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High prevalence of peripheral atherosclerosis in a rapidly developing country

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Abstract

Cardiovascular disease is rapidly increasing in developing countries experiencing epidemiological transition. We investigated the prevalence of peripheral atherosclerosis in a rapidly developing country and compared our findings with data previously reported in Western populations. A cardiovascular risk factor survey was conducted in 1067 individuals aged 25–64 randomly selected from the general population of Seychelles. High-resolution ultrasonography of the right and left carotid and femoral arteries was performed in a random subgroup of 503 subjects (245 men and 258 women). In each of the four arteries, arterial wall thickness (in plaque-free segments) and atherosclerotic plaques (i.e. focal wall thickening at least 1.0 mm thick) were measured separately. The prevalence of peripheral atherosclerosis was high in this population. For instance, at least one plaque ≥ 1.0 mm was found in, respectively, 34.9 and 27.5% of men and women aged 25–34 and at least one plaque ≥ 2.5 mm was found in, respectively, 58.2 and 36.9% of men and women aged 55–64. With reference to data found in the literature, the prevalence of carotid atherosclerosis appeared to be significantly higher in Seychelles than in Western populations. This study provides further evidence for the importance of cardiovascular disease in developing countries. Determinants should be identified and relevant prevention and control programs implemented.

Keywords: Atherosclerosis; Arteries; Carotid arteries; Ultrasonography; Developing countries

1. Introduction

Accumulating data support the view of an emerging epidemic of cardiovascular disease (CVD) in developing countries [1,2]. Increasing CVD in developing countries relate, among other factors, to ageing populations, changing lifestyles accompanying industrialisation and urbanisation and nutrition transition [1,3].

As developing countries will certainly not be able to afford the high costs of CVD treatments for large portions of their populations, appropriate preventive strategies should be promptly implemented after specific determinants of CVD epidemic in these countries have been identified [4,5].

In Seychelles, a survey conducted in 1989 demonstrated high levels of several cardiovascular risk factors (CVRF) in the general population [6–9]. Subsequently, a national program for the prevention and control of CVD was designed and implemented [10,11]. In 1994, a second independent population-based survey (‘Seychelles Heart Study II’) was conducted to assess trends in CVRF levels in the population. The survey also included high-resolution ultrasonography of the carotid and femoral arteries. This new non-invasive technique permits precise quantification of atherosclerotic changes in peripheral arteries and is now frequently used in observational studies or clinical trials on atherosclerosis [12]. Although many reports based on these measurements have been published, especially with regard to their relation with CVRF [13–28], data from non-selected populations are sparse and no such data have

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been collected systematically in populations from developing countries so far.

The aim of this study was therefore to determine the prevalence of persons with peripheral atherosclerosis in the general population of Seychelles and to subsequently compare these findings with data previously reported in Western populations.

2. Methods

2.1. General population

The Republic of Seychelles consists of 115 islands lying in the Indian Ocean, 1800 km east of Kenya and 1800 km north of Mauritius. The islands were first inhabited when French colonials settled in Seychelles in 1770, joined over the next decades by larger number of African slaves and indentured labourers (coming mainly from East and Central Africa and Madagascar) and, later, by small numbers of Indian and Chinese immigrants [29]. Eighty-nine percent of the total population lives on the largest island, Mahé. According to a census carried out in 1994, the total population was 73 442 with 49% aged less than 25 years and 45% aged 25–64. Although intermarriage has blurred racial differences in many Seychellois, ethnic descent of the population is considered to be predominantly African in 67%, Caucasian in 8%, Indian or Chinese in 2% and evidently mixed in 23% [6,30]. The opening of an international airport in 1971 was followed by a rapid increase of tourism, fast economic development (the gross domestic product per year and per inhabitant increased from $600 to 6565 from 1970 to 1994) and major changes in lifestyles [9,30]. CVD currently accounts for approximately 40% of the total mortality according to the vital statistics (all deaths in the country are certified by a doctor). Stroke mortality is higher in Seychelles than in several industrialised countries while ischemic heart disease mortality is intermediate (Table 1) [8,31,32]. Major tropical scourges such as malaria, leishmaniasis, bilharziasis, yellow fever, and sleeping sickness are unknown in Seychelles. Apart from a small private medical sector, medical care is delivered without fees to all residents within a national health system operated by the Ministry of Health.

2.2. Survey methods

The Seychelles Heart Study II was designed as a cross-sectional survey of the general population and detailed methods have been published elsewhere [30] (full text available on www.seychelles.net/smdj). The study protocol was approved by the review committee of the Ministry of Health. Selection of eligible subjects was performed using computerised population data from a census carried out in 1987, which were thereafter regularly updated by the local Ministry of Administration. A sex- and age-stratified sample of 1280 eligible subjects was randomly drawn from the population of 28 695 Seychellois aged 25–64 years and residing on the main island of Mahé. Eligible subjects were sent a letter to invite them to participate in the study. The subjects were free to participate and extensive information on the study was largely disseminated through the media and delivered on-site. Fifty-four subjects turned out to be dead or abroad at the time of the survey and were therefore excluded. Out of the remaining 1226 eligible individuals, 1067 (504 men and 563 women) attended the study, hence a participation rate of 87%. Among the 159 eligible persons who did not attend the study, letters were returned unopened by the postal services to the study centre for 38 (24%) suggesting that these persons had moved. The proportions of eligible participants who did not attend the survey were similar in all sex- and age-categories with the exception of a lower participation of men aged 25–34 years (76% participation). The survey took place from July to December 1994. During this period, 14 persons were invited to report to the study centre every day in a sequence determined by the alphabetical order of their family name. Bus transportation to the study centre, which did not exceed 1 h from any place in the island, was reimbursed.

A face-to-face structured questionnaire was administered to all participants by a team of nurses who had previous experience in the conduct of surveys. The questionnaire focused on CVD, CVRF and knowledge, attitudes and practices on cardiovascular health. Ethnicity was assessed according to the phenotypic appearance by a single examiner at the time the participants arrived and registered in the survey centre. Blood pressure, weight and height were measured according to common standards [33,34]. Several other tests (including comprehensive echocardiography, 12-lead resting

Table 1
Age standardised death rates (per 100 000) for ischemic heart disease (IHD, code 27 from ICD-9) and cerebrovascular disease (CBVD, code 29 from ICD-9) in selected developing and industrialised countries in the late 1980s according to the WHO data [31]

	IHD		CBVD	
	Men	Women	Men	Women
Seychelles (1985–1987)	104	97	118	69
San Tomé[a] (1984–1985)	16	18	45	54
Japan (1987)	32	17	72	51
Switzerland (1987)	105	40	40	30
US (1986)	172	86	35	31
UK (1987)	218	95	60	53

[a] Sao Tome is a little insular country of the west African coast which has not yet experienced a significant epidemiological transition.

electrocardiogram, blood thiamine concentration, extensive serum lipid analyses and urinary dipstick) were also performed and are described in detail elsewhere [30].

2.3. High-resolution arterial ultrasonography

High-resolution B-mode ultrasonography of the right and left carotid (CA) and femoral (FA) arteries was expected to be performed in approximately half of the study participants. This restriction was necessary as only up to 7 of the 14 convoked participants every day could materially be submitted to ultrasonography (vascular and cardiac ultrasonography lasted approximately 1 h per subject) [30]. Participants undergoing ultrasonography were selected randomly by matching each participant's rank of arrival at the study centre with a list of seven numbers (comprised between 1 and 14) randomly generated every day. Finally, 245 men and 258 women (47% of participants) underwent high-resolution arterial ultrasonography.

All scans were performed by the same examiner (FPe), a cardiologist with a long experience in ultrasonic exploration of arteries [35,36] and who had been previously specifically trained for the present procedure. This cardiologist was kept blind to all CVRF data throughout the study. The echographic system (Vingmed CFM 800C, Horten, Norway) was equipped with a mechanical 7.5 MHz annular phased array probe having a theoretical axial resolution of 0.3 mm. Except for image depth, settings of the system (e.g. image gain and compression) were maintained unchanged throughout the study. Calibration of the ultrasound system was verified several times during the study period and no adjustment was needed.

In this study, we followed the methodological recommendations made by Devereux who advised to measure intima–media thickness (IMT) 'avoiding segments with discrete atheromass' and to 'separately identify and measure atherosclerotic plaques' [37]. The examination protocol had therefore two distinct parts, the first one aimed to measure basal arterial wall thickness in specific arterial segments visually free of plaques (this part will subsequently be referred to as 'IMT protocol') while the second part intended to identify and quantify the largest atherosclerotic plaque on the whole range of the examined vessels (this part will subsequently be referred to as the 'plaque protocol'). All measurements were performed using a computer equipped with a digital frame-grabbing board and a specific software for arterial wall analysis (Eurequa™ 2.5, TSI, Meudon, France). Calibration of this system (along the vertical and horizontal axes) was checked daily with reference to distance markers on the echographic images and remained stable throughout the survey.

2.3.1. IMT protocol

When imaged perpendicularly with high-resolution ultrasonography, longitudinal views of arterial walls typically appear as two parallel lines. This echographic double-line pattern has proved to correspond to the lumen–intima and the media–adventitia histologic interfaces [38] so that the distance between these two lines represents the combined thickness of the intima and media layers of the arterial wall [39].

In this study, the best far-wall double-line images were obtained for the right and left common carotid arteries (20–40 mm prior to the central edge of flow divider) and the right and left superficial femoral arteries (20–40 mm after the central edge of flow divider). An end-diastolic frame (snapped at the onset of the QRS on the ECG monitoring) was downloaded on-line on the analysis computer. After further magnification, IMT was precisely measured using the software's automatic line edge detection capability [40]. Three measurements (sampled at the left, middle and right parts of the double-line image, respectively) were recorded on each artery and averaged. The arterial lumen diameter, defined as the distance between the near-wall intima–lumen interface and the far-wall intima–lumen interface, was measured using electronic calipers on the same image. From IMT and lumen diameter (LD) values, the walls-to-lumen ratio ($WLR = 2 \times IMT/LD$) and the cross-sectional wall area ($CSWA = [[\pi \times LD/2] + IMT]^2 - [\pi \times LD/2]^2$) were calculated.

2.3.2. Plaque protocol

The 'plaque protocol' consisted of a thorough scan of the right and left carotid artery (common part from the base of the neck, bifurcation and first 20 mm of the internal and external branches from the central edge of flow divider) and the right and left femoral arteries (common part from the groin, bifurcation and first 20 mm of the superficial and deep branches from the central edge of flow divider). Multiple views were performed to identify all atherosclerotic plaques along the defined artery segments. A plaque was defined as a focal wall thickening of at least 1.0 mm. Plaques were imaged in centred longitudinal view (crossing the most prominent part of the lesion) and in transversal view (at the site of the largest lumen stenosis) and corresponding frozen frames were downloaded on-line on the computer. When more than one plaque were present on the same arterial tree, only the thickest one (as assessed on the longitudinal view) was recorded.

Measurements of plaques were performed after survey completion by the examiner who was still blind to CVRF data. Several measurements were performed for all recorded plaques using the Eurequa™ software and

Table 2
Levels of selected cardiovascular risk factors by gender[a]

	Men ($n=245$)				Women ($n=258$)				P
	Percentage or mean	S.D.	Minimum	Maximum	Percentage or mean	S.D.	Minimum	Maximum	
Age (years)	43.6	11.2	25	64	44.3	11.6	25	64	0.47
Blacks (%)	66.5	–	–	–	67.4	–	–	–	0.85
Smokers (%)	39.5	–	–	–	8.5	–	–	–	‡
BMI (kg/m^2)	24.6	4.5	16	56	27.0	5.6	15	46	‡
Systolic BP (mmHg)	138	23	88	238	132	25	90	248	†
Diastolic BP (mmHg)	91	14	60	165	86	15	59	125	‡
Total chol (mmol/l)	5.5	1.3	2.5	10.2	5.7	1.2	3.1	8.9	*
Triglycerides (mmol/l)	1.4	0.9	0.4	5.7	1.1	0.6	0.3	6.0	‡

[a] *, $P \leq 0.05$; †, $P \leq 0.01$; ‡ $P \leq 0.001$.

have been described in detail elsewhere [30]. Among these, maximum plaque thickness (i.e. the distance from the plaque–lumen interface to the media–adventitia interface) was measured on the longitudinal view using electronic calipers. Plaque and total vessel areas were planimetered on the transversal view and the resulting lumen stenosis computed.

2.3.3. Feasibility

Adequate images allowing IMT to be measured could be obtained in all 503 subjects for the common CA. Femoral arteries IMT could not be measured in two subjects (on both sides) because of excessively irregular and poorly defined double-line image. Noticeably, these two subjects had severe atherosclerosis with large plaques in all four examined sites. There was no missing data for the plaque protocol.

2.3.4. Reproducibility protocols

Reproducibility of IMT and maximum plaque thickness (MPT) measurements was tested in 20 randomly chosen participants who were re-examined by the same examiner 2–6 weeks after their first session, with the examiner kept blind to the first results and using the same protocol. Mean difference for paired IMT measurements was 3.3 ± 3.0 mm $\times 10^{-2}$ for carotid arteries and 3.3 ± 2.9 mm $\times 10^{-2}$ for femoral arteries (which represented, respectively, 6.5 and 8.4% of the corresponding IMT values). Correlation coefficients for the two sets of measurements were 0.88 and 0.80, respectively. The reproducibility of the MPT measurements was examined with the κ-statistic after having classified each artery in four lesion categories (i.e. 1, no plaque; 2, plaques measuring 1.00–1.49 mm; 3, 1.50–2.49 mm; 4, 2.50 mm or more). Inter-rating agreement reached 70.0 and 87.5% (κ values of 0.51 and 0.71) for carotid and femoral arteries, respectively.

2.4. Statistical analysis

Statistics were performed using Stata™ 4.0 for Windows™ software (Stata Corp., College Station, TX, USA). Differences between two or more means were respectively assessed with unpaired t-test and one-way ANOVA, while differences between two or more proportions were respectively assessed with the Fisher's exact test and the χ^2-test. P values equal to or lower than 0.05 were considered statistically significant. When not stated otherwise, values mentioned in the text are means $\pm$ S.D.

3. Results

3.1.1. Study group characteristics

Table 2 displays characteristics of the subjects selected for ultrasonography. The distribution of age and black phenotype was similar in both genders. Men had higher prevalence of smoking (≥ 1 cigarette every day), higher systolic and diastolic BP and higher triglycerides concentration. Women had higher BMI and marginally higher total cholesterol concentration. The distribution of these characteristics was not statistically different between the 503 participants selected for ultrasonography and the 564 who were not.

3.1.2. Epidemiology of IMT and plaques in Seychelles

Table 3 lists the values of IMT, lumen diameter (LD), walls-to-lumen ratio (WLR) and cross-sectional wall area (CSWA) according to age and gender for each of the four investigated arteries. IMT, walls-to-lumen

Table 3
Values (mean ± S.D.) of intima–media thickness (IMT), lumen diameter (LD), walls-to-lumen ratio (WLR) and cross-sectional wall area (CSWA) by gender, age and artery[a]

		Men				*A*	Women				*A*	*B*
	(*n*)	25–34 (63)	35–44 (68)	45–54 (59)	55–64 (55)		25–34 (69)	35–44 (63)	45–54 (61)	55–64 (65)		
IMT ($mm \times 10^{-2}$)	Right carotid	44.0 ± 7.6	46.3 ± 8.8	50.6 ± 8.4	61.8 ± 11	‡	41.4 ± 6.6	44.6 ± 5.4	54.1 ± 11	57.2 ± 11	‡	0.27
	Left carotid	45.1 ± 6.4	49.1 ± 8.5	52.3 ± 8.6	63.1 ± 13	‡	43.8 ± 5.5	45.9 ± 6.4	55.7 ± 12	57.1 ± 11	‡	0.12
	Right femoral	37.9 ± 6.7	43.3 ± 6.6	47.7 ± 8.5	55.1 ± 11	‡	33.9 ± 7.7	38.1 ± 6.4	45.4 ± 7.1	49.2 ± 6.3	‡	‡
	Left femoral	38.0 ± 6.0	42.5 ± 6.7	46.1 ± 7.1	52.3 ± 10	‡	33.6 ± 7.9	37.1 ± 7.4	44.7 ± 6.0	47.1 ± 5.0	‡	‡
LD ($mm \times 10^{-2}$)	Right carotid	558 ± 49	565 ± 61	553 ± 51	577 ± 69	0.14	534 ± 55	523 ± 41	530 ± 58	542 ± 59	0.26	‡
	Left carotid	550 ± 41	566 ± 59	543 ± 52	572 ± 78	*	517 ± 45	505 ± 42	526 ± 56	547 ± 48	‡	‡
	Right femoral	609 ± 80	607 ± 69	619 ± 77	635 ± 82	0.19	486 ± 58	495 ± 61	537 ± 67	559 ± 63	‡	‡
	Left femoral	599 ± 73	602 ± 69	610 ± 74	632 ± 70	0.55	483 ± 58	495 ± 63	530 ± 72	560 ± 57	‡	‡
WLR (%)	Right carotid	13.6 ± 2.2	14.1 ± 2.4	15.5 ± 2.7	17.7 ± 2.8	‡	13.5 ± 1.9	14.6 ± 1.7	17.0 ± 3.0	17.5 ± 3.3	‡	0.10
	Left carotid	14.1 ± 1.7	14.8 ± 2.3	16.2 ± 2.4	18.1 ± 3.3	‡	14.5 ± 1.5	15.4 ± 2.1	17.5 ± 3.4	17.3 ± 3.1	‡	0.10
	Right femoral	11.2 ± 2.0	12.5 ± 2.0	13.4 ± 2.1	14.9 ± 3.0	‡	12.3 ± 2.4	13.4 ± 2.3	14.5 ± 2.0	15.1 ± 1.8	‡	‡
	Left femoral	11.3 ± 1.8	12.5 ± 2.0	13.2 ± 1.9	14.3 ± 2.7	‡	12.2 ± 2.2	13.1 ± 2.6	14.5 ± 2.1	14.5 ± 1.6	‡	‡
CSWA (mm^2)	Right carotid	8.4 ± 1.8	9.0 ± 2.4	9.6 ± 1.8	12.5 ± 3.0	‡	7.5 ± 1.7	8.0 ± 1.3	10.0 ± 2.4	10.8 ± 2.3	‡	‡
	Left carotid	8.5 ± 1.5	9.5 ± 2.1	9.8 ± 2.1	12.7 ± 3.6	‡	7.8 ± 1.4	8.0 ± 1.4	10.2 ± 2.6	10.8 ± 2.5	‡	‡
	Right femoral	7.8 ± 1.9	8.9 ± 1.8	10.1 ± 2.6	12.0 ± 3.0	‡	5.6 ± 1.7	6.4 ± 1.5	8.4 ± 1.9	9.5 ± 2.0	‡	‡
	Left femoral	7.6 ± 1.7	8.6 ± 1.8	9.6 ± 2.2	11.3 ± 2.7	‡	5.5 ± 1.9	6.2 ± 1.7	8.1 ± 1.6	9.0 ± 1.5	‡	‡

[a] *A*, one-way ANOVA for age; *B*, *t*-test for gender (all ages together); *, $P \leq 0.05$; †, $P \leq 0.01$; ‡ $P \leq 0.001$.

ratio and cross-sectional wall area of carotid and femoral arteries were all significantly associated with age (in both genders) while the relation of lumen diameter with age was less consistent (especially in men). All values were higher in men than women although carotid IMT and walls-to-lumen ratio were not statistically different between genders.

Table 4 lists the proportion of arteries with at least one plaque while Fig. 1 displays the proportions of subjects with at least one plaque (in any of the four examined arteries) by gender, age group and plaque thickness. Carotid and femoral plaque prevalence were strongly associated with age (in both genders) and with male sex, irrespective of plaque size. At least one plaque ≥ 1.0 mm was found in, respectively, 34.9 and 27.5% of men and women aged 25–34 and these numbers reached, respectively, 92.7 and 89.2% in men and women aged 55–64. Largest plaques (≥ 2.5 mm) were found in 9.5% of men aged 25–34 (none in women) and in, respectively, 58.2 and 36.9% of men and women aged 55–64 years. Individuals with only small plaques (1.0–1.4 mm) had them more in their carotid than femoral arteries (26.0 vs. 10.4%; $P < 0.0005$) while individuals with large plaques (2.5 mm or more) had them more in their femoral than carotid arteries (9.9 vs. 16.7%; $P < 0.002$), suggesting a different time-course of atherosclerosis in these two territories.

3.1.3. Comparison with plaque prevalence data originating from industrialised countries

Table 5 compares the prevalence of carotid atherosclerosis in Seychelles and in Western populations. We could identify four studies from Western countries (US, Italy, France and Finland) which were population-based, reached satisfactory participation rates, and used measurement protocols compatible with our study [13,41–43]. To permit valid comparisons, prevalence of carotid atherosclerosis in Seychelles were each time calculated using same or similar categories of gender, age and lesion size as in the study taken for comparison.

Carotid atherosclerosis was systematically found to be more frequent in Seychelles than in Western countries within all categories of age, gender and plaque size used to define atherosclerosis. Few exceptions concerned categories with small numbers of subjects (hence having poor statistical power to demonstrate a difference) or categories for which Western subjects were significantly older than Seychellois subjects (in the American study). Prevalence differed particularly largely when comparing Seychelles individuals to Italian or Finnish subjects, both for small lesions occurring before age 50 or for large lesions occurring after age 40. In these instances, prevalence of carotid atherosclerosis was often found to be several times higher in Seychelles than in the considered Western populations.

Table 4
Proportions of subjects with at least one plaque by gender, age, plaque thickness and artery[a]

		Men				*A*	Women				*A*	*B*
	(*n*)	25–34 (63)	35–44 (68)	45–54 (59)	55–64 (55)		25–34 (69)	35–44 (63)	45–54 (61)	55–64 (65)		
Plaque ≥1.0 mm (%)	Right carotid	17.5	39.7	62.7	70.9	‡	17.4	30.2	44.3	58.5	‡	*
	Left carotid	14.3	38.2	54.2	65.5	‡	10.1	22.2	36.1	61.5	‡	*
	Right or left carotid	23.8	52.9	71.2	81.8	‡	21.7	36.5	54.1	76.9	‡	*
	Right femoral	15.9	29.4	50.8	70.9	‡	5.8	20.6	29.5	60.0	‡	†
	Left femoral	15.9	27.9	57.6	63.6	‡	8.7	22.2	36.1	55.4	‡	*
	Right or left femoral	23.8	39.7	64.4	72.2	‡	13.0	33.3	44.3	70.8	‡	*
	Carotid or femoral	34.9	66.2	81.4	92.7	‡	27.5	54.0	67.2	89.2	‡	*
Plaque ≥1.5 mm (%)	Right carotid	4.8	7.4	25.4	56.4	‡	1.4	9.5	21.3	33.8	‡	0.10
	Left carotid	1.6	11.8	25.4	52.7	‡	1.4	4.8	8.2	29.2	‡	‡
	Right or left carotid	6.4	16.2	35.6	67.3	‡	2.9	11.1	27.9	44.6	‡	*
	Right femoral	9.5	22.1	39.0	63.6	‡	2.9	12.7	19.7	46.2	‡	†
	Left femoral	9.5	20.6	47.5	61.8	‡	2.9	7.9	23.0	49.2	‡	‡
	Right or left femoral	15.9	30.9	55.9	70.9	‡	4.4	17.5	27.9	61.5	‡	‡
	Carotid or femoral	19.1	38.2	64.4	85.5	‡	7.3	27.0	42.7	67.7	‡	*
Plaque ≥2.5 mm (%)	Right carotid	3.2	2.9	5.1	21.8	‡	0.0	0.0	8.2	9.2	‡	0.10
	Left carotid	0.0	1.5	8.5	25.5	‡	0.0	0.0	1.6	13.8	‡	*
	Right or left carotid	3.2	4.4	11.9	38.2	‡	0.0	0.0	9.8	16.9	‡	*
	Right femoral	3.2	5.9	18.6	29.1	‡	0.0	1.6	6.6	10.8	*	‡
	Left femoral	4.8	7.4	23.7	27.3	†	0.0	0.0	6.6	27.7	‡	*
	Right or left femoral	7.9	8.9	33.9	47.3	‡	0.0	1.6	8.2	32.3	‡	‡
	Carotid or femoral	9.5	11.8	44.1	58.2	‡	0.0	1.6	18.1	36.9	‡	‡

[a] *A*, χ^2-test for age; *B*, Fisher's exact test for gender (all ages together); *, $P \leq 0.05$; †, $P \leq 0.01$; ‡, $P \leq 0.001$.

Table 5
Prevalences of carotid atherosclerosis in Seychelles and in selected Western populations[a]

Country (author)	Sex and age of subjects				Definition of plaque	Scanning range	Prevalence (%)			*A*
	Western (*n*)		Seychelles (*n*)				Western	Seychelles	S/W ratio	
United States (O'Leary) [41]	M 65–69	(688)	M 55–64	(55)	Stenosis <25%	dCCA+BIF+pICA	67.9	81.8	1.2	*
	M 65–69	(688)	M 55–64	(55)	Stenosis ≥25%	dCCA+BIF+pICA	28.1	27.3	1.0	n.s.
	W 65–69	(1126)	W 55–64	(65)	Stenosis <25%	dCCA+BIF+pICA	54.2	76.9	1.4	‡
	W 65–69	(1126)	W 55–64	(65)	Stenosis ≥25%	dCCA+BIF+pICA	22.8	24.6	1.1	n.s.
Italy (Prati) [42]	M 30–39	(101)	M 30–39	(75)	Thickness ≥1.0 mm	dCCA+BIF+pICA	1.0	34.7	35.0	‡
	M 40–49	(135)	M 40–49	(63)	Thickness ≥1.0 mm	dCCA+BIF+pICA	7.4	71.4	9.6	‡
	M 50–59	(112)	M 50–59	(54)	Thickness ≥1.0 mm	dCCA+BIF+pICA	36.6	64.8	1.8	‡
	W 30–39	(112)	W 30–39	(73)	Thickness ≥1.0 mm	dCCA+BIF+pICA	1.0	27.4	27.4	‡
	W 40–49	(127)	W 40–49	(58)	Thickness ≥1.0 mm	dCCA+BIF+pICA	3.9	44.8	11.5	‡
	W 50–59	(124)	W 50–59	(66)	Thickness ≥1.0 mm	dCCA+BIF+pICA	9.7	59.1	6.1	‡
	M 40–69	(337)	M 40–64	(143)	Stenosis ≥40%	dCCA+BIF+pICA	2.1	4.7	2.2	n.s.
	W 40–69	(355)	W 40–64	(157)	Stenosis ≥40%	dCCA+BIF+pICA	0.8	4.3	5.1	*
France (Bonithon–Kopp) [13]	W 45–54	(517)	W 45–54	(61)	Thickness ≥0.75 mm	CCA+BIF	39.1	55.7	1.4	*
	W 45–54	(517)	W 45–54	(61)	Thickness ≥1.75 mm	CCA+BIF	8.7	21.3	2.4	*
Finland (Salonen) [3]	M 42	(92)	M 38–46	(52)	Thickness ≥1.2 mm	CCA+BIF	14.1	48.1	3.4	‡
	M 42	(92)	M 38–46	(52)	Stenosis ≥20%	CCA+BIF	0.0	13.5	∞	‡
	M 60	(105)	M 56–64	(51)	Thickness ≥1.2 mm	CCA+BIF	81.9	76.5	0.9	n.s.
	M 60	(105)	M 56–64	(51)	Stenosis ≥20%	CCA+BIF	4.8	35.3	7.4	‡

[a] Prevalence of carotid atherosclerosis in Seychelles were calculated using same categories of gender, age and lesion size (thickness or degree of stenosis) as in the compared populations. M, men; W, women; CCA, common carotid artery; dCCA, distal common carotid artery; BIF, carotid bifurcation; pICA, proximal internal carotid artery; other abbreviations as in Table 3; A, Fisher's exact test for difference; *, $P \leq 0.05$; †, $P \leq 0.01$; ‡, $P \leq 0.001$; n.s., non-significant ($P > 0.05$).

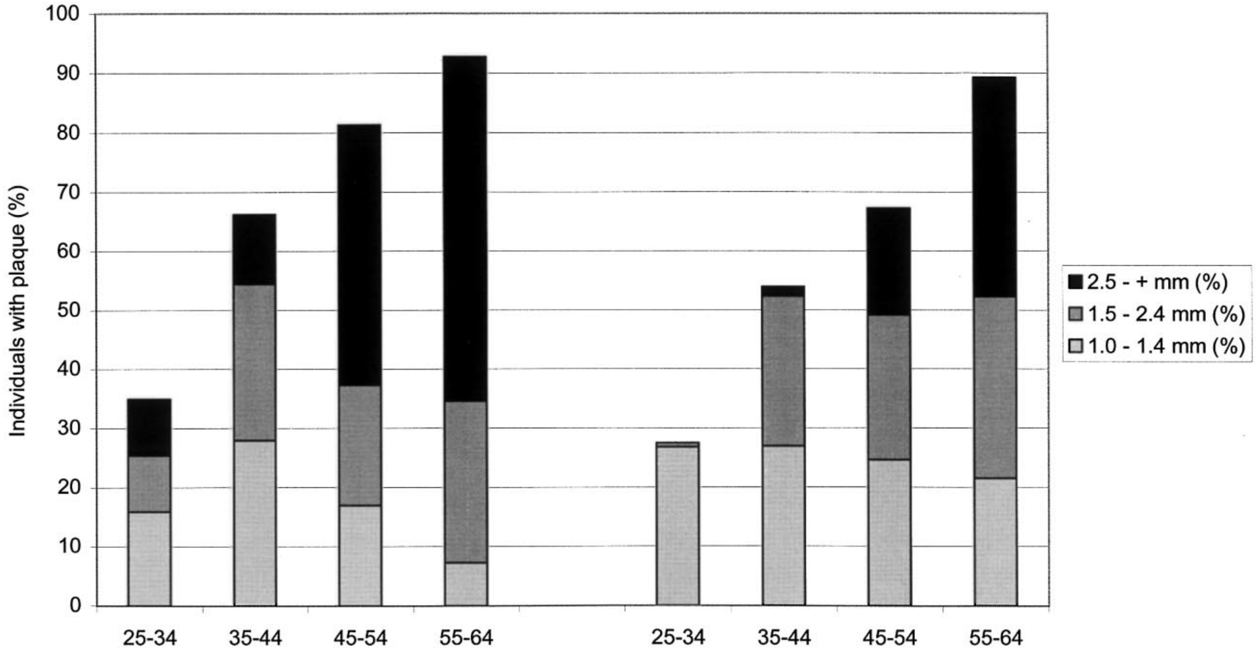

Fig. 1. Proportions of men (left) and women (right) with carotid or femoral atherosclerosis (at least one carotid or femoral plaque) by gender, age, plaque thickness and artery.

4. Discussion

This study aimed at quantifying peripheral atherosclerosis in the general population of a developing country. We used high-resolution ultrasonography and measured arterial wall thickness (IMT) and atherosclerotic plaque prevalence in carotid and femoral arteries. The study included fairly large numbers of subjects of both genders and several age categories, and participation rate was high.

4.1.1. IMT measurement

The IMT measurement protocol used in this study followed the recommendations recently made by Devereux et al. to measure IMT by avoiding segments with discrete atheromass and to separately identify and measure atherosclerotic plaques [37]. Furthermore, we systematically measured IMT in rectilinear segments, thereby avoiding sites with complex blood rheology such as turns or bifurcations [44]. It is now well known that some lipid deposition often occurs early in such atherosclerosis-prone regions but the true significance of these changes is still debated and could be considered physiological ('eccentric intimal thickening') [45]. This methodological approach (used here for the first time in a large population-based study) should permit to better distinguish arterial wall changes due to atherosclerosis or hypertrophy and to investigate the factors associated with each of these pathologic processes separately.

Our data confirm that IMT is associated with age. In our series, IMT was larger by 30–45% in the oldest than youngest subjects (depending on gender and arterial territory). Previous histological studies of plaque-free arterial segments have shown that this ageing phenomenon mainly relates to a proliferation of collagen fibres and smooth muscle cells in the intima and media layers, together with quantitative and qualitative alterations of the matrix [44,46,47]. Despite arterial wall thickening, lumen diameter (LD) tended to be larger in older than younger subjects and external arterial diameter (LD + [2 × IMT]) was associated with age for both carotid and femoral arteries and for both genders ($P < 0.001$). This association of peripheral artery diameter with age, which has already been described by others [48–50], was weaker than the association of IMT with age so that both the walls-to-lumen ratio and the cross-sectional wall area were associated with age, with respective proportionate changes of up to 33 and 70% between the 25–34 and 55–64 age categories.

As previously mentioned, few data are available in general populations on truly 'basal' IMT (i.e. sampled in segments visually free of atherosclerotic plaques). Table 6 nevertheless lists some average IMT reported in several Western selected populations [51–54]. Although IMT values appeared to be lower in our series than in these studies, this most probably relates to our option to sample IMT away from any focal thickening. This explanation is supported by the fact that Gariepy, who is the only cited author to use the same measurement method as that used in this study, obtained IMT values very close to ours. Although this needs confirmation, basal IMT values might be similar in the Seychelles and Western populations.

4.1.2. High prevalence of peripheral atherosclerosis

Prevalence of subjects with at least one carotid plaque appeared to be at least twice as high in Seychelles as in several Western populations after adjustment for age and gender. In selected instances, particularly for young subjects, prevalence of carotid atherosclerosis was up to several times more frequent in Seychelles than in Western populations of same age and gender. Although this descriptive study cannot provide definitive explanations for this discrepancy, areas for discussion include methodological issues, prevalence of classical CVRF in the population and hypothetical conditions likely to have accelerated atherosclerosis in this population.

An overestimation of the prevalence of subjects with plaques in Seychelles is not likely for several reasons. Indeed, the use of a sophisticated echographic system, the protocol requirement to visualise each plaque in two perpendicular planes, the plaque measurements made after study completion based on videotaped images and the frequent controls of the system calibration should all have minimised the risk of an overestimation of the measurements and false-positive findings. On the other hand, an underestimation of the prevalence of carotid atherosclerosis might have occurred in the cited studies from Western countries as these studies were performed several years ago and used potentially less discriminative echographic systems. In this situation, one would nevertheless assume that large lesions would not have been easily missed so that a presumed underestimation in the plaque prevalence would have occurred predominantly for small lesions. This is clearly not the case here, as we found higher prevalence of subjects with both small and large plaques in Seychelles compared to Western countries. These observations support the view that the prevalence of peripheral atherosclerosis found in Seychelles is valid and truly high.

The high prevalence of atherosclerotic plaques in Seychelles might be secondary to a particularly adverse CVRF profile in this population. The prevalence of the main CVRF in the Seychelles population has been thoroughly investigated in the two population-based surveys conducted in 1989 [6–8,32,55] and in 1994 [30] and, as in the WHO-MONICA project, have been age-standardized to the world population for individuals aged 35–64 years. In the 1994 Seychelles Heart Study II, such prevalence in men and women were, respectively, 41.7 and 27.4% for hypertension (BP $\geq$ 160/95 mmHg), 41.2 and 8.4% for smoking (at least one cigarette per day), 9.7 and 33.6% for obesity (BMI ≥ 30 kg/m^2), 7.8 and 4.6% for diabetes (fasting glycosuria or history of diabetes), 21.1 and 31.6% for hypercholesterolemia (cholesterol ≥ 6.5 mmol/l). These data demonstrate very high prevalence of hypertension and obesity (women), and fairly high prevalence of smoking (men), hypercholesterolemia and diabetes in Seychelles compared to Western countries [56,57] In addition, a larger proportion of the population had high serum lipoprotein (a) levels (>300 mg/l) in Seychelles than, for example, in Switzerland (38 and 25%, respectively) [55], Not unexpectedly in a rapidly developing country, sedentary lifestyle is also being adopted by an increasing proportion of the populations. As an example, 36.3% of men and of 7.0% women reported heavy exercise at work in 1989 compared to no more than 13.6 and 2.3% in 1994 ($P < 0.001$ for both). Overall, the markedly adverse CVRF profile documented recently in the Seychelles population is therefore consistent with high prevalence of peripheral atherosclerosis in Seychelles.

Other factors have been linked to high CVD frequency in developing countries and might therefore also account for high peripheral atherosclerosis in Seychelles.

Table 6
Average intima–media thickness (IMT; mean ± S.D.) reported in several Western populations[a]

Country (author)	Subjects	(n)	Artery site	IMT (mm × 10^{-2})
US (Crouse) [51]	M 45–49, (ARIC study participants)	1272	Both dCCA	77*
	M 60–64 (ARIC study participants)	1268	Both dCCA	93*
	W 45–49 (ARIC study participants)	1796	Both dCCA	68*
	W 60–64 (ARIC study participants)	1252	Both dCCA	83*
Sweden (Lemne) [52]	M 50 ± 6 (normotensive controls)	68	Right dCCA	67 ± 10
	M 50 ± 6 (normotensive controls)	68	Left dCCA	71 ± 13
Finland (Salonen) [53]	M 42 (population of Kuopio)	257	Both CCA	73 ± 26
	M 60 (population of Kuopio)	334	Both CCA	115 ± 49
France (Gariepy) [54]	M 42 ± 10 (healthy volunteers)	40	Right CCA	50 ± 6
		40	Right CFA	50 ± 8

[a] CFA, common femoral artery; other abbreviations as in Table 5; *, S.D. not available.

Dietary factors have strong relationship with CVD and special diet characteristics could be involved in the high peripheral atherosclerosis found in Seychelles. Similarly to other developing countries [58,59], Seychelles currently experiences rapid dietary transition. It is characterised by a rapid increase in the intake of fat (especially from cheap vegetable hydrogenated oils rich in saturated fats), a decline in complex carbohydrates consumption, an increase in salt intake (partly subsequent to increased consumption of processed food) and a decrease in dietary fibres and micro-nutrients intake. In Seychelles, the energy intake derived from fats increased from 21 to 26% over a decade according to serial household expenditure surveys in 1983/1984 and 1992/1993 [60]. In addition, consumption of fruits and vegetables has been shown to be low in Seychelles [60], which related, e.g. to low thiamin blood levels in the population [61]. It could then be speculated that the current diet in Seychelles provides limited amounts of those micronutrients and antioxidants, which are increasingly believed to protect against atherosclerosis.

The recently reported inverse relation between birth size and CVD in later life ('Barker hypothesis') may have special relevance to developing countries [62]. If this effect can be adequately validated, populations of developing countries would be at enhanced cardiovascular risk as substantial numbers of poorly nourished infants born in the past decades would nowadays reach ages at which atherosclerosis becomes apparent. Although severe famines are uncommon in tropical countries, some degree of undernutrition has probably occurred in segments of the Seychelles population in the past so that such a mechanism could play a role in the high prevalence of peripheral atherosclerosis found in this study.

Mounting evidence relates infectious organisms (e.g. *Chlamydia pneumoniae*) to coronary heart disease and, specifically, to atherosclerotic plaques [63,64]. It is however still unknown whether such organisms could have a role at the initiation of the disease, in the progress of the disease or in the complicating events so that speculations on a role of such agent in the aetiology of atherosclerosis in developing countries seems premature. This hypothesis could nevertheless have special relevance to developing countries where infectious diseases account for a particularly large burden of disease and antibiotics have traditionally been used less extensively than in Western countries.

Ethnic factors may also be considered to explain high prevalence of peripheral atherosclerosis in Seychelles, as much of the population is of predominantly African descent and CVD (or CVRF) generally seem to be more frequent in African than Caucasian populations [65–67]. Sub-group analysis of our data did not however support substantial difference in peripheral atherosclerosis prevalence between persons of African or Caucasian descent. For instance, 61.4% of black Africans versus 70.0% of white Caucasian were, respectively, found to have at least one plaque (carotid or femoral of at least 1 mm) in this survey ($P = 0.31$). These results have admittedly inherent limited significance due to low statistical power (small number of Caucasian subjects) and lack of adjustment for concomitant CVRF. However, carotid atherosclerosis was similarly not found to be more prevalent in African Americans than white Americans in the ARIC study [68].

Some genetic factors, other than those determining ethnicity, could also be involved in the high prevalence of atherosclerosis in Seychelles. Although such considerations remain purely speculative due to the lack of data on this aspect in Seychelles, the insular situation of the country has potential for amplification of such phenomena. Moreover, genetic factors that predispose to CVRF (e.g. those modulating lipoprotein (a) levels, central obesity, glucose intolerance or dyslipidemia) have been shown to be particularly detrimental in populations experiencing rapid environmental changes (e.g. leading to weight gain, rise in plasma cholesterol and blood pressure levels), which may point to detrimental environment–genetic interactions [1,69].

Findings of this study have important public health significance. It has been established that peripheral atherosclerosis detected by ultrasonography closely relates to coronary atherosclerosis [16,22,28,70,71], subsequent coronary [17,24] or cerebral [24,72] ischemic events, cardiovascular mortality [73] and all cause mortality [14]. The high prevalence of peripheral atherosclerosis (particularly carotid atherosclerosis) in Seychelles is consistent with high stroke mortality (Table 1). However, ischemic heart disease mortality seemed no higher in Seychelles than in Western countries. Several hypotheses can be speculated to explain this discrepancy. Under-reporting of ischemic heart disease could occur in Seychelles due to limited availability of sophisticated diagnostic tools. Second, specific protective factors could be present in Seychelles which decrease ischemic heart disease incidence or case-fatality, e.g. by protecting the coronary tree from plaque occurrence, decreasing the tendency of plaques to rupture or exhibiting antithrombotic properties. Third, prevalence of peripheral atherosclerosis in Seychelles could have reached high levels only recently and incidence of coronary events would subsequently be expected to increase in a near future.

In conclusion, prevalence of peripheral atherosclerosis was found to be high in the adult population of Seychelles, possibly higher than in several Western populations. These findings emphasise the need to identify specific causal factors and to implement promptly appropriate preventive and control measures. These observations could generalise to other developing countries currently experiencing epidemiological transition.

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