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Distribution of a subclinical marker of cardiovascular risk, the ankle brachial index, in a rural African population: SASPI study

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Abstract

Background—In sub-Saharan Africa, hypertension and stroke are emerging as an important cause of death and disability whereas coronary heart disease appears to still be uncommon. The aim of our study was to measure for the first time in an African population the ankle brachial index which is known to be a good marker of subclinical atheroma and of the risk of future cardiovascular events.

Methods—The study was part of the Southern African Stroke Prevention Initiative (SASPI). It comprised a cross-sectional survey conducted in rural north-east South Africa in the sub-district of Agincourt in which the demography of the population has been closely monitored. A stratified sample of 10 villages were selected and within these a random sample was chosen of 526 men and women 35 years and older. Subjects were visited on up to three occasions to be interviewed and have a clinical examination by specially trained nurses. This included assessment of cardiovascular risk factors and measurement of the ankle brachial index (ABI) (ratio of ankle: brachial systolic pressure) using a Doppler ultrasound machine.

Results—The sample comprised 322 subjects in which the mean ABI (lower of either leg) was 1.05 in both men and women. The distribution of ABI was negatively skewed and a low ABI of 0.9, indicative of significant atheroma and higher cardiovascular risk, increased with age from 3.9% in 40–49 year olds to 39.7% in those 70 years and older. Lower ABI was related to current cigarette smoking ($p = 0.02$) and higher systolic and diastolic blood pressure ($p < 0.01$, $p = 0.02$ respectively) but not total cholesterol levels which were relatively low in this population (mean 4.47 mmol/L).

Conclusion—The distribution of the ABI in this rural African population was very similar to that reported in Western populations and suggests that this population has subclinical peripheral atheroma and is at increased risk of future cardiovascular events, thus providing further evidence of an epidemiological transition towards cardiovascular disease.

Keywords

Cardiovascular disease; subclinical; peripheral arterial disease; ankle brachial index; cross sectional survey; rural; sub-Saharan Africa; South Africa

INTRODUCTION

In many developing countries, coronary heart disease and stroke are emerging as major causes of morbidity and mortality.^{1,2} Such deaths account for around two thirds of worldwide mortality from cardiovascular disease and stroke and for about one quarter of total mortality in the developing world.³ This epidemiological transition from a predominant burden of infectious diseases to one of chronic diseases would appear to be dependent upon complex interactions between genetic, environmental and lifestyle factors. The emergence of chronic vascular diseases commonly begins with an increase in hypertension and related conditions, such as haemorrhagic stroke, followed by atherosclerotic conditions such as coronary heart disease and ischaemic stroke.^{2,4,5}

Among the population in sub-Saharan Africa, valid figures on mortality and morbidity from cardiovascular and cerebrovascular diseases are not available.⁶ Reviews of studies of hospital admissions and postmortems in different countries have concluded that coronary heart disease and stroke were negligible in the 1950s and 60s.⁶⁻⁸ More recently, stroke may be emerging as an important cause of death⁹ and disability^{10,11} whereas coronary heart disease appears to have shown only a modest increase and may still be uncommon.^{12,13} Lifestyle surveys among black South Africans however indicate that many populations have a moderate to high prevalence of cardiovascular risk factors, including hypertension, total cholesterol, smoking (especially in men), diabetes, and obesity (especially in women).^{12,14,15}

In the Agincourt sub district of Limpopo Province in the rural northeast of South Africa, we have shown recently as part of the Southern African Stroke Prevention Initiative (SASPI) that the prevalence of stroke was higher than previously documented in Africa.¹⁰ Cardiovascular diseases appeared to be still relatively uncommon but we wondered if there was any evidence of subclinical atheroma implying an impending future risk of ischaemic cardiovascular events. Also we wished to find out for the first time in a developing rural community if there was any evidence of peripheral arterial disease in the legs. In a prevalence survey of cardiovascular risk factors we therefore measured the ankle brachial index which is known to be a good marker of subclinical peripheral arterial disease and the risk of future cardiovascular events.¹⁶

METHODS

Setting

The Agincourt sub-district is in South Africa's rural north-east, adjacent to Mozambique, where the University/Medical Research Council Rural Public Health and Health Transitions Research Unit has been monitoring causes of death, births and migration in a population of around 70,000 people since 1992¹⁷ providing a well categorised sampling frame. The sub-district has 21 villages of varying sizes and is densely populated at about 170 persons per sq km. Electricity is available in most villages, but not all households, while access to clean water is severely limited. There is high unemployment and considerable labour migration, especially among men but increasingly in women. Household plots are too small for subsistence agriculture, although crops supplement the family diet.

Sample recruitment

In selecting our sample, the Agincourt villages were stratified by size (less than 500 households, and 500 households or more) and by whether the village was predominantly a formal settlement (officially recognised) or an informal settlement (settled following an influx of refugees during the Mozambican civil war). Ten villages were randomly selected: four informal, three small formal, and three large formal villages. A 10% random sample of the population (excluding migrant workers) aged 35 years or older in the selected villages provided 526 individuals (representing 3% of the 16,705 sub-district population aged 35 years or older).

The only means of communication was through visiting households and we made three attempts to visit each individual. If individuals were found to be ineligible (for example, too young, or not currently resident) they were replaced from a reserve random sample. Information on age, gender and household asset score were available from the Agincourt database. The household asset score is based on the type and size of dwelling; access to water and electricity; appliances and livestock owned; and transport available.

We obtained community assent from the village headman and through community meetings, before starting work in a village. Following thorough explanation, informed consent was sought from each participant. Ethics committee approval was granted by both the London School of Hygiene and Tropical Medicine (No. 755) and the University of the Witwatersrand (M02-04-63).

Interview and clinical examination

In 12 months from July 2002, two specially trained senior nurses from the local community carried out interviews and clinical examinations. They were trained by a member of staff from the Medical Research Council which carried out the South African Demographic and Health Survey.^{14,15} They were trained in the measurement of the ankle brachial index by one of us (MC). The interview covered a past history of cardiovascular symptoms, diabetes, hypertension, and smoking. The nurses measured height with the participant barefoot using a stadiometer, and weight with the participant barefoot and wearing light clothing. Waist circumference was measured with a tape 2.5cms above the umbilicus.

Sitting blood pressure was measured using an OMRON 705CP blood pressure monitor and an appropriately sized cuff after the participant had been sitting for five minutes with their arm supported. Three measures were taken two to three minutes apart. Supine arm blood pressure was measured with the same monitor after the participant had been lying for 2 to 3 minutes. Ankle systolic pressures were measured in the posterior tibial artery of both legs using a Doppler ultrasound probe (Huntleigh Mini-Dopplex) and a Mandaus manual digital blood pressure monitor (PMS instruments) with the cuff placed just above the malleoli. The pulse was located using the Doppler probe and the cuff then inflated until the pulse was obliterated. The cuff was then deflated at a pre-set deflation speed and the digital reading stopped at the point when the pulse reappeared. The pressure reading was documented and the ankle brachial index calculated using the supine arm blood pressure.

A nonfasting venous blood sample was taken and transported in cold boxes, centrifuged locally, and transferred by courier to the University of the Witwatersrand Contract Laboratory Services. Analysis was done using the Roche Cobas Integra 400 System. Total and HDL cholesterol were measured using an enzymatic, colorimetric method, and plasma glucose was measured using an enzymatic reference method with hexokinase.

Data analysis

The ABI for each leg was calculated by dividing the ankle systolic pressure by the brachial pressure. The lower of the two indexes was taken as the measure of disease severity. The mean of the second two blood pressure measurements was used in the analysis of systolic and diastolic pressure. When the random glucose was above 11 mmol/l, a subsequent fasting sample was taken. Diabetes mellitus was diagnosed if participants had a fasting blood glucose of 6.1 mmol/l or more, or were on anti-diabetic treatment. Mean ABI according to age group was compared using ANOVA. The X^2 test for trend was used to examine associations between ABI group and age group. Finally, ANCOVA was used to calculate and compare age and sex adjusted ABI per tertile of risk factors. Homogeneity of variance assumption was tested when we performed either ANOVA or ANCOVA. All analyses were performed using SPSS version 12 for windows. Throughout all analyses a two sided p value 0.05 was taken to denote statistical significance.

RESULTS

In this cross-sectional survey, 402 out of the random sample of 526 individuals participated. The non responders included 87 who refused and 25 who missed appointments. Among the 402 participants, an ankle brachial index (ABI) could not be measured in 80 subjects, mostly because of non functioning equipment which could not be quickly and easily repaired. Thus 322 subjects were included in the analysis of ABI and comprised 252 women (78.3%) and 70 men (21.7%). The preponderance of women reflected a long-standing male bias in labour migration to jobs far from the study site. The mean (SD) age of the women was 53.5 (13.9) years and of the men was 58.5 (13.7) years. A comparison of the 322 who had their ABI measured with all 402 participants showed no difference in age, sex and distribution of cardiovascular risk factors.

The distribution of the ABI in all participants was similar in the right and left legs. Figure 1 shows the distribution in the right leg in which there was evidence of a negative skew with a few subjects having very low levels (< 0.7). Two subjects had a level of 1.4 which is often considered to be artefactual due to hardening of peripheral arteries associated with conditions such as diabetes mellitus. Taking the lower ABI of the left and right leg as the measure for each subject, the mean ABI (95% CI) adjusted for age was 1.046 (1.010, 1.081) in men and 1.044 (1.025, 1.062) in women. Given the relatively small number of men in the study and the similarity in ABI between the sexes, further analysis was conducted for men and women combined.

Table 1 shows that the mean ABI fell with increasing age (< 0.001) from a mean (95%CI) of 1.085 (1.049, 1.122) in those < 40 years of age to 0.971 (0.930, 1.012) in those ≥ 70 years of age. Likewise, the proportion with a low ABI of ≤ 0.9 increased with age so that over 25% of those 60 years or older had a low ABI. Surprisingly those < 40 years of age had a slightly higher proportion with a low ABI (8.6%) compared to those aged 40-49 years (3.9%), but otherwise an increasing trend of low ABI with age was apparent ($p = 0.001$).

The relationship between the ABI and potential cardiovascular risk factors, adjusted for age and sex, is shown in Table 2. The number of diabetics was too few ($n=7$) to include in the analysis. No statistically significant difference was found in mean ABI between the top and bottom tertiles of total cholesterol but mean ABI was lower in the top tertile of HDL cholesterol ($p = 0.03$) resulting in a higher mean ABI in the top tertile of the total: HDL cholesterol ratio ($p = 0.03$). Mean ABI was higher in the top tertile of weight ($p < 0.001$), but not height, and correspondingly body mass index ($p < 0.01$) and waist hip ratio ($p = 0.04$) were related to higher ABI. Both systolic ($p < 0.01$) and diastolic blood pressure ($p = 0.02$) were associated with lower ABI in the top tertiles. The relatively small proportion of

individuals who currently smoked cigarettes (17.4%) also had a lower mean ABI compared to nonsmokers ($p = 0.02$).

DISCUSSION

In developed populations the ABI is considered to be a good marker of overall atherosclerosis as well as in the lower limb. A low ABI has been associated with increased frequency of other indicators of cardiovascular disease, such as angina pectoris¹⁸ and carotid stenosis,¹⁹ and with risk factors, such as cigarette smoking, hypercholesterolaemia and hyperfibrinogenaemia.¹⁸ In addition, a low ABI is related to an approximately two fold increased risk of death and major vascular events such as myocardial infarction and stroke.²⁰ Conventionally an ABI cut off point of 0.9 has been taken to distinguish high and low risk individuals, although the degree of risk would appear to relate to the ABI value at least up to 1.0 or 1.1 above which would be considered normal.¹⁹

Our study is the first to report on the distribution of the ABI in a sub-Saharan African population and, indeed, in any developing country. We found that the distribution was very similar to that found in Western populations. The skewing to lower levels, also observed in studies such as the Edinburgh Artery Study²¹ and Cardiovascular Health Study,¹⁸ may have been due to the effects of atheroma superimposed on a healthy normal distribution. The mean ABI would have been affected by the age and sex of the population and method of measurement but was comparable to that found in other studies.^{18,21,22} The decreasing ABI with age is also universally observed and is compatible with an increase in the prevalence and severity of atheroma with age.

We also found that the ABI was related to certain cardiovascular risk factors, notably cigarette smoking – known to be particularly important in the aetiology of peripheral atheroma.²³ Also a lower ABI was associated with both higher systolic and diastolic blood pressure. Blood pressure has not been shown consistently to be related to ABI²³ and any associations need to be interpreted with caution because of a lack of independence between the variables. ABI was not related to plasma total cholesterol which was not surprising given the low mean plasma levels, as has been observed in some other African populations.²⁴ High HDL cholesterol is known to be protective of atherosclerotic disease in Western populations but in this population was associated with lower ABI. This may have been a chance finding or may reflect different associations of lipids with disease in populations with naturally low fat diets compared to those in Western countries. Likewise the inverse associations with measures of obesity may be due to a similar phenomenon although in studies in the developed world, the relationship between peripheral arterial disease and obesity has been quite inconsistent between studies.²³ Furthermore, in our study, obesity was uncharacteristically unrelated to blood pressure²⁵ – an association commonly found in developed populations.

What are the significance of our findings on the ABI in relation to the epidemiological transition towards cardiovascular diseases that appears to be taking place in sub-Saharan Africa? Recent surveys in equatorial and southern Africa have shown that hypertension is relatively common in the population affecting for example, 29% of men and women in Ghana²⁶ and 30% in Tanzania.²⁷ Our own population study in Agincourt¹⁰ and others in Tanzania¹¹ have demonstrated that stroke occurs frequently, although not as commonly as in the West and with relatively more haemorrhagic than ischaemic cases. Despite an apparent increase in the frequency in some African populations of conventional cardiovascular risk factors, such as cigarette smoking and hypertension, the occurrence of overt coronary heart disease, such as myocardial infarction, remains extremely low.²⁴ The

findings of our study however suggests the existence of subclinical atheroma which could be a prelude to clinical disease.

There are several limitations to our study which need to be considered when interpreting the results. Firstly, due to logistical reasons our study sample was relatively small. In particular, the number of men was low due predominantly to their long term absence as migrant workers. We are confident that the measurement of the ABI was adequate due to the care taken to train staff and the quality control measures carried out during the study. However, breakdown of the Mandaus blood pressure instruments or the Doppler ultrasound machines meant that some subjects did not have an ABI measured resulting in their exclusion from this part of the study. Nevertheless, those included appeared to be representative of the whole study population. A further limitation was that we were not able to collect data on any symptoms of cardiovascular disease, such as angina or intermittent claudication, because validated questionnaires have not been developed for use in this population. Indeed, the advantage of using the ABI was that it is an objective indicator of disease.

Despite these limitations, this study is based on a proper population based sample in a deprived rural area and is the first to use the ABI to assess subclinical atheroma in a developing country. We have no reason to believe that the meaning and interpretation of the ABI should be any different in this population than in studies conducted in developed countries. In the Multi-Ethnic Study of Atherosclerosis in the United States, no significant differences were found in distributions of the ABI between ethnic groups, including black Americans, and in the relationship of ABI to other measures of subclinical atheroma such as carotid intima media thickness and coronary calcification.¹⁹ Recently another survey of risk factors in Limpopo Province, South Africa, found using the Framingham formulae a higher than expected risk of cardiovascular disease.²⁸ Our findings on the distribution of the ABI are also highly suggestive that atheroma is forming and that such populations are at increased risk of developing overt coronary heart disease in future.

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Figure 1. Distribution of ankle brachial index (ABI) in right leg in study sample (n = 322)

Table 1
Mean Ankle Brachial Index (ABI) and percentage 0.9 by age group

Age (years)	N	ABI Mean (95% CI)	ABI %	0.9
< 40	58	1.085 (1.049, 1.122)	8.6	
40-49	77	1.072 (1.045, 1.099)	3.9	
50-59	82	1.074 (1.039, 1.108)	11.0	
60-69	47	0.986 (0.934, 1.039)	25.5	
70+	58	0.971 (0.930, 1.012)	39.7	

Test for trend: $p < 0.001$ $p = 0.001$

Table 2
Mean Ankle Brachial Index (ABI) by tertile or presence of cardiovascular risk factor

Risk factor	Risk factor Mean (SD) or % (n)	Mean ABI (SD) ^a		P value
		In bottom tertile or with risk factor	In top tertile or without risk factor	
Total cholesterol (mmol/L)	4.47 (0.99)	1.05 (.017)	1.05 (.018)	0.81
HDL cholesterol (mmol/L)	1.47 (0.45)	1.07 (.016)	1.01 (.017)	0.03
Total/HDL cholesterol	3.35 (1.48)	1.02 (.017)	1.07 (.017)	0.03
Weight (Kg)	67.41 (14.51)	1.00 (.014)	1.09 (.015)	< 0.001
Height (cms)	161.99 (8.78)	1.02 (.016)	1.04 (.017)	0.36
Body mass index (Kg/M ²)	25.81 (5.73)	1.00 (.015)	1.07 (.015)	< 0.01
Waist hip ratio	0.84 (0.09)	1.02 (.014)	1.06 (.015)	0.04
Systolic blood pressure (mmHg)	133.37 (27.13)	1.07 (.014)	1.00 (.015)	< 0.01
Diastolic blood pressure (mmHg)	80.31 (13.58)	1.06 (.013)	1.01 (.015)	0.02
Smoking ^b	17.4 (56)	1.05 (.024)	1.00 (.021)	0.02

^a Adjusted for age and sex

^b Smoking: currently smoking cigarettes daily