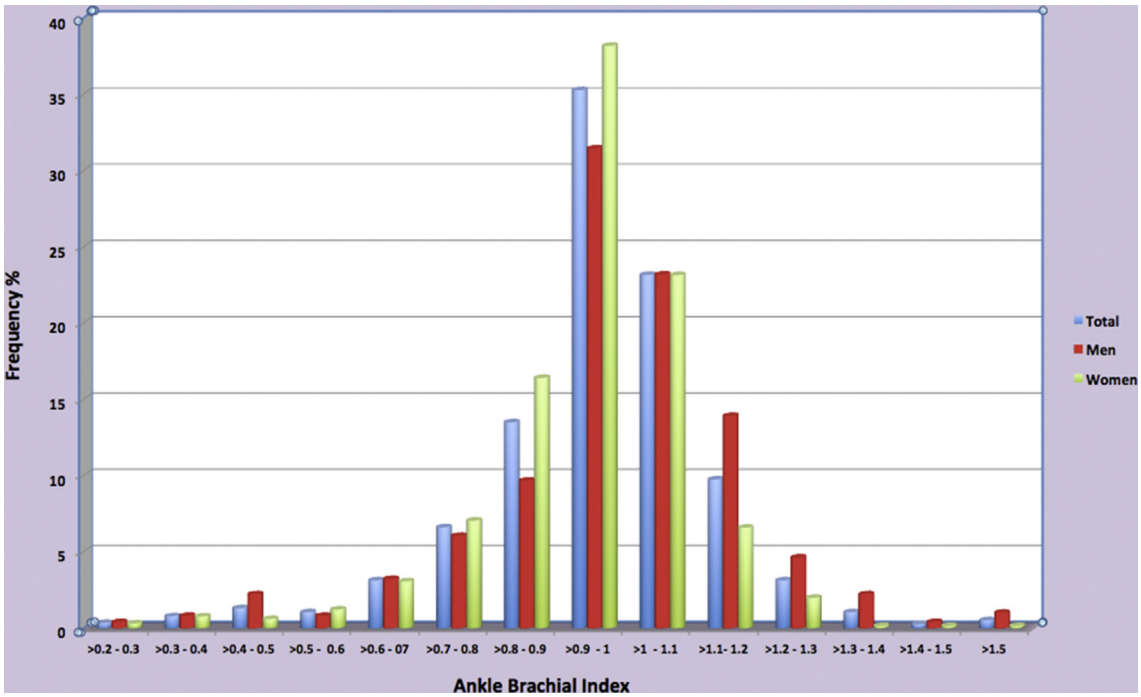

Fig. 2. Distribution of ankle brachial index among men and women.

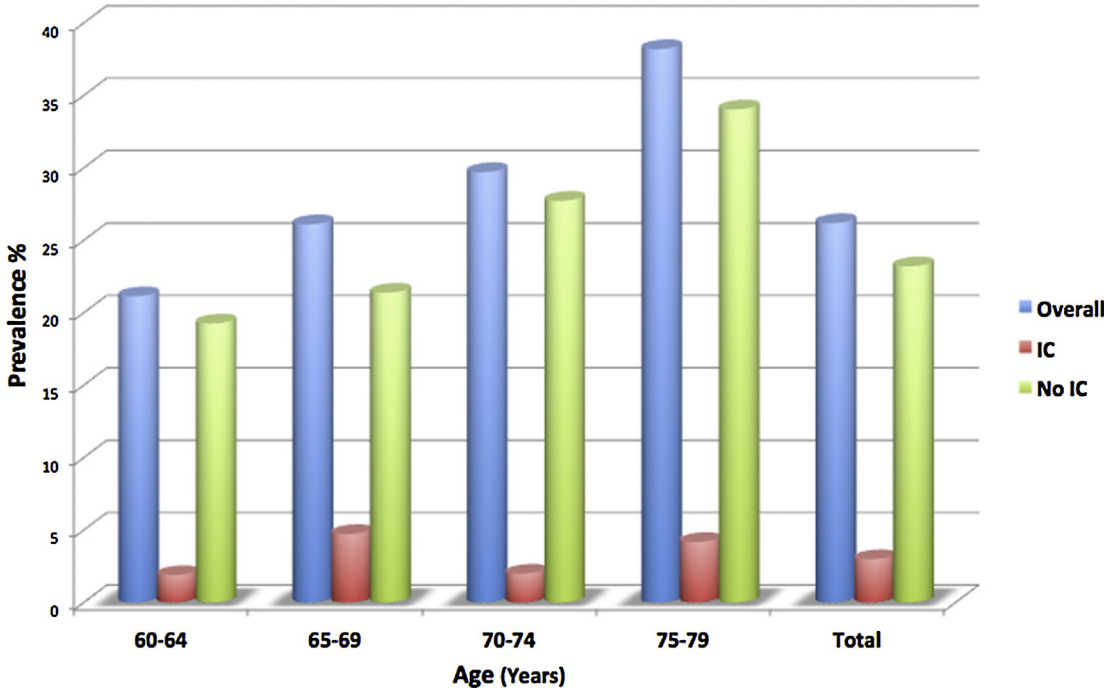

Fig. 3. Age-wise prevalence of symptomatic and asymptomatic peripheral artery disease.

(0.21); p = < 0.001] (Table 2). However, height-adjusted mean ABI among men and women showed no significant difference (0.98 vs.0.95, 95% CI (-0.005,0.06), p = 0.092).

3.2. Prevalence of peripheral artery disease

There were 299 subjects with ABI <0.9. An additional 9 subjects had ABI equal to 0.9. The age- standardized prevalence of PAD among the sample was 26.74% [95%CI (24.23, 29.41)]. The overall occurrence of symptomatic and asymptomatic PAD was 2.98% [95%CI (2.13, 4.14)] and 23.20% [95% CI (20.84, 25.75)], respectively. There was a steady increase in the prevalence of the disease with age (Fig. 4); prevalence in the 60- 64 years and 75 to 79 years groups was 21.13% and 38.19% (p <0.001), respectively. This was true for asymptomatic cases (19.25% vs. 34.03%; p = 0.0002) while in symptomatic group, a significant difference by age was not found (1.88% vs. 4.17%; p = 0.1173). The overall occurrence of PAD was more in women; but the difference between men and women was seen only in the 70–79 years age group (Table 3).

Table 2
Distribution of ankle brachial index among men and women by region.

	Ankle Brachial Index											
	Overall			Male			Female			Difference	95% CI	P value
	n	Mean	SD	n	Mean	SD	n	Mean	SD			
Urban	492	0.97	0.19	193	1.00	0.23	299	0.95	0.16	0.05	(0.01, 0.08)	0.0141
Rural	656	0.96	0.19	303	0.98	0.19	353	0.95	0.18	0.04	(0.01, 0.07)	0.0101
Overall	1148	0.97	0.19	496	0.99	0.21	652	0.95	0.17	0.04	(0.02, 0.06)	0.0004

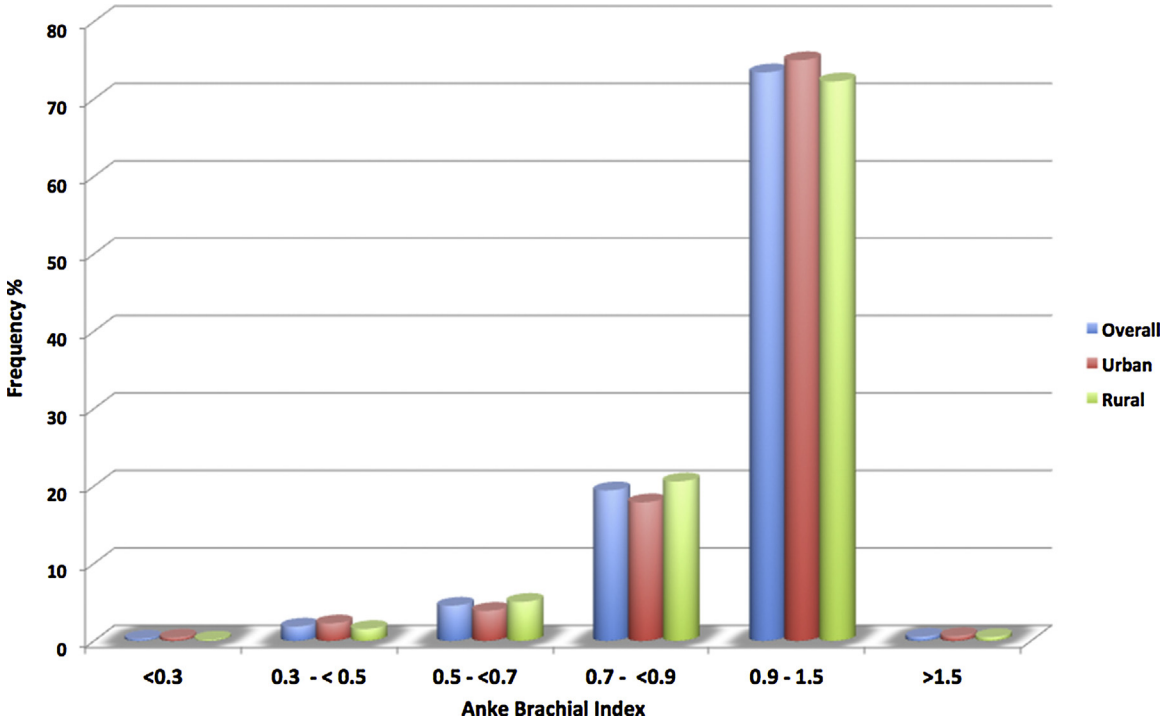

Fig. 4. Region-wise distribution of ankle brachial index.

3.3. Intermittent claudication

Symptomatic PAD was more prevalent in urban sample (4.50% vs. 1.84%; p = 0.0088) whereas asymptomatic PAD was more often seen in rural population (25.57% vs. 20.04%; p = 0.0284). Prevalence of symptomatic PAD was similar in men and women (2.65% and 3.23%; p = 0.5693). However, asymptomatic PAD was more common in women (25.35% vs. 20.37%; p = 0.0485).

Intermittent claudication by RQ was observed in 79 subjects (6.92%); 5.34% of patients with ABI 0.9 to 1.5 and 11.37% in the ABI <0.9 group; the prevalence of IC was significantly more in those with ABI <0.9 (95% CI for difference: (2.13, 9.94); p = 0.0004). The prevalence of IC among patients with PAD was 11.37%, equally divided between men and women (11.50% vs. 11.29%); urban men and women with PAD had much more prevalent symptoms than rural.

3.4. CAD and risk factors

Among the 1148 subjects the prevalence of diabetes, hypertension, high cholesterol and low HDL was25.50%, 62.94%, 61.61%, and 35.93%, respectively. Sedentary habit was prevalent in 38.07%; smoking was exclusively seen in men (30.65%).

Table 4 shows the univariate and multivariate associations between PAD and various subject charecteristics. On univariate analysis we found that age, sex, diabetic status and physical inactivity were associated with presence of PAD. Smoking showed a trend for higher prevalence of PAD. Hypertension, high

Table 3
Age and gender-wise prevalence of peripheral artery disease.

	Overall			Men			Women			Diff. (%)	95% CI	P value
Age (years)	N	n	%	N	n	%	N	n	%			
60–64	478	101	21.13	216	41	18.98	262	60	22.90	−3.92	(−11.22, 3.38)	0.2962
65–69	318	83	26.10	122	34	27.87	196	49	25.00	2.87	(−7.13, 12.87)	0.5711
70–74	202	60	29.70	88	20	22.73	114	40	35.09	−12.36	(−24.75, 0.03)	0.0566
75–79	144	55	38.19	65	18	27.69	79	37	46.84	−19.14	(−34.62, −3.67)	0.0186
Overall	1142	299	26.18	491	113	23.01	651	186	28.57	−5.56	(−10.65, −0.47)	0.0344

Table 4
Univariate and multivariate association of peripheral artery disease.

Variables	Univariate			Multivariate		
	PR	95% CI	P value	PR	95% CI	P value
Age						
60–69 years		Referent			Referent	
> = 70 years	1.44	(1.18, 1.75)	<0.001	1.37	(1.12, 1.67)	0.002
Gender						
Male		Referent			Referent	
Female	1.24	(1.01, 1.52)	0.036	1.39	(1.08, 1.80)	0.010
Abdominal Obesity						
Yes	1.09	(0.89, 1.32)	0.412	1.10	(0.88, 1.39)	0.409
No		Referent			Referent	
BMI						
<25		Referent			Referent	
> = 25	0.89	(0.72, 1.12)	0.318	0.87	(0.68, 1.12)	0.279
Diabetic Status						
Diabetics	1.29	(1.03, 1.60)	0.025	1.26	(1.00, 1.57)	0.047
IFG	1.03	(0.79, 1.33)	0.845	1.05	(0.81, 1.36)	0.725
Non Diabetic		Referent			Referent	
Hypertension						
Normal		Referent			Referent	
Pre Hypertensive	0.77	(0.56, 1.07)	0.120	0.82	(0.60, 1.13)	0.225
Hypertensive	0.90	(0.70, 1.17)	0.439	0.89	(0.69, 1.15)	0.375
High Cholesterol						
Normal		Referent			Referent	
High	1.19	(0.96, 1.46)	0.108	1.21	(0.98, 1.50)	0.077
Low HDL						
Normal		Referent			Referent	
Low	1.06	(0.87, 1.30)	0.540	0.99	(0.81, 1.21)	0.907
Smoking						
Yes	1.09	(0.83, 1.44)	0.521	1.45	(1.04, 2.02)	0.028
No		Referent			Referent	
Physical Activity						
Yes		Referent			Referent	
No	1.44	(1.18, 1.74)	<0.001	1.36	(1.12, 1.66)	0.002
Any CAD						
Yes	1.001	(0.81, 1.24)	0.991	0.82	(0.62, 1.09)	0.172
No		Referent			Referent	
Definite CAD						
Yes	1.18	(0.90, 1.54)	0.221	1.44	(1.01, 2.07)	0.047
No		Referent			Referent	

PR – Prevalence ratio; HDL – high density lipoproteins; CAD – coronary artery disease; IFG – impaired fasting glucose after Prevalence ratio.

cholesterol, low HDL, high BMI or abdominal obesity did not have any association with PAD prevalence. Among 332 subjects with any CAD, 87 had PAD (26.20%); the proportion was nearly similar for presence of PAD among 149 subjects with definite CAD (30.20%). Likewise, about one-third of subjects with PAD had any CAD; the figure for definite CAD was 15.05%. On multivariate analysis age, smoking and physical inactivity were strong predictors of PAD; diabetes and female sex were also independently associated. Hypertension, high cholesterol, low HDL obesity or abdominal obesity did not show association. There was independent association of PAD with definite CAD.

4. Discussion

Peripheral arterial disease is being recognized as a major health problem in the elderly. Our study tried to estimate the prevalence of PAD among men and women between the age of 60 years and 79 years in central and northern parts of Kerala, South India. We could achieve a response rate of 86.3%, comparable to other major studies.[5,6]

In our study, ABI at rest was used to define presence of PAD. Ankle brachial index is a very sensitive (97%) and specific (100%) tool for diagnosis of PAD.[19,20] In a number of surveys, ABI measurement during exercise or during reactive hyperemia was used.[5,21,22] We employed resting ABI only, as used in other major surveys on PAD, as other maneuvers are generally not useful.[23]

There has been disagreement in the way ABI is calculated in studies in the past. Some of the major studies[6] have used lower ankle pressure (LAP) for calculation of ABI while others have used the average of ankle pressures[24,25] or the higher of the ankle pressures (HAP).[26] There are two studies comparing LAP with HAP for sensitivity and specificity; both found that the LAP used for calculation of ABI conferred more reliable estimate of PAD, notwithstanding the 2016 AHA statement recommendation of HAP for calculation of ABI.[27,28] The sensitivity of ABI for diagnosis of PAD is better when LAP is used; since ABI has lower sensitivity and high specificity for diagnosis of PAD we used a higher sensitivity measurement as the numerator.

The threshold of ABI for diagnosis of PAD is still debated. In this study, we chose <0.9 as the threshold ABI for PAD diagnosis. Although the ABI cut off currently accepted is $\leq$0.9.[29] most major studies have taken <0.9 as the cut-off for diagnosis of PAD.[6,7,24,30] and hence we also chose this value for comparison.

4.1. Distribution of ABI

As expected, the distribution of ABI had a skew for the range of >0.9 to 1.5; more than 70% of ABI fell in this range. Mean ABI was lower in women, which may be partly explained by the shorter stature of women. Shorter stature causes lower ABI, and this is unlikely to be related to the difference in actual prevalence of PAD. Aboyans et al. found that on an average, ABIs are slightly lower in women independent of height.[31] while Hiatt et al. found that in normal subjects, the influence of height on the ABI is small.[32] While such differences may not affect the assessment in individuals, but may lead to overestimation of prevalence of PAD among women. When ABI was adjusted for height, we found no significant difference in ABI in men and women.

4.2. Prevalence of PAD

The overall crude prevalence of PAD was high in our study. The prevalence was much higher than most of the western studies where figures between 4 and 19% were found. Data from National Health and Nutrition Examination Survey found12.2% prevalence of PAD in US subjects at or above the age of 60.[33] In the Strong Heart Study with participants aged 45–74 years, PAD was seen in 5.3%.[34] The highest prevalence among major western studies on unselected population was 19.1% (Rotterdam Study).[6] It is difficult to make reliable comparisons with other large population surveys on PAD on account of differences in age of the study population, ethnicity and time frame. In Rotterdam study, the approximate prevalence in the subset between ages 60 and 79 was 19% vis-à-vis 26.7% in our study. However, it may be noted that the frequency of risk factors in our sample was much higher than most major studies (diabetes25.5% vs. 10%; hypertension 62.9% vs. 29 to 47%; high cholesterol 61.6% vs. 30 to 46% and smoking 31% vs. 14 to 21%).[6,24,31] The high frequency of vascular risk factors would probably account for the high prevalence of PAD in our study. There was no difference in the occurrence of PAD in urban and rural areas. The lack of a rural-urban divide was akin to similar finding in the prevalence of CAD in Kerala, due to the fact that in Kerala, the urban- rural differences in the socioeconomic status, risk factors, and dietary habits were negligible.

The prevalence of PAD was more in women despite the fact that major risk factors like diabetes and hypertension were not higher in women. We found only high BMI, abdominal obesity, high cholesterol and low HDL more prevalent in women and none of these was found to have an independent association with PAD. The gender-specific prevalence of PAD by ABI seems to be highly variable in studies from the West. The Rotterdam study showed clear female preponderance in PAD prevalence. However, most

other studies have found PAD prevalence more in men or equal in both sexes.[34,35] Higher occurrence of PAD in women mirrors the unadjusted low ABI in women; thus it may be partly related to the effect of height on ABI and may not reflect truly higher prevalence in women.

Rose Questionnaire is widely used for assessment of IC in PAD, however it is insensitive for diagnosis of lower extremity obstructive arterial disease.[36] The Rose questionnaire for claudication was developed for epidemiological surveys. It is moderately sensitive (60–68%), and highly specific (90–100%) for diagnosis of PAD. The Edinburgh Claudication Questionnaire (ECQ) is an improved version of the Rose Questionnaire. It was found to be 91.3% sensitive and 99.3% specific in detecting IC in the general population, compared with the diagnosis of PAD by clinical examination.[37] In our study we have used Rose Questionnaire as has been utilized in other major studies on PAD.[5,6] Only a small minority (~3%) of the participants in this study reported symptom of IC. The prevalence of IC was same in men and women, where as asymptomatic PAD tended to be more in women. Other studies reported prevalence of IC in the range of 5.3% to 18.9%.[5,6,34,38] Among patients with PAD, the prevalence of IC was 11% with no difference in men and women. The low prevalence of IC may underlie the fact that elderly individuals are unlikely to walk vigorously enough to the point of symptoms.

4.3. Peripheral artery disease, coronary artery disease and risk factors

There was high prevalence of major CVD risk factors in the subjects studied. The association with PAD was found with age, female gender, physical inactivity, smoking and diabetes by multivariate regression analysis. Surprisingly, hypertension, low HDL, obesity or abdominal obesity did not show any significant association; high cholesterol and tended to have some relation with PAD. The prevalence ratio was highest for smoking (1.5) followed by definite CAD, age, female gender and physical inactivity (1.4 each), diabetes (1.3) and high cholesterol (1.2). Most large studies on PAD have found significant association between PAD and major CVD risk factors like smoking, diabetes and hypertension while failed to find relation between obesity and PAD. Dyslipidemia has been found to be an independent factor in most studies except the Framingham Offspring Study.[24] Our study, for unexplained reasons, did not show any association between hypertension and high cholesterol or low HDL in either univariate or multivariate analysis, although high cholesterol showed a trend. Another unique finding in our data was the strong association between physical inactivity and PAD (PR = 1.4; $p = 0.002$).

Among subjects with PAD, nearly 1/3 had any CAD and 15% had definite CAD in our study. Major western studies have shown much higher proportion of CAD in participants with PAD. Subherwal and associates, analyzed data from a large registry concluded that patients with PAD had higher risk of long-term cardiovascular events compared to those with incident MI alone and suggested that PAD should be considered as a coronary artery disease risk-equivalent.[39] The Edinburgh Artery Study observed CAD in 71% of individuals with symptomatic PAD and 54% in asymptomatic subjects.[5] Other studies evaluating angiographic CAD in patients with proven PAD report prevalence of CAD between 50 and 70%.[40,41] In the ARIC study, individuals with ABI <0.9 were twice likely to have CAD than those with ABI >0.9.[25] Similar relation was noted in the Cardiovascular Health Study.[35] These figures are higher than what we have found; the differences may be partly explained by the differences in the criteria for defining CAD in these studies. On multivariate analysis, our study did not show any correlation between PAD and any CAD, but correlation with definite CAD was significant.

4.4. Studies from India and other Asian countries

Studies on PAD prevalence from Asian countries are limited. A study from urban sample at or above the age of 20 years from South India showed PAD prevalence of 3.2%.[8] The prevalence of PAD was more in women among Indian patients with type 2 diabetes.[42] A cross-sectional population study from Sri Lanka on more than 2900 persons between the ages of 50 to 70 years revealed 3.6%age and sex-adjusted prevalence of PAD.[43] A Chinese population study of men and women aged >=60 years showed age-standardized PAD prevalence of 15.3%; the prevalence was higher in women.[44]

Our study was the first population survey of PAD in unselected elderly population from India. We were able to get a good response rate for our study with very little missing data. One important limitation of the study was that we did not use a random-zero sphygmomanometer for assessment of ABI; moreover, we did not make multiple measurement of the leg and arm blood pressures to estimate ABI. Taking the mean of consecutive measurements, as for example in the Limburg PAOD Study[45] would have been more appropriate. We could not estimate observer variation in this study; however, Aboyans et al in a study found high inter- and intra-observer reliability of various ABI calculation methods.[46]

In conclusion, our cross-sectional survey on PAD diagnosed on the basis of ABI from urban and rural regions of Kerala showed high prevalence of PAD among elderly men and women, with no urban rural difference. Intermittent claudication was uncommon in our sample. Age, female gender, smoking, physical inactivity, diabetes were independent predictors for presence of PAD while hypertension, high cholesterol, obesity did not have significant association.

Funding

The study was funded by the Cardiological Society of India, Kerala Chapter; the funding source had no role in the design, data collection, analysis or interpretation or writing up of the article.

Conflict of interest

None of the authors has any conflict of interest to declare.

Acknowledgements

None.

References

1. Hertzer NR. The natural history of peripheral vascular disease: implications for its management. *Circulation*. 1991;(Suppl. I):12–19.
2. Criqui MH, Langer RD, Fronek A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med*. 1992;326:381–386.
3. Smith GD, Shipley MJ, Rose G. Intermittent claudication, heart disease risk factors, and mortality: the Whitehall Study. *Circulation*. 1990;82:1925–1931.
4. Newman AB, Sutton-Tyrrell K, Vogt MT, et al. Morbidity and mortality in hypertensive adults with a low ankle/arm blood pressure index. *JAMA*. 1993;270:487–489.
5. Fowkes FGR, Housley E, Cawood EHH. et al. Edinburgh Artery Study: prevalence of asymptomatic and symptomatic PAD in the general population. *Int J Epidemiol*. 1991;20:384–392.
6. Meijer WT, Hoes AW, Rutgers D, et al. Peripheral arterial disease in the elderly: the Rotterdam study. *Arterioscler Thromb Vasc Biol*. 1998;18:185–192.
7. Fabsitz RR, Sidaway AN, Go O, et al. Prevalence of peripheral arterial disease and associated risk factors in American Indians: the Strong Heart Study. *Am J Epidemiol*. 1999;149:330–338.
8. Premalatha G, Shanthirani S, Deepa R, et al. Prevalence and risk factors of peripheral vascular disease in a selected South Indian population: the Chennai Urban Population Study. *Diabetes Care*. 2000;23(9):1295–3000.
9. Pradeepa R, Chella S, Surendar J, et al. Prevalence of peripheral vascular disease and its association with carotid intima-media thickness and arterial stiffness in type 2 diabetes: the Chennai urban rural epidemiology study (CURES 111). *Diab Vasc Dis Res*. 2014;11(3):190–200.

10. Zachariah G, Harikrishnan S, Krishnan MN, et al. Prevalence of coronary artery disease and coronary risk factors in Kerala, South India: a population survey –design and methods. *Indian Heart J*. 2013;65:243–249.
11. Krishnan MN, Zachariah G, Venugopal K, et al. Prevalence of coronary artery disease and its risk factors in Kerala: a community-based cross-sectional study. *BMC Cardiovas Disord*. 2016;16:12–23.
12. Rose GA. The diagnosis of ischemic heart pain and intermittent claudication in field surveys. *Bull World Health Org*. 1962;27:646–658.
13. Mendis S, Thygesen K, Kuulasmaa K, et al. World Health Organization definition of myocardial infarction: 2008-09 revision. *Int J Epidemiol*. 2010;1–8.
14. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33(Suppl. 1):S62–S69.
15. Chobanian AV, Bakris GL, Black HR, et al. The Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 Report. *JAMA*. 2003;289:2560–2572.
16. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486–2497.
17. Misra A, Chowbey P, Makkar BM, et al. for Consensus Group. Consensus Statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. *J Assoc Phys India*. 2009;57:163–170.
18. Tamhane AR, Westfall AO, Burkholdera GA, et al. Prevalence odds ratio versus prevalence ratio: choice comes with consequences. *Statist Med*. 2016;35:5730–5735.
19. Yao ST, Hobbs JT, Irvine WT. Ankle systolic pressure measurements in arterial disease affecting the lower extremities. *Br J Surg*. 1969;56:676–679.
20. Ouriel K, McDonnell AE, Metz CE, et al. Critical evaluation of stress testing in the diagnosis of peripheral vascular disease. *Surgery*. 1982;91:686–693.
21. Fowkes FGR. The measurement of atherosclerotic peripheral arterial disease in epidemiological surveys. *Int J Epidemiol*. 1988;17:248–254.
22. Laing S, Greenhalgh RM. The detection and progression of asymptomatic peripheral arterial disease. *Br J Surg*. 1983;70:628–630.
23. Hiatt WR, Marshall JA, Baxter J, et al. Diagnostic methods for peripheral arterial disease in the San Luis Valley Diabetes Study. *J Clin Epidemiol*. 1990;43:597–606.
24. Murabito JM, Evans JC, Nieto K, et al. Prevalence and clinical correlates of peripheral arterial disease in the Framingham Offspring Study. *Am Heart J*. 2002;143:961–965.
25. Zheng Zhi-Jie, Sharrett AR, Chambless LE, et al. Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study. *Atherosclerosis*. 1997;131:115–125.
26. Allison MA, Criqui MH, McClelland RL, et al. The Effect of Novel Cardiovascular Risk Factors on the Ethnic-Specific Odds for Peripheral Arterial Disease in the Multi-Ethnic Study of Atherosclerosis (MESA). *J Am Coll Cardiol*. 2006;48:1190–1197.
27. Niazi K, Khan TH, Easley KA. Diagnostic utility of the two methods of ankle brachial index in the detection of peripheral arterial disease of lower extremities. *Catheter Cardiovasc Interv*. 2006;68:788–792.
28. Schroder F, Diehm N, Kareem S, et al. A modified calculation of ankle-brachial pressure index is far more sensitive in the detection of peripheral arterial disease. *J Vasc Surg*. 2006;44:531–536.
29. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. *Circ Res*. 2015;116:1509–1526.
30. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States. Results from the National Health and Nutrition Examination Survey. 1999–2000. *Circulation*. 2004;110:738–743.
31. Aboyans V, Criqui MH, McClelland RL, et al. Intrinsic contribution of gender and ethnicity to normal ankle-brachial index values: the Multi-Ethnic Study of Atherosclerosis (MESA). *J Vasc Surg*. 2007;45:319–327.
32. Hiatt WR, Hoag S, Hamman RF. Effect of diagnostic criteria on the prevalence of peripheral arterial disease: the San Luis Valley Diabetes Study. *Circulation*. 1995;91:1472–1479.
33. Ostchega Y, Paulose-Ram R, Dillon CF, et al. Prevalence of peripheral arterial disease and risk factors in persons aged 60 and older: data from the National Health and Nutrition Examination Survey 1999–2004. *J Am Geriatr Soc*. 2007;55(4):583–589.
34. Stoffers HE, Rinkens PE, Kester AD, et al. The prevalence of asymptomatic and unrecognized peripheral arterial occlusive disease. *Int J Epidemiol*. 1996;25:282–290.
35. Newman AB, Siscovick DS, Manolio TA, et al. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. Cardiovascular Heart Study (CHS) Collaborative Research Group. *Circulation*. 1993;88:837–845.
36. Criqui MH, Fronek A, Klauber MR, et al. The sensitivity, specificity, and predictive value of traditional clinical evaluation of peripheral arterial disease: results from noninvasive testing in a defined population. *Circulation*. 1985;71:516–522.
37. Leng GC, Fowkes FG. The Edinburgh Claudication Questionnaire: an improved version of the WHO/Rose Questionnaire for use in epidemiological surveys. *J Clin Epidemiol*. 1992;45(10):1101–1109.
38. Criqui MH, Fronek A, Barrett-Connor E, et al. The prevalence of peripheral arterial disease in a defined population. *Circulation*. 1985;71:510–515.
39. Subherwal S, Patel MR, Kober L, et al. Peripheral artery disease is a coronary heart disease risk equivalent among both men and women: results from a nationwide study. *Eur J Prev Cardiol*. 2015;22(3):317–325.
40. Hur DJ, Kizilgul M, Aung WW, et al. Frequency of coronary artery disease in patients undergoing peripheral artery disease surgery. *Am J Cardiol*. 2012;110(5):736–740.
41. Cho SW, Kim BG, Kim DH, et al. Prediction of coronary artery disease in patients with lower extremity peripheral artery disease. *Int Heart J*. 2015;56(2):209–212.
42. Eshcol J, Jebarani S, Anjana RM, et al. Prevalence, incidence and progression of peripheral arterial disease in Asian Indian type 2 diabetic patients. *J Diabetes Complications*. 2014;28(5):627–631.
43. Weragoda J, Seneviratne R, Weerasinghe MC, et al. A cross-sectional study on peripheral arterial disease in a district of Sri Lanka: prevalence and associated factors. *BMC Public Health*. 2015;15:829–836.
44. He Y, Jiang Y, Wang J, et al. Prevalence of peripheral arterial disease and its association with smoking in a population-based study in Beijing. *China J Vasc Surg*. 2006;44(2):333–338.
45. Hooi JD, Stoffers HE, Kester AD, et al. Risk factors and cardiovascular diseases associated with asymptomatic peripheral arterial occlusive disease. The Limburg PAOD Study. *J Primary Health Care*. 1998;16(3):177–182.
46. Aboyans V, Lacroix P, Lebourdon A, Preux PM, Ferrires J, Laskar M. The intra- and interobserver variability of ankle-arm blood pressure index according to its mode of calculation. *J Clin Epidemiol*. 2003;56:215–220.