Risk Factors Associated With Myocardial Infarction in Africa

The INTERHEART Africa Study

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***Background*—**Cardiovascular disease (CVD) is rising in low-income countries. However, the impact of modifiable CVD risk factors on myocardial infarction (MI) has not been studied in sub-Saharan Africa (SSA). Therefore, we conducted a case-control study among patients with acute MI (AMI) in SSA to explore its association with known CVD risk factors.

***Methods and Results*—**First-time AMI patients (n=578) were matched to 785 controls by age and sex in 9 SSA countries, with South Africa contributing ≈80% of the participants. The relationships between risk factors and AMI were investigated in the African population and in 3 ethnic subgroups (black, colored, and European/other Africans) and compared with those found in the overall INTERHEART study. Relationships between common CVD risk factors and AMI were found to be similar to those in the overall INTERHEART study. Modeling of 5 risk factors (smoking history, diabetes history, hypertension history, abdominal obesity, and ratio of apolipoprotein B to apolipoprotein A-1) provided a population attributable risk of 89.2% for AMI. The risk for AMI increased with higher income and education in the black African group in contrast to findings in the other African groups. A history of hypertension revealed higher MI risk in the black African group than in the overall INTERHEART group.

***Conclusions*—**Known CVD risk factors account for ≈90% of MI observed in African populations, which is consistent with the overall INTERHEART study. Contrasting gradients found in socioeconomic class, risk factor patterns, and AMI risk in the ethnic groups suggest that they are at different stages of the epidemiological transition. **(*Circulation.* 2005;112:3554-3561.)**

Key Words: apolipoproteins ■ cardiovascular diseases ■ myocardial infarction ■ population ■ risk factors

Africa is a continent of great diversity, extending from highly industrialized cities where people follow an urban Westernized lifestyle to remote rural regions with traditional lifestyles. Consequently, populations reflect different stages of the epidemiological health transition across Africa. Reliable data on cardiovascular diseases (CVD) and their risk factors are limited. Studies in the 1970s and 1980s suggested that the prevalence and death rates from coronary artery disease (CAD) were low in the black African population.[1–4] However, many reports from different African countries suggest that the spectrum and pattern of CVD along with their risk factors are changing rapidly, particularly in urban areas.[5–9]

Current knowledge about prevention of CVD is derived mainly from studies done in populations of European origin.[10] However, African populations include individuals of various ethnicities (black, colored, Asian, and European), and it is not known whether information derived from studies conducted in North America or Western Europe is applicable. The INTERHEART is an international, standardized, case-control study conducted in 52 countries, designed for the first time to assess the association of CVD risk factors and acute myocardial infarction (AMI).[11,12] The aim of the data analysis of INTERHEART Africa was to determine the strength of the association between various CVD risk factors individually and in combination with AMI in the overall African study population and in 3 African subgroups: black Africans, colored Africans, and European/other Africans. Differences in the CVD risk profiles among the 3 African groups will be explored to assess the stages of the health transition in each group.

Methods

The methods used in the INTERHEART study[11,13] were followed in 9 sub-Saharan Africa (SSA) countries to recruit 578 AMI incident cases and 785 age- and sex-matched controls in urban settings during 1999–2003. Patients admitted to the coronary care units or medical

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wards at hospitals of participating centers were screened to identify first incident AMI cases and were enrolled when possible within 24 hours of onset of symptoms. Criteria used for the definition of AMI have been described previously.[11] The controls included visitors or relatives of patients from noncardiac wards or unrelated visitors of cardiac patients. Alternatively, the controls were patients with conditions unrelated to the known AMI risk factors who were admitted to the same hospital as the cases.

Staff trained in study procedures utilizing standard manuals and videotapes collected the data at site visits. These data included demographic factors, socioeconomic status, and lifestyle factors including tobacco use, physical activity, and dietary patterns and were collected with the use of standardized INTERHEART questionnaires. Personal and family patterns of CVD and risk factors were recorded, and histories of hypertension and diabetes were self-reported. Questions were included about psychosocial conditions to identify depressive mood and psychological stress.[12] Height, weight, and waist and hip circumferences were measured with the use of standard protocols.[11]

Nonfasting blood samples (20 mL) were drawn soon after admission and centrifuged, and aliquots were frozen immediately at −20°C or −70°C. Courier services shipped samples from each site in nitrogen vapor tanks to the National Blood Storage Site, where they were stored in liquid nitrogen (−160°C). Blood analyses for total cholesterol, HDL cholesterol, and apolipoprotein B (ApoB) and apolipoprotein A-1 (ApoA-1), the latter 2 with the use of immunoturbidimetric assays on a Roche/Hitachi 917 apparatus with the Tina-quant ApoB ver-2 and Tina-quant ApoA-1 ver-2 kits (Roche Diagnostics GmbH, D-68298), were performed in Hamilton, Ontario, Canada. The ApoB method was standardized against the IFCC SP3-07 reference standard,[8] and the ApoA-1 method was standardized against the IFCC SP1-01 reference preparation.[9] Because apolipoprotein levels are not affected by the fasting status of the individual, we used the ApoB/ApoA-1 ratio as the major index of abnormal lipids in the analysis. Blood samples were available in 76% of cases and controls. Although centers attempted to draw blood within 24 hours of symptom onset in cases, this was only achieved in 31%. In Africa, the AMI patients presented to health services long after the onset of symptoms, probably because of limited access to health services and delays in diagnosing their condition.

Current smokers were defined as those who smoked any tobacco in the previous 12 months. Former smokers were defined as those who had quit more than a year before. For waist/hip ratio (WHR), tertiles were calculated separately for men and women on the basis of the overall control data.[11] The cutoff points used were 0.90 and 0.96 in men and 0.83 and 0.90 in women, to divide participants into thirds. Cutoff points for ApoB/ApoA-1 ratio tertiles were derived from all controls. Individuals were considered physically active if they were regularly involved in moderate or strenuous exercise for ≥4 hours per week. Regular alcohol use was defined as consumption ≥3 times per week. The cases and controls are grouped as black Africans, European/other Africans, and colored Africans. This last group is predominantly from South Africa and of mixed race ancestry including Khoi, San, European, black African, and Malay descent.

Statistical Methods

The methods used by all countries participating in the INTERHEART study are described by Yusuf et al.[11] To account for potential differences in the age structure of the 3 ethnic groups, all comparisons among groups were statistically adjusted for age and sex. Means and medians were calculated to summarize continuous effects and compared with the use of *t* tests or appropriate nonparametric tests when distributional assumptions were in doubt. Simple associations were tested with the use of the Pearson χ^2 test or the Cochran-Armitage trend test for frequencies if >2 levels were being tested for linear trend. Findings of relative risk and population attributable risk (PAR) presented are for models fit with unconditional logistic regression and adjusted for age, sex, and potential confounders.

Relative risk estimates are reported as odds ratios (ORs) and accompanying 95% CIs. Statistical analyses and graphics were produced with the use of the SAS System 9.1 and S-Plus Version 6 (Insightful). All statistical tests of hypotheses are 2 sided. PAR (ie, the proportion of all cases attributable to the relevant factor) and 95% CI were calculated for various CVD risk factors by the methods of Breslow and Day,[14] Bruzzi et al,[15] Benichou and Gail,[16] and Walter.[17] The PARs presented are adjusted for confounders in a fashion similar to the corresponding logistic regression models for odds ratio estimates. PAR estimates were calculated with the Interactive Risk Attributable Program software of the US National Cancer Institute.[18]

The ethics committees in all participating countries and centers approved the INTERHEART. All participants provided informed consent before participating in the study.

TABLE 1. Overall African Cases and Controls by Ethnicity and Participating Country

	Controls		Cases	
	Women	Men	Women	Men
All participants	275	510	193	385
Major ethnic groups				
Black African	134	218	52	92
Colored African	120	212	115	192
European/other African	25	80	26	101
Countries				
Benin	...	8	...	4
Botswana	10	20	4	12
Cameroon	5	14	2	15
Kenya	34	14	17	10
Mozambique	5	15	3	13
Nigeria	...	7	1	6
Seychelles	...	2	...	1
South Africa	224	410	165	308
Zimbabwe	1	10	1	16

Results

Participants were recruited from 9 countries in Africa and constituted 578 cases and 785 controls, with >80% from South Africa (Table 1). The study population comprised 36.3% black African people (144 cases and 352 controls), 46.7% colored African people (307 cases and 332 controls), and 17% European and other African people (127 cases and 105 controls). Almost 75% of the cases and controls were male, and their ages were similar.

The mean age at which the African cases presented with a MI for the first time was 54.3 (SD ±11.3) years. African cases presented 3.8 years earlier than the overall INTERHEART study cases, which is a statistically significant difference ($P<0.0001$) (Table 2). Men (53.2±11.6 years) presented at a younger age than did women (56.4±11 years; $P=0.0014$). There were no age differences seen among the 3 ethnic groups.

Effect of Individual Risk Factors

CVD risk factor profiles among cases and controls for the global INTERHEART and African sample are shown in Table 2, after adjustment for age, sex, and smoking rates of the overall INTERHEART study population.[11] The degree of association for each of the major risk factors with AMI in the African sample is consistent with that found in the global study. The risk factors with the strongest relationship to AMI in the African

TABLE 2. Comparison of the Overall INTERHEART Study and the African INTERHEART Study Risk Factor Profiles

	Overall INTERHEART Study			African INTERHEART Study			
Characteristics	Controls, % (n=14 637)	Cases, % (n=12 461)	OR (95% CI)	Controls, % (n=785)	Cases, % (n=578)	OR (95% CI)	Heterogeneity *P**
Male sex	74.1	75.9	...	64.6	66.6	...	<0.0001
Hypertension, self-reported	21.9	39.0	2.49 (2.35, 2.63)	18.8	42.3	3.44 (2.64, 4.48)	0.0023
Diabetes	7.5	18.5	3.07 (2.84, 3.33)	7.6	23.6	3.55 (2.53, 4.99)	0.23
Current smoker	26.8	45.2	2.95 (2.72, 3.20)	38.1	52.3	2.42 (1.86, 3.15)	0.017
Current/former smoker	48.1	65.2	2.27 (2.11, 2.44)	56.3	72.3	2.17 (1.70, 2.77)	0.90
Exercise	19.3	14.3	0.70 (0.65, 0.76)	17.0	15.0	0.88 (0.65, 1.20)	0.15
Alcohol	24.5	24.0	0.81 (0.76, 0.87)	26.8	22.2	0.66 (0.50, 0.87)	0.07
Fruits and vegetables, daily	42.4	35.8	0.70 (0.65, 0.75)	39.4	37.4	0.87 (0.63, 1.18)	0.19
Depression	17.5	24.0	1.54 (1.44, 1.64)	22.3	31.8	1.73 (1.34, 2.25)	0.23
Stress, permanent	4.3	7.7	2.19 (1.95, 2.47)	4.5	9.6	2.92 (1.76, 4.85)	0.43
Continuous Variables	Controls, Mean (SD)	Cases, Mean (SD)	*P*, Cases vs Controls	Controls, Mean (SD)	Cases, Mean (SD)	*P*, Cases vs Controls	*P**
Age	56.9 (12.2)	58.1 (12.2)	<0.0001	52.21 (11.53)	54.3 (11.29)	0.0017	<0.0001
BMI	25.84 (4.15)	26.11 (4.15)	<0.0001	26.79 (5.31)	27.59 (5.11)	0.0006	<0.0001
WHR	0.91 (0.08)	0.93 (0.08)	<0.0001	0.91 (0.08)	0.95 (0.08)	<0.0001	<0.0001
Total cholesterol	5.14 (1.2)	5.29 (1.29)	<0.0001	4.91 (1.26)	5.22 (1.31)	<0.0001	<0.0001
HDL cholesterol	1.08 (0.39)	1.03 (0.34)	<0.0001	1.14 (0.44)	1.00 (0.35)	<0.0001	0.20
LDL cholesterol	3.18 (1.03)	3.41 (1.11)	<0.0001	2.94 (1.04)	3.38 (1.13)	<0.0001	<0.0001
ApoA-1	1.21 (0.29)	1.12 (0.25)	<0.0001	1.22 (0.32)	1.10 (0.26)	<0.0001	0.58
ApoB	0.91 (0.25)	0.97 (0.27)	<0.0001	0.86 (0.27)	1.00 (0.29)	<0.0001	0.08
ApoB/ApoA-1 ratio	0.80 (0.35)	0.91 (0.36)	<0.0001	0.76 (0.33)	0.94 (0.32)	<0.0001	0.87

BMI indicates body mass index.
*African INTERHEART study vs overall INTERHEART study.

sample were previous history of diabetes and hypertension. The history of hypertension was significantly stronger in the total African population than in the global INTERHEART population (OR 3.44; 95% CI 2.64 to 4.48 for the African sample versus OR 2.49; 95% CI 2.35 to 2.63 in the global study) ($P=0.0023$ for tests of heterogeneity of effects). Abdominal obesity (top 2 tertiles compared with lowest tertile of the WHR) (Table 3) was also a significantly stronger risk factor for AMI in the African group than the overall INTERHEART group ($P<0.0001$ for tests of heterogeneity of effects). Subsequently, the strongest risk factors in the African sample were current (OR 2.42; 95% CI 1.86 to 3.15) and current/former tobacco smoking (OR 2.17; 95% CI 1.7 to 2.77) and permanent stress (OR 2.92; 95% CI 1.76 to 4.85).

The CVD risk profile among cases and controls for the 3 ethnic African groups, after adjustment for age and sex, with respect to the overall INTERHEART study population is compared in Table 4.[11] The AMI risk associated with each of the major CVD risk factors is generally consistent across the 3 ethnic groups and the overall INTERHEART study. The exceptions are (1) a history of hypertension in which the strength of the relationship is stronger in the black African group (OR 6.99; 95% CI 4.23 to 11.55) compared with the colored African group (OR 2.31; 95% CI 1.61 to 3.32) and (2) the risk of AMI associated with current smoking in the black African group (OR 1.14; 95% CI 0.69 to 1.89) is significantly lower than that found in the global INTERHEART study.

The atherogenic elements of the lipid profile of the controls in the black African group were lower than those of the other 2 groups. This included lower levels of total cholesterol, LDL cholesterol, ApoB, and ApoB/ApoA-1 ratio.

The Figure shows heterogeneity across the 3 ethnic groups in the magnitude of the associations between level of education, income, and AMI. The data have been adjusted for differences in age, sex, and smoking status. In the black African group, relative to those with <8 years of schooling, those with tertiary education have increased risk for AMI (OR 1.86; 95% CI 1.06 to 3.25). No difference was seen in the colored African sample (OR 0.71; 95% CI 0.30 to 1.68). The direction of the association was reversed for the European/other African sample, in which those with tertiary education had a significantly lower risk for AMI than those with <8 years of schooling (OR 0.30; 95% CI 0.15 to 0.58).

This same pattern was observed when we examined the relationship between income and AMI in each of the subgroups (Figure). Relative to those in the lowest income tertile, black Africans in the highest income tertile had a higher risk of AMI (OR 2.75; 95% CI 1.53 to 4.94). No relationship was observed in the colored African group (OR 0.69; 95% CI 0.33 to 1.43), whereas high income in the European/other African groups was associated with lower risk for AMI (OR 0.35; 95% CI 0.18 to 0.68). The probability values for the education-ethnicity interactions and the income-ethnicity interactions are <0.0001.

TABLE 3. Risk of AMI Associated With Individual Risk Factors in Africa

Risk Factor	Prevalence		OR (95% CI) Adjusted for Age, Sex, and Smoking (OR 1)	PAR (95% CI)
	% Controls	% Cases		
Current smoking				
Overall INTERHEART study	26.8	45.2	2.95 (2.72, 3.20)	...
Overall African population	38.1	52.3	2.42 (1.86, 3.15)	...
Black Africans	29.8	26.6	1.14 (0.69, 1.89)	...
Colored Africans	46.2	64.6	2.34 (1.53, 3.59)	...
European/other Africans	39.1	51.6	2.73 (1.44, 5.17)	...
Current/former smoking				
Overall INTERHEART study	48.1	65.2	2.27 (2.11, 2.44)	36.4 (33.9, 39.0)
Overall African population	56.3	72.3	2.17 (1.70, 2.77)	38.94 (29.75, 48.99)
Black Africans	38.4	45.3	1.48 (0.95, 2.30)	14.23 (4.33, 37.80)
Colored Africans	74.9	83.6	1.79 (1.20, 2.69)	37.37 (20.25, 58.37)
European/other Africans	55.2	75.4	2.76 (1.51, 5.02)	48.05 (29.50, 67.15)
Diabetes				
Overall INTERHEART study	7.5	18.5	3.08 (2.77, 3.42)	12.3 (11.2, 13.5)
Overall African population	7.6	23.6	3.55 (2.53, 4.99)	16.70 (12.88, 21.39)
Black Africans	4.0	23.6	5.79 (2.91, 11.53)	18.25 (11.80, 27.13)
Colored Africans	11.5	23.4	2.53 (1.61, 3.96)	14.14 (8.91, 21.72)
European/other Africans	7.6	24.0	4.04 (1.67, 9.77)	18.20 (10.38, 29.94)
Hypertension				
Overall INTERHEART study	21.9	39.0	2.48 (2.30, 2.68)	23.4 (21.7, 25.1)
Overall African population	18.8	42.3	3.44 (2.64, 4.48)	29.56 (24.34, 35.39)
Black Africans	13.1	50.4	6.99 (4.23, 11.55)	41.91 (32.46, 51.98)
Colored Africans	26.5	41.7	2.31 (1.61, 3.32)	23.42 (15.75, 33.34)
European/other Africans	13.3	34.4	3.90 (1.92, 7.94)	25.79 (16.42, 38.08)
Abdominal obesity (tertiles 2, 3 vs 1)				
Overall INTERHEART study	66.7	76.5	1.77 (1.67, 1.88)	33.7 (30.2, 37.4)
Overall African population	68.8	87.3	2.99 (2.20, 4.07)	58.35 (47.6, 68.4)
Black Africans	66.8	80.6	2.01 (1.21, 3.34)	40.35 (20.23, 64.34)
Colored Africans	71.3	89.2	3.73 (2.35, 5.92)	65.88 (51.97, 77.50)
European/other Africans	66.7	90.3	5.53 (2.51, 12.19)	74.00 (55.10, 86.84)
Elevated ApoB/ApoA-1 ratio (tertiles 2, 3 vs 1)				
Overall INTERHEART study	66.7	81.06	2.29 (2.13, 2.45)	46.24 (43.50, 49.01)
Overall African population	58.2	84.0	3.78 (2.75, 5.19)	61.86 (52.04, 70.79)
Black Africans	45.8	72.6	3.43 (2.06, 5.71)	51.59 (35.86, 67.01)
Colored Africans	67.8	86.7	3.44 (2.11, 5.60)	61.54 (45.45, 75.45)
European/other Africans	67.14	91.01	6.88 (2.60, 18.21)	77.51 (56.78, 90.05)

Table 3 illustrates the risk for AMI associated with 5 CVD risk factors in the global INTERHEART study,[11] the total African population, and the 3 ethnic subgroups. It shows the ORs and PAR for the 5 individual risk factors and the combinations of these risk factors, after adjustment for age and sex of the overall INTERHEART population. The PAR for a history of hypertension in the black African sample (PAR 41.9; 95% CI 32.5 to 52.0) is markedly higher than that of the global INTERHEART study (PAR 23.4; 95% CI 21.7 to 25.1).

Abdominal obesity (expressed as the WHR) and the ApoB/ApoA-1 ratio are included with a comparison of the top two thirds compared with the lowest third values for the 2 variables. The risk for AMI for both these risk factors is significantly higher in the total African group than that in the global INTERHEART group. This is reflected in a higher PAR for the total African group for abdominal obesity (PAR 58.4; 95% CI 32.5 to 52) than for the global INTERHEART group (PAR 33.7; 95% CI 30.2 to 37.4). The risk for AMI in terms of ApoB/ApoA-1 ratio is also higher in the total African group than in the global INTERHEART group. This is reflected in the higher PAR found in the African group (PAR 61.8; 95% CI 52 to 70.8) than in the global INTERHEART group (PAR 46.2; 95% CI 43.5 to 49).

TABLE 4. Comparison of CVD Risk Factor Profile Among the 3 Ethnic Groups in Africa

	Black Africans			Colored Africans			European/Other Africans			
Characteristics	Controls, % (n=352)	Cases, % (n=144)	OR (95% CI)	Controls, % (n=332)	Cases, % (n=307)	OR (95% CI)	Controls, % (n=105)	Cases, % (n=127)	OR (95% CI)	Heterogeneity *P* by Ethnicity*
Male sex	61.9	63.9	...	63.9	62.5	...	76.2	101 (79.5)	...	<0.0001
Hypertension, self-reported	13.1	50.4	6.99 (4.23, 11.55)	26.5	41.7	2.31 (1.61, 3.32)	13.3	43 (34.4)	3.90 (1.92, 7.94)	0.0002
Diabetes	4.0	23.6	5.79 (2.91, 11.53)	11.5	23.4	2.53 (1.61, 3.96)	7.6	30 (24.0)	4.04 (1.67, 9.77)	0.04
Current smoker	29.8	26.6	1.14 (0.69, 1.89)	46.2	64.6	2.34 (1.53, 3.59)	39.1	65 (51.6)	2.73 (1.44, 5.17)	0.0002
Current/former smoker	38.4	45.3	1.48 (0.95, 2.30)	74.9	83.6	1.79 (1.20, 2.69)	55.2	95 (75.4)	2.76 (1.51, 5.02)	0.22
Exercise	15.9	17.7	1.22 (0.70, 2.10)	13.25	11.2	0.86 (0.52, 1.42)	32.4	26 (20.6)	0.54 (0.29, 1.01)	0.23
Alcohol	27.3	32.4	1.44 (0.86, 2.39)	24.2	18.0	0.56 (0.37, 0.86)	33.3	26 (20.8)	0.41 (0.21, 0.77)	0.09
Fruits and vegetables, daily	39.4	37.0	0.61 (0.36, 1.06)	36.2	35.0	0.98 (0.63, 1.53)	50.0	50 (43.86)	1.04 (0.44, 2.47)	0.31
Depression	23.9	36.9	1.96 (1.26, 3.08)	19.8	27.3	1.69 (1.13, 2.50)	25	43 (36.8)	1.76 (0.95, 3.25)	0.79
Stress, permanent	2.9	9	3.45 (1.27, 9.36)	14.2	9.6	3.53 (1.69, 7.37)	8.7	13 (10.5)	0.87 (0.29, 2.62)	0.003
Continuous Variables	Mean (SD)	Mean (SD)	*P*	Mean (SD)	Mean (SD)	*P*	Mean (SD)	Mean (SD)	*P*	*P* by Ethnicity*
Age	50.6 (12.0)	53.0 (12.3)	0.03	53.5 (11.1)	54.6 (11.1)	0.21	53.3 (10.4)	54.9 (10.6)	0.28	0.005
BMI	26.8 (5.2)	28.4 (5.2)	0.003	26.9 (5.6)	27.4 (5.1)	0.31	26.2 (4.9)	27.2 (5.0)	0.14	0.11
WHR	0.90 (0.081)	0.92 (0.085)	0.01	0.92 (0.072)	0.96 (0.069)	<0.0001	0.92 (0.081)	0.98 (0.089)	<0.0001	<0.0001
Total cholesterold†	4.42 (1.12)	4.50 (1.18)	0.58	5.29 (1.19)	5.53 (1.27)	0.03	5.29 (1.45)	5.33 (1.25)	0.85	<0.0001
HDL cholesterol†	1.16 (0.46)	0.99 (0.45)	0.0006	1.14 (0.42)	1.03 (0.32)	0.004	1.10 (0.46)	0.93 (0.29)	0.01	0.18
LDL cholesterol†	2.57 (0.92)	2.82 (0.97)	0.04	3.27 (1.02)	3.66 (1.15)	<0.0001	3.07 (1.08)	3.42 (1.02)	0.04	<0.0001
ApoA-1	1.20 (0.33)	1.08 (0.31)	0.0002	1.22 (0.29)	1.11 (0.24)	<0.0001	1.27 (0.35)	1.12 (0.25)	0.0018	0.20
ApoB	0.753 (0.24)	0.851 (0.24)	0.0012	0.942 (0.26)	1.04 (0.28)	<0.0001	0.941 (0.29)	1.06 (0.31)	0.0056	<0.0001
ApoB/ApoA-1 ratio	0.681 (0.33)	0.855 (0.37)	<0.0001	0.811 (0.27)	0.982 (0.31)	<0.0001	0.838 (0.48)	0.963 (0.25)	0.0147	<0.0001

BMI indicates body mass index.

*Black Africans vs colored Africans vs European/other Africans.

†From nonfasting blood sample, after infarct in cases (and at varying times after initial chest pain).

Cumulative Effects of Risk Factors

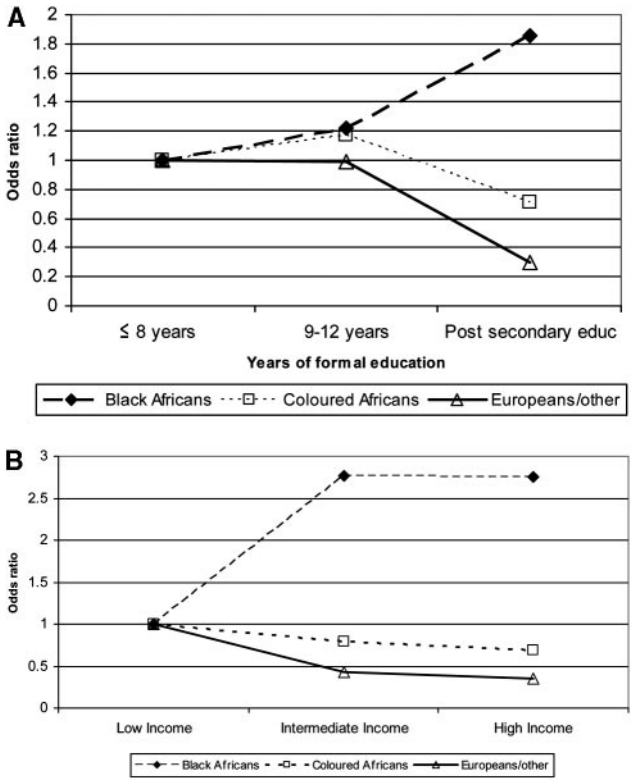
Table 5 shows the effect of combinations of risk factors on the level of risk for AMI for the overall INTERHEART study population, the total African population, and the 3 African ethnic groups. When we considered the group of participants who had 1 or more of the 3 risk factors of current/former smoker, history of diabetes, and hypertension, the overall risk of suffering an AMI by the total African group was represented by an OR of 17.4 (95% CI 10.5 to 28.7) and a PAR of 64.5% (95% CI 56.7 to 71.5). When the fourth risk factor, ApoB/ApoA-1 ratio, was added to the analysis, the OR increased to 28.9 (95% CI 14.8 to 56.3) and PAR is 80.6 (95% CI 72.7 to 86.7). When the fifth risk factor, WHR, was added to the combined analyses, the magnitude of the OR increased to 49.3 (95% CI 22.8 to 106.8), with a PAR of 89.2 (95% CI 82.8 to 93.4). There were no differences between the overall INTERHEART group and the total African group when the impact of 3 and 4 risk factors combined was assessed. However, when all 5 risk factors were combined, the PAR for the African group was higher than that for the overall INTERHEART group (PAR 78.4; 95% CI 76.6 to 80.1). Yusuf et al[11] showed that 9 risk factors (the aforementioned factors plus irregular consumption of fruits and vegetables, no alcohol intake, physical inactivity, and psychosocial stressors) provided a PAR of 97.4% for all of the African participants in the INTERHEART study.

Discussion

Overall Impact of CVD Risk Factors

The INTERHEART Africa data show for the first time that only 5 risk factors account for 89.2% of the risk for an initial MI. These are as follows: current/former tobacco smoking, self-reported hypertension and diabetes, abdominal obesity measured as the WHR, and lipoprotein ApoB/ApoA-1 ratio. Four of these risk factors can be determined by taking a medical history and simply measuring the waist and hip circumferences of patients attending primary healthcare services. Additionally, actual blood pressure can be measured easily, thereby improving the sensitivity of this risk factor. These 4 risk factors account for a PAR of 83.1% of the risk. These data confirm that people from Africa who are exposed to these known major CVD risk factors are at risk to develop AMI, as are other people across the globe.[11] Note that several of the risk factors have much higher ORs and PAR values in Africa compared with the global study, suggesting that uncontrolled major CVD risk factors will have a larger impact on the burden of CVD in Africa than elsewhere.

Our data showed heterogeneity in relation to the magnitude of the risk for AMI for the level of education and income among the 3 ethnic groups. These variations reflect that the 3 ethnic groups are at different points of the epidemiological transition and therefore the development of the CVD epidemic.[19] This difference in the epidemiological transition is also



Socioeconomic status in Africa: OR associated with increasing formal education by ethnic group (A) and OR associated with increasing income by ethnic group (B). Analysis is adjusted for age, sex, and smoking status. $P<0.0001$ for education×ethnicity interaction.

reflected in the mortality patterns recorded by Statistics South Africa in 2000.[20] Burden of disease estimates that adjust for underregistration and misclassification of cause show that the black African group in South Africa had ischemic heart disease and stroke mortality rates of 70/100 000 and 143/100 000, respectively. For the colored African group, these values were 171/100 000 and 139/100 000, respectively, whereas mortality rates for the white South African group were 230/100 000 and 72/100 000, respectively (D. Bradshaw, DPhil, unpublished data, 2005).

In the overall INTERHEART study,[11] the median age at which AMI presented was significantly older than in Africa, where no differences were observed across the 3 ethnic groups. This suggests that more premature AMIs occur in Africa than in the rest of the INTERHEART study areas and probably reflects a pervasive lack of prevention, early detection, and effective management of the MI risk factors across the participating countries. Furthermore, this highlights the need for initiating interventions to reduce the impact of CVD and possibly truncating the CVD epidemic in the black African group in the region. In Africa, the age of presentation may be lower because these patients are able to present to hospitals that are possibly farther away or more difficult to reach than in the other INTERHEART countries.

European/Other African Group

The CVD risk factor profile of this group reflects an advanced stage of the epidemiological transition, with high prevalence rates of dyslipidemia, tobacco addiction, and abdominal obesity, whereas lower prevalence rates of hypertension and diabetes occurred in cases and controls. The risk of an elevated ApoB/ApoA-1 ratio was significantly higher in the European/other African group than that found in the global INTERHEART study. Furthermore, the Figure illustrates that the wealthiest and most educated third of the European/other African group had the lowest risk of having an initial AMI. This pattern corresponds to the lower ischemic heart disease risk factor levels and rates found in the wealthier sector of the population in the United Kingdom.[21] Their risk profile is also congruent with the mortality pattern reported above. In the European group in Africa, the median age for cases to present was 54 years (interquartile range, 46 to 60 years), whereas that of Europeans participating in other regions of the INTERHEART study was 62 years (interquartile range, 52 to 71 years).[11] This shows that the Europeans in Africa present with AMI at a much earlier age than those in other areas.

Colored African Group

The colored African group in this study is predominantly from South Africa and represents a group of mixed race ancestry descending from the first South African nations, the Khoi and San people, as well as European, African, and Malaysian people. The epidemiological transition has been associated with marked degrees of urbanization and the adoption of a typical Westernized/industrialized lifestyle during the last part of the 20th century. Recruitment took place at the public sector health services that serve poor working-class people from this group.

The CVD risk profile of the controls in this ethnic group illustrates the adoption of a hazardous Westernized/industrialized lifestyle. Men and women have very high smoking rates. High rates of overweight and obesity have also been reported,[22] which lead to high diabetes rates compared with the other ethnic groups (11.5% versus 4% and 7.6% in the colored, black, and European/other control groups, respectively) and hypertension (27% versus 13% and 13% in the colored, black, and European/other control groups, respectively). The risk profile is indeed in agreement with the mortality pattern reported above, in which the differences between the mortality rates for stroke and ischemic heart disease are smaller than those between the other 2 groups.

Black African Group

Unhealthy lifestyles and the resultant emerging CVD risk factors impart at least the same level of risk for AMI as that found in the overall INTERHEART study and, in the case of hypertension, a higher level.[11] Consequently, our data contradict the theory that black African people, with exposure to the known CVD risk factors, are immune to developing AMI.[4] Reports from various African countries document a changing pattern and spectrum of CVD and their risk factors, especially in urban areas.[5–9] This must be understood in the context of lifetime exposure to unhealthy lifestyles before CVD risk factors have a sufficient impact and subjects present with CVD. Supporting this position is the fact that 2 to 3 decades ago, African Americans had lower CVD rates than white North Americans. However, over time and with extended exposure to risk factors, this has changed,

TABLE 5. Risk of AMI Associated With Combinations of Risk Factors

Risk Factor	OR (95% CI) Adjusted for Age, Sex, and Smoking (OR 1)	PAR (95% CI)
Current and former smoking, diabetes, hypertension		
Overall INTERHEART study	13.04 (11.63, 14.62)	57.72 (56.04, 59.38)
Overall African population	17.35 (10.51, 28.66)	64.46 (56.69, 71.54)
Black Africans	37.96 (14.10, 102.23)	56.95 (43.46, 70.44)
Colored Africans	7.67 (3.69, 15.93)	61.47 (45.92, 74.98)
European/other Africans	32.72 (8.52, 125.74)	69.49 (52.42, 82.49)
Current and former smoking, diabetes, hypertension+ApoB/ApoA-1 ratio (tertiles 2, 3 vs 1)		
Overall INTERHEART study	22.83 (19.69, 26.47)	74.24 (72.44, 75.97)
Overall African population	28.89 (14.83, 56.29)	80.62 (72.73, 86.65)
Black Africans	89.64 (24.52, 327.66)	73.80 (58.19, 85.08)
Colored Africans	14.29 (5.35, 38.14)	80.98 (66.07, 90.30)
European/other Africans	130.76 (15.50, 1103.02)	92.59 (78.71, 97.69)
Current and former smoking, diabetes, hypertension+ApoB/ApoA-1 ratio (tertiles 2, 3 vs 1)+WHR (tertiles 2, 3 vs 1)		
Overall INTERHEART study	27.78 (23.64, 32.65)	78.41 (76.59, 80.12)
Overall African population	49.28 (22.75, 106.75)	89.18 (82.77, 93.39)
Black Africans	136.50 (30.71, 606.66)	83.74 (68.42, 92.44)
Coloured Africans	22.06 (7.28, 66.85)	89.14 (77.02, 95.26)
European/other Africans	1622.56 (95.49, 27 569.75)	99.13 (94.82, 99.86)
Current and former smoking, diabetes, hypertension+WHR (tertiles 2, 3 vs 1)		
Overall INTERHEART study	18.71 (16.42, 21.31)	69.48 (67.67, 71.24)
Overall African population	34.20 (18.64, 62.74)	83.06 (76.62, 88.00)
Black Africans	52.05 (16.52, 163.99)	73.11 (58.21, 84.14)
Colored Africans	17.09 (7.20, 40.59)	84.08 (72.94, 91.19)
European/other Africans	399.46 (54.42, 2932.41)	95.65 (88.20, 98.48)

with African Americans now having higher CVD rates than whites in the United States.

The CVD risk profile of the black African group illustrates a population in the early stages of the CVD epidemic and the epidemiological transition. The data in the Figure further illustrate this trend in the black African group among the more educated and wealthier sector of society in which the risk for AMI is much higher than in the poor sector. This parallels the findings in European societies early in the 20th century at the beginning of the CVD epidemic.[21] One phenomenon that was observed during this study was the low number of AMI cases that were recruited among black Africans, particularly outside of South Africa. This suggests that in the less-developed areas of SSA, AMI in black Africans may still be relatively rare, and in these countries the black African population may be at an even earlier stage of the epidemiological transition than those in South Africa. However, with growing urbanization and economic development, the rates may increase and resemble those seen in South Africa.

The risk associated with hypertension in relation to AMI is more marked in this group than in the overall INTERHEART study, and with increasing urbanization, the prevalence is rising in Africa. Kearney et al[22] estimated that there were 38.2 million men and 41.6 million women in SSA with hypertension in 2000 and that these figures will increase to 73.6 million men and 77.1 million women by 2025. Data from South Africa's first demographic and health survey showed that of all the ethnic groups, the black African people with hypertension had the poorest degree of hypertension diagnosis and control, which is reflected by their high mortality rates for stroke. The high OR observed for a history of hypertension as a risk factor for AMI may be explained in part by higher levels of uncontrolled blood pressure in comparison to those found in the other INTERHEART regions.

Limitations

As part of the overall INTERHEART study, the African data have the same potential limitations as those reported previously.[11] These include possible confounding if there is differential ascertainment of risk factors between cases and controls, such as possible recall bias when cases of AMI are influenced more because of stress than in controls. The inclusion of patients with first AMI reduces the possibility that individuals with previous CVD may have altered their lifestyles and risk factor patterns. To minimize bias in the selection of controls, individuals in whom the risk factors of

interest in this study were implicated as being protective or harmful were excluded. In addition, the African data have specific limitations because of the relatively small sample size of some of the African ethnic groups. However, it still is the largest study of its kind in SSA. We only recruited 144 cases of AMI in black African patients in total, with 80 cases recruited from South Africa, although extensive efforts were made. Although the mortality rate for this group reported in South Africa is much lower than that for the other 2 groups, we are uncertain why this was the case. However, it is plausible that AMI in black Africans may be uncommon in parts of Africa or that these patients have high prehospital mortality rates. Long distances to hospitals and lack of transport, including ambulances, may be contributing factors. Several African countries have no coronary care units or equivalent cardiology wards in state hospitals and do not provide formal specialist training for cardiologists. A more plausible possibility is that the expected epidemiological transition in SSA is being radically altered by the HIV/AIDS pandemic, and the drastically shortened life expectancy in the region means that the age structure is skewed to those who are younger and therefore not at risk for CAD.

Conclusions

The association of major risk factors with AMI in the African population is consistent with that found in the overall INTERHEART study. Five major, modifiable risk factors could be attributed to 89.2% of the AMI found in the people from Africa. This study demonstrated that the 3 ethnic groups are at different stages of the epidemiological transition. The black African group is at an earlier stage and the European/other Africans group is at a later stage of the transition. These data suggest that lifestyle modification, early diagnosis, and cost-effective treatment of CVD risk factors are of utmost importance, especially in the black African population, to prevent a CVD epidemic in Africa of the same magnitude as seen elsewhere on the globe in the future.

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Disclosure

None.

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