CORONARY HEART DISEASE AND RISK FACTORS IN BLACK SOUTH AFRICANS: A CASE-CONTROL STUDY

Magriet Loock, MD; Krisela Steyn, MD; Piet Becker, PhD; Jean Fourie, MPhil

Background: Coronary heart disease (CHD) was uncommon in Black people living in Africa before 1970. Since then CHD risk factor levels have increased, while CHD rates have remained low.

Objective: This case-control study aims to assess the relationship between CHD and known risk factors in urban Black South Africans.

Methods: Eighty-nine cases with CHD and 356 controls attending the Kalafong hospital were recruited between 1982 and 1986 and followed up until 1994. Family and personal medical histories were recorded, along with a clinical examination and special investigations to assess risk factor profiles, clinical presentation and target organ damage. The relationship of the risk factors, target organ damage, and the development of CHD was assessed by using a stepwise multiple logistic regression procedure.

Results: Far more cases than controls had a family and personal medical history and risk factors related to CHD. Those relating to the development of CHD were family history of myocardial infarction (odds ratio [OR] 17.29; 95% confidence interval [CI] 5.48-54.51), hypertension (OR 8.38, 95% CI 3.66-19.17), family history of hypertension (OR 4.33, 95% CI 2.21-8.52), low high-density lipoprotein cholesterol/low-density lipoprotein cholesterol ratio (OR 2.82, 95% CI 1.24-7.22), and type 2 diabetes (OR 2.99, 95% CI 1.19-6.68). Hypercholesterolemia was marginally associated (OR 2.53, 95% CI .92-6.89).

Conclusions: Evidence is provided that an association exists between CHD and the major risk factors for cardiovascular diseases in urban Black South Africans. A relationship between genetic factors and the development of CHD was also identified in this population group. (*Ethn Dis*. 2006;16:872–879)

Key Words: Case-Control Study, Coronary Diseases, Ethnic Groups, South Africa

From the Department of Internal Medicine, University of Pretoria, Pretoria (ML); Chronic Diseases of Lifestyle Unit (KS, JF) and Biostatics Unit (PB), Medical Research Council, Tygerberg; South Africa.

Address correspondence to Krisela Steyn, MD; Chronic Diseases of Lifestyle Unit; Medical Research Council; P.O. Box 19070; Tygerberg 7505; South Africa; +27 21 938 0345 / 0423; +27 21 933 5519 (fax); krisela.steyn@mrc.ac.za

INTRODUCTION

Before 1970, coronary heart disease (CHD) and other cardiovascular diseases (CVD) were virtually unknown in Black people in Africa, and prevalence of risk factors was low.[1–6] This history is in stark contrast with the high rates of CHD in people of African descent living in typically westernized/industrialized settings.[7,8] During the latter part of the 20th century, research showed that as developing countries were undergoing an epidemiologic transition, chronic diseases in general, and CVD in particular, were increasing.[9] This transition was associated with the adoption of unhealthy lifestyles, such as smoking, resulting in an ever-increasing prevalence of known CHD risk factors,[9–11] which predict CVD in African Americans.[12,13] However, few data exist that show the same relationship in Black people living in Africa.

Although the caseload of Black people in Africa with CHD has increased since 1970, particularly in urban settings, they may not be at risk for CVD in the near future. Walker and Sareli[14] deduced in 1997 that, "The global epidemic of cardiovascular diseases predicted to occur early in the 21st century is unlikely to have a significant effect on the Black populations of Africa, at least those dwelling in Sub-Saharan Africa." This statement came irrespective of significant CVD risk factor levels, which are now being recorded in Black populations in Africa.[15,16]

The primary objective of this report is to describe a case-control study conducted in urban Black South Africans to assess the relationship between CHD and its known risk factors.

The primary objective of this report is to describe a case-control study conducted in urban Black South Africans to assess the relationship between CHD and its known risk factors. A post-hoc secondary objective is to examine the relationship found between the CHD risk factors and other atherosclerosis-related target organ damage in the control group of this study.

METHODS

Setting

All the cases and controls lived in the Black townships of Atteridgeville, Saulsville, and Mamelodi outside Pretoria, South Africa. The Kalafong hospital, a tertiary-level referral hospital, serves the population of these three townships. The inhabitants are mainly of Pedi, Tswana, and Ndebele origin.

Data were collected from acute myocardial infarction (MI) cases during their hospitalization. The data for chronic CHD patients were collected during their outpatient visits or from patient

Table 1. Presentation and diagnosis of the 89 cases with coronary heart disease

Initial Diagnosis	Presenting Symptoms	Diagnostic Criteria: Serial ECG (Minnesota coding [MC])[17,18] and cardiac enzymes levels
Acute myocardial infarction (AMI) (n=46)	Chest pain	Q-waves: MC 1-1 to 1-3 Hyper-acute ST-segment changes: MC 9-2 ST-T-wave changes and non-Q waves: MC 4-1 to 4-4; 5-1 to 5-4; 6-4-1; 7-1-1; 7-1-2; 8-2-1 Serial elevated cardiac enzymes: CK; CK-MB-fraction; LDH and LDH isoenzymes I Coronary angiogram confirmed CAD
Previous MI (n=25)	History of chest pain typical of previous MI	Q waves: MC 1-1 to 1-3 Cardiac enzyme levels within normal limits Coronary angiogram confirmed CAD
Chronic angina (n=18)	History of chest pain typical of angina pectoris	Non-Q waves: MC 4-1 to 4-4; 5-1 to 5-4 Cardiac enzyme levels within normal limits Coronary angiogram confirmed CAD

ECG=electrocardiogram; CK=creatine kinase; LDH=lactate dehydrogenase; CAD=coronary artery disease.
Acute chest pain with AMI: severe chest pain across anterior chest wall lasting for ≥30 minutes.
Typical chest pain of angina: chest pain of effort lasting ≤10 minutes and relieved by sublingual nitrates and/or rest.

files for previous admissions for acute MI. Controls were matched to the cases as soon as possible; data collection began in 1982 and was completed in 1986.

CHD Cases

Eighty-nine Black people presented at Kalafong with two or more World Health Organization (WHO) criteria for the diagnosis of CHD (international classification of diseases codes 410 – 414).[17] Acute MI was diagnosed in 46 patients admitted for chest pain and who were found to have typical serial electrocardiogram (ECG) changes and elevated cardiac enzymes (Table 1).[18] Coronary angiograms confirmed the diagnosis during their stay in the hospital.

Previous MI was diagnosed in 25 patients attending cardiac outpatient clinics for follow-up after admission for a previous MI and history similar to the acute MI cases described above. In addition, 18 patients with chronic chest pain typical of angina pectoris and positive ECGs according to the Minnesota code (MC) were entered.[17,19] All these patients had previous coronary angiograms confirming coronary artery disease (CAD).

Of the 89 cases, those deemed clinically fit by a cardiologist underwent a stress ECG test. Only 54 of these cases completed this test to enable stress ECG coding according to Selzer and Cohn,[19] which fulfilled the criteria for CAD (grade III-V). As of 1994, 76 of these CHD patients had died, and we could confirm underlying CAD in 51 necropsies.[20]

Control Group

A control group of 356 Black people was selected from the outpatients attending Kalafong hospital for minor complaints. Other controls without medical complaints were voluntary participants who were accompanying these patients. They had no evidence of the symptoms and signs of underlying CHD. They presented with fewer than two WHO criteria for the diagnosis of CHD. All controls completed a stress ECG and were classified either negative (grade I) or doubtful (grade II) according to the stress ECG criteria.[17,19,21,22] The two study groups were matched according to age, sex, and ethnicity. No controls underwent a coronary angiogram. The case-to-control ratio was 1:4 (Table 2).

Table 2. Sociodemographic characteristics of cases and controls

Characteristics	CHD Cases (n=89) (%)	Controls (n=356) (%)	P value
Age in years*	28 to 91 54.3 (± 11.6)	26 to 85 53.6 (± 11.7)	.519
Age groups (years)			
25 – 44	19.1	19.4	677
45 – 54	29.2	28.1	
55 – 64	31.5	32.9	
≥65	20.2	19.7	
Sex			
Male	82.0	81.7	.951
Female	18.0	18.3	
Marital status			
Married	80.9	81.5	.903
Single	19.1	18.5	
Education			
None	44.9	22.5	.0001
Primary school (1 – 7 years)	23.6	36.0	
Secondary school (8 – 12 years)	27.0	33.4	
Tertiary education	4.5	8.2	
Duration of stay in study area			
Years*	40.6 (± 12.5)	43.1 (± 11.3)	.169

The Student t and Pearson chi-square tests were used to calculate P values.
* Range and/or mean (standard deviation).

Questionnaires

A qualified doctor interviewed the cases and controls with questionnaires developed by WHO to collect demographic characteristics, such as age, sex, and family history of CHD for first-, second- and third-degree relatives.[17] A personal medical history inquired about CHD risk factors and atherosclerosis-related target organ damage. The London School of Hygiene cardiovascular questionnaire provided evidence of chest pain on effort, possible previous myocardial infarction, and intermittent claudication.[17] Smoking history was similarly collected, and the duration of smoking and the amount of tobacco consumed was recorded to calculate the pack-years of tobacco use (number of cigarettes x years of smoking/20).[17,18]

Clinical Examination

The physical examination, also based on WHO criteria, focused on the cardiovascular system and included clinical evaluation of the heart and examination for signs of left ventricular hypertrophy (LVH) or congestive cardiac failure.[17] An ophthalmologist confirmed the fundoscopic findings classified according to WHO criteria.[17]

Peripheral vascular disease (PVD) was diagnosed with a history of claudication.[17] Criteria included absent or diminished peripheral pulses on physical examination and the development of claudication pain in the extremities during the first two stages of the ECG stress test.[17]

The blood pressure (BP) of cases and controls was measured by using a mercury sphygmomanometer, according to WHO guidelines.[17] For an arm circumference <33 cm, a standard cuff was used, while a broad cuff was used for those patients with a larger arm circumference. The classification of hypertension, stratification for risk, and the presence of target organ disease were based on WHO criteria.[17,18]

Special Investigations

Standard 12-lead electrocardiograms were recorded and classified according to the MC of 1982 (WHO criteria).[17] A symptom-limited and/or 90% of the predicted heart-rate response was used to confirm or contest the possibility of ischemia in the cases and controls during a standardized ergometric procedure according to the Bruce Protocol.[22] A treadmill was used for the stress test, according to a simple graded procedure.[19,22]

Heights and weights of the cases and controls were measured, and the body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared kg/m^2.[23] Urinary dipsticks were used to assess proteinuria, glycosuria, and blood in the urine. The urine sample was centrifuged, and the pellet was examined, microscopically, for red and white blood cells.

Fasting blood samples were collected to determine multiparameter biochemical profiles with a Technicon-SMA-11 multi-channel auto-analyzer, with the necessary internal and external controls according to Wellcome International Quality Control. Serum glucose, serum creatinine and urea levels, electrolytes, liver function tests, and cardiac enzyme levels were measured. The latter included creatine kinase (CK), CK-MB-fraction, lactate dehydrogenase (LDH), and LDH isoenzyme I, according to the GEMSTAR system and Helena Laboratoria.

The Boehringer-Mannheim enzymatic kits were used to measure total cholesterol (TC), high-density lipoprotein cholesterol (HDLC), and triglycerides (TG). The low-density lipoprotein cholesterol (LDLC) level was calculated by using the Friedewald equation.[24]

Statistical and Analytical Methods

Categorical data are presented as frequencies and percentages, while continuous data are reported as means and standard deviations. Internationally accepted WHO criteria are used to identify the prevalence of risk factors and target organ damage. Comparison between cases and controls used chi-square tests for categorical data and *t* tests for continuous data.

To address the primary objective of the study, a stepwise multiple logistic regression analysis was used to determine the association between CHD outcome and major risk factors and other related variables. The variables were family histories of diabetes, hypertension, stroke, and myocardial infarction; a personal history of diabetes, hypertension, stroke, or peripheral vascular disease; all fasting lipid-related measurements; an elevated BP; fasting blood glucose ≥ 7 mmol/L; BMI; tobacco pack-years; sex; and age >55 years. The second objective was achieved by conducting logistic regression analyses in the control group (ie, those without CHD), after categorizing them with or without target organ damage according to the same variables.

The diagnosis of hypertension according to WHO criteria was confirmed with a BP reading of $\geq 140/90$ mm Hg on three or more occasions and/or being on appropriate antihypertension medication.[17,18,25] The averages of three measurements were analyzed.

The diagnosis of type 2 diabetes mellitus was confirmed by using WHO criteria adopted for South Africa, with the following cutoff points: a fasting glucose level ≥ 7 mmol/L and/or a non-fasting (random) blood glucose level ≥ 11.1 mmol/L and/or the use of anti-diabetes medication with a clinical history of type 2 diabetes.[26] Retinopathy was categorized according to the Keith Wagener Barker classification, and $\geq$Gr II retinopathy was considered abnormal.[27]

The diagnosis of LVH was defined by clinical examination of the apical impulse, outside the mid-clavicular line, below and/or lateral to the fifth intercostal space confirmed by ECG MC 3-1, MC 3-3, and MC 3-4 when both

were present.[21,22] Additional confirmation of LVH included the following: chest radiograph showing a cardiothoracic ratio >50% and echocardiographic LV mass ≥294 g in males and ≥198 g in females.[17]

The diagnosis of renal target organ damage was confirmed by two or more of the following: proteinuria and/or hematuria with associated serum urea levels ≥6 mmol/L, serum uric acid levels >.35 μmmol/L, and serum creatinine levels ≥97 mmol/L on more than one occasion.[17]

Calculation of the absolute risk of having an MI or acute CHD incident within 10 years in individuals without CHD was done by using a point system (weights) that was developed by the Framingham study for certain risk factor categories for the control group.[28] Because the CHD cases had confirmed evidence of underlying coronary artery disease, their risk scores were adjusted with a conservative one per conventional risk factor.[28]

Ethical Considerations

The ethical committee of the University of Pretoria approved the protocol. All CHD cases and controls provided written informed consent to enter into the study.

Table 3. The clinical presentation and risk factors that contributed significantly to the development of CHD

Variables	CHD cases (*n*=89) (%)	Controls (*n*=356) (%)	*P* value*
Family history			
Diabetes	27.0	4.8	<.0001
Hypertension	62.9	13.8	<.0001
Cerebrovascular disease (stroke)	12.4	2.5	<.0001
Myocardial infarction	33.7	1.4	<.0001
Personal medical history and clinical signs			
Diabetes mellitus	27.0	3.4	<.0001
Hypertension	88.8	20.2	<.0001
Cerebrovascular disease	14.6	.8	<.0001
Peripheral vascular disease	16.9	.8	<.0001
Arcus cornealis	67.4	22.5	<.0001
Dorsalis pedis and/or tibialis posterior pulse absent	53.9	12.4	<.0001
Body weight in kg†	75.1 (±11.8)	74.4 (± 10.6)	.6201
Height in meters†	1.69 (± .6)	1.69 (± .6)	.6830
Some special investigations			
Proteinuria	66.3	17.7	<.0001
Glycosuria	31.5	6.5	<.0001
Blood urea ≥6.0 mmol/L	32.6	23.4	.0533
Blood creatinine ≥97 μmol/L	50.0	12.9	<.0001
Target organ damage			
Red blood cells in urine	21.7	10.2	.01
White blood cells in urine	31.0	17.4	.005
Renal target organ damage‡	67.4	17.1	<.0001
Left ventricular hypertrophy§	83.2	13.8	<.0001
≥Grade II retinopathy (KWB)||	95.5	30.6	<.0001
Peripheral vascular disease¶	50.6	14.3	<.0001
Claudication	57.3	3.7	<.0001

* The Fisher exact and chi-square tests were used to calculate *P* values.
† Mean (standard deviation).
‡ Defined as having at least one finding of proteinuria, hematuria, raised serum urea and/or creatinine.
§ Defined as having an electrocardiogram with Minnesota coding 3-1, 3-3, or 3-4 and/or a displaced apical impulse on clinical examination.
|| KWB is the Keith-Wagener-Barker classification used to classify ≥Gr. I ophthalmologist-confirmed retinopathy.
¶ Defined as having at least one finding of absent peripheral pulses and/or claudication during an ECG stress test.
CHD=coronary heart disease; ECG=electrocardiogram.

RESULTS

The sociodemographic characteristics of the 89 cases and 356 controls are shown in Table 2. The two groups were similar, with the exception of higher education levels in the control group. A univariate analysis of the variables, which contributed significantly to the development of CHD, as identified during a multiple logistic regression procedure, appears in Table 3. The family histories of the CHD cases show significantly higher rates of the major risk factors and manifestations of CVD. This group also reported significantly higher personal histories of CVD risk factors and related conditions. The indirect evidence of major risk factors (hypertension and type 2 diabetes) as well as target organ damage (LVH, renal target organ damage, and PVD) was confirmed at necropsy. The latter also provided evidence of poorly controlled CHD risk factors during the lifetime of the CHD patients. In addition, 33% of the cases and 7.6% of the controls had elevated cholesterol levels (≥6.5 mmol/L). All cases and controls had triglyceride levels <4.5 mmol/L and were thus included in the LDLC calculation.

The CHD risk factor patterns of the cases and controls are shown in Table 4. All these risk factors occurred more frequently in the cases than in the controls, with the exception of overweight and obesity. Although not statistically significant, 80% of females and 29% of males in both study groups had BMIs ≥25 kg/m^2 (data not shown). A significantly higher Framingham total CVD risk score was calculated for the cases compared to the controls.

The post-hoc secondary regression analysis of target organ damage in the control group, displayed in Table 5, found that LVH was associated with hypertension, male sex, and family histories of type 2 diabetes and MI.

Table 4. Coronary heart disease (CHD) risk factors in cases and controls

Variables	CHD cases (n=89) (%)	Controls (n=356) (%)	P value*
Systolic BP in mm Hg†	169.0 (± 26.0)	146.0 (± 21.0)	<.0001
Diastolic BP in mm Hg: (Korotkoff IV)†	110.0 (± 16.0)	93.0 (± 12.0)	<.0001
(Korotkoff V)†	98.0 (± 17.0)	84.0 (± 12.0)	<.0001
Hypertension: BP ≥140/90 mm Hg and/or antihypertensive medication	95.5	71.7	<.0001
Hypertension: BP ≥160/95 mm Hg and/or antihypertensive medication	46.1	10.7	<.0001
Total serum cholesterol (TC) in mmol/L†	6.1 (± 1.2)	5.4 (± .8)	<.0001
TC ≥5 mmol/L	81.8	61.8	<.0001
TC ≥6.5 mmol/L	33.0	7.6	<.0001
HDLC in mmol/L†	1.05 (± .3)	1.2 (± .3)	<.0001
HDLC ≤1.2 mmol/L	74.2	44.6	<.0001
Triglyceride in mmol/L†	1.75 (± 1.1)	1.4 (± .8)	.0034
LDLC in mmol/L†	4.7 (± 1.2)	3.9 (± .8)	<.0001
LDLC ≥3 mmol/L	95.5	83.7	<.0001
LDLC ≥4 mmol/L	69.3	39.0	<.0001
HDLC:TC ratio as %†	17.3 (± 2.8)	22.6 (± 3.9)	<.0012
HDLC:TC ratio <25%	88.8	66.6	<.0001
HDLC:LDLC ratio as %†	22.3 (± 3.4)	31.3 (± 3.7)	<.0001
HDLC:LDLC ratio <20%	44.9	11.2	<.0001
Patients who ever smoked tobacco regularly	79.8	38.2	<.0001
Patients who ever smoked in past but quit	24.7	12.9	.0236
Patients who never smoked tobacco	20.2	60.3	<.0001
Pack-years (of ever smokers)†	16.5 (± 15.6)	6.7 (± 13.0)	<.0001
Years of smoking (of ever smokers)†	23.8 (± 17.5)	8.6 (± 13.0)	<.0001
Fasting blood glucose in mmol/L†	7.3 (± 4.2)	5.5 (± 1.2)	<.0001
Diagnosis of type 2 diabetes mellitus: Fasting glucose ≥7 mmol/L	31.5	5.9	<.0001
Body mass index (BMI) (kg/m^2)	26.4 (±3.7)	26.1 (± 3.3)	.4538
BMI ≥25 kg/m^2	38.2	36.8	.8078
BMI ≥30 kg/m^2	8.9	7.9	.6697
Framingham total CVD risk score†	14.9 (± 3.4)	7.5 (± 3.6)	<.0001
Predicted 10-year CHD mortality as % (Framingham)	53.0	9.0	<.0001

* Fisher exact, chi-square, Student, and Welch t tests were used to calculate P values.

† Mean (standard deviation).

BP=blood pressure; LDLC=low-density lipoprotein cholesterol; HDLC=high-density lipoprotein cholesterol; CVD=cardiovascular disease.

Retinopathy was significantly associated with a family history of stroke, hypertension, and type 2 diabetes and inversely associated with HDLC levels. PVD was significantly associated with elevated TC levels ≥ 6.5 mmol/L, hypertension and family history of type 2 diabetes, and age >55 years. Renal TOD was significantly associated with family history of stroke and hypertension and marginally with age >55, male sex, and pack-years of smoking.

DISCUSSION

These data show that the known major CHD risk factors commonly found in Caucasians are independently associated with having CHD in Black South Africans. Family histories of MI and hypertension were strong predictors of CHD. Therefore, genetic factors may play a role in the predisposition of this community to develop CHD.

Furthermore, the risk factors and family histories were associated with target organ damage of the eyes, kidneys, and peripheral vessels and with LVH also in the control group, who were free of CHD. The presence of these major CHD risk factors and the genetic influences along with type 2 diabetes and smoking seemed to contribute significantly to the development of CHD and target organ damage, similar to data reported in African Americans with confirmed CHD.[12,13] These findings finally challenge the notion that Black people of Africa are "immune" to CHD.

These data show that the known major CHD risk factors commonly found in Caucasians are independently associated with having CHD in Black South Africans.

The low CHD rates reported in Black people of Africa could be ascribed to previously low prevalence rates of the known CHD risk factors. Alternatively, observations could have been made during the extended period of recently raised levels of risk factors and before the development of extensive atherosclerosis that is necessary for CHD and related target organ damage to emerge.

In a recent publication by Leeder et al,[29] in people of working age (35 – 64 years), CVD mortality rates in South Africa in 2000 had already increased to levels higher than those found in the United States and Portugal. The report also shows that the projected CVD mortality in South Africa for this age group will increase by 41% between 2000 and 2030.[29] These premature deaths will have a major impact on the country, which at the same time will have to deal with the HIV/AIDS pandemic.

Table 5. The stepwise multiple logistic regression analyses of the relationship between known risk factors and coronary heart disease and target organ damage. (Risk factors that contributed to the area under the ROC curves are shown.)

	Odds Ratio	95% CI	*P* value
Primary analysis (89 cases; 356 controls)			
Coronary heart disease Area under the ROC curve =.9268			
Family history of myocardial infarction	17.29	5.48–54.51	<.0001
Hypertension (BP ≥140/90 mm Hg and/or treatment)	8.38	3.66–19.17	<.0001
Family history of hypertension	4.33	2.21–8.52	<.0001
Ratio of HDLC:LDLC ≤ 20%	2.82	1.24–7.22	.0157
Type 2 diabetes (fasting glucose ≥7 mmol/L and/or treatment)	2.99	1.19–6.68	.0184
Hypercholesterolemia (TC ≥6.5 mmol/L)	2.53	.92–6.89	.0692
Tobacco pack-years	1.02	.99–1.04	.1407
Post-hoc secondary regression analyses (356 controls)			
Left ventricular hypertrophy (49 with, 307 without LVH) Area under the ROC curve =.7159			
Hypertension	4.27	2.25–8.08	<.0001
Family history of myocardial infarction	3.87	.57–26.09	.1652
Men compared to women	3.19	1.07–9.51	.0386
Family history of diabetes	3.07	.98–9.63	.0543
≥Gr 2 retinopathy (109 with, 247 without retinopathy) Area under the ROC curve =.8104			
Family history of stroke	6.61	1.13–38.71	.0369
Hypertension	5.64	3.23–9.86	<.0001
Type 2 diabetes	4.16	1.29–13.40	.0175
Family history of diabetes	2.96	.90–9.78	.0742
Age >55 years	2.33	1.35–4.03	.0024
HDLC <1.2 mmol/L	1.80	1.05–3.11	.0348
Tobacco pack-years	1.02	.99–1.04	.1459
Men compared to women	.59	.30–1.18	.1393
Peripheral vascular disease (51 with, 305 without PVD) Area under the ROC curve=.7873			
Hypercholesterolemia	8.63	2.74–27.15	<.0001
Hypertension	4.09	2.11–7.93	<.0001
Family history of diabetes	3.22	.92–1.33	.0681
Age >55 years	2.47	1.25–4.93	.0106
HDLC <1.2 mmol/L	1.67	.82–3.39	.1568
HDLC:LDLC ratio <20%	.22	.06–.84	.0275
Renal target organ damage (61 with, 295 without renal damage) Area under the ROC curve =.6983			
Family history of stroke	3.37	.74–15.44	.1182
Hypertension	3.14	1.69–5.82	<.0001
Men compared to women	1.89	.84–4.26	.1218
Age >55 years	1.57	.87–2.81	.126
Tobacco pack years	.96	.92–1.00	.0092
Hypercholesterolemia	.31	.07–1.39	.1275

ROC=receiver operator characteristic; CI=confidence interval; BP=blood pressure; HDLC=high-density lipoprotein cholesterol; LDLC=low-density lipoprotein cholesterol; TC=total cholesterol; PVD=peripheral vascular disease.

Approximately 80% of the cases included in this study were younger than 65 years and fell within the working-age group (Table 2); most came from a low socioeconomic background with limited education. This finding questions the common myth that CHD occurs predominantly in the wealthier sector of society in low- or middle-income countries.[30]

High levels of the major risk factors, such as hypertension, hypercholesterolemia, diabetes, and the use of tobacco, are shown in the CHD cases. In addition, these data identify poor levels of control for manageable major CHD risk factors in patients who attend hospital. Inadequate care of the major risk factors in these patients could have been longstanding, as reflected by the high levels of target organ damage. This finding is of great concern in patients admitted to the hospital after suffering an MI or chronic angina.

The inadequate management of CHD risk factors has also been found in community-based surveys in South Africa.[30,31] Therefore, an intervention to prevent these risk factors is urgently needed in the Black community of South Africa to avert the projected CVD mortality patterns.

The results of the stepwise multiple logistic regression analyses shown in Table 5 provide a predictive model for CHD based on the most important risk factors. These suggest that genetic factors represented by the strong association between family history of MI or hypertension and CHD may be important in Black South Africans. Lack of significant association between smoking pack-years and CHD could be the result of the low levels of exposure to tobacco in these patients (Table 4). However, these are not definite epidemiologic models that fully describe the degree of association between risk factors and CHD. To develop such models would require a detailed exploration of all the other possible confounders in this population and those described in the literature.

Limitations of this study require consideration in interpreting the data. The CHD patients were defined as those having a confirmed angiography diagnosis, and most had had an acute or previous MI. Therefore, they were likely to have had severe disease and not been representative of the spectrum of CHD among Black South Africans. On the other hand, a diagnosis of CHD in the controls was excluded because of absent

signs and symptoms and negative stress ECG testing. Possibly some of the controls could have had clinically occult CHD, causing biased study results. Most of the exposure variables were relatively objective measures. However, some exposures, ie, a family history of CHD, could have been prone to recall bias, depending on whether or not the subject had CHD. The data are ≈20 years old, limiting applicability to current populations. However, very little data show this association between risk factors and CHD to allow for publication of the data. Furthermore, the findings are similar to those reported by the INTER-HEART study that was conducted in nine African countries.[32] The results from a case-control study may further be limited because of biases resulting from the selection of the study subjects, the collection of covariates, and the possibility of unmeasured confounding.

The data presented here should alert health policy makers in South Africa and elsewhere that an epidemic of CHD and other atherosclerosis-related CVD could become manifest in the first half of the twenty-first century. If the projections by Leeder et al[29] that CVD will increase dramatically by 2030 are correct, this epidemic will have an impact on the population and the economy of South Africa that will strongly aggravate that of the current HIV/AIDS pandemic.

ACKNOWLEDGMENTS

This study was supported financially by Cardiovascular Research Grants from Squibb South Africa 1982 – 1985 and 1986 – 1988; short-term grants from the Medical Research Council South Africa 1982 – 1985 and 1986 – 1988; the Heart Foundation of South Africa 1985 and 1986, the University of Pretoria, 1986 and 1987, Jurgens and Van der Berg 1986 and 1987, Noristan Laboratories 1986; and the Adam Loock Trust 1993 and 1995.

We are indebted to Professor N. J. Temple for editing the manuscript.

REFERENCES

1. Brockington IF, Edington GM. Adult heart disease in western Nigeria: a clinicopathological synopsis. *Am Heart J*. 1972;83:27–40.
2. Vaughan JP. A brief review of cardiovascular disease in Africa. *Trans R Soc Trop Med Hyg*. 1977;71:226–231.
3. Bertrand E. Coronary heart disease in Black Africans: an overview. *East Afr Med J*. 1995;72:37–41.
4. Gelfand M. Cardiac and vascular disorders in the African. *West Afr Med J*. 1952;1:91–94.
5. Schrire V, Uys CJ. Infarction in the Bantu. *Am J Cardiol*. 1958;2:453–463.
6. Cosnett JE. Heart disease in the Zulu: especially cardiomyopathy and cardiac infarction. *Br Heart J*. 1962;34:76–82.
7. Gillum RF. Cardiovascular disease in the United States, an epidemiologic overview. In: Saunders E, Brest AN, eds. *Cardiovascular Disease in Blacks*. Philadelphia, Pa: FA Davis Co; 1991.
8. Gillum RF, Mussolino ME, Madans JH. Coronary heart disease incidence and survival in African American women and men. The NHANES 1 Epidemiologic Follow-up Study. *Ann Intern Med*. 1997;127: 111–118.
9. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation*. 1998;97:596–601.
10. World Health Organization. *World Health Report 2002: Reducing Risks, Promoting Healthy Life*. Geneva: World Health Organization; 2002.
11. World Health Organization. *Secondary Prevention of Non-Communicable Disease in Low and Middle Income Countries Through Community-Based Interventions*. Geneva: World Health Organization; 2002.
12. Husten L. Global epidemic of cardiovascular disease predicted. *Lancet*. 1998;352:1530.
13. Potts JL, Thomas J. Traditional coronary risk factors in African Americans. *Am J Med Sci*. 1999;317:189–192.
14. Walker ARP, Sareli P. Coronary heart disease: outlook for Africa. *J R Soc Med*. 1997;90: 23–27.
15. Van der Sande MAB, Milligan PJM, Nyan OA, et al. Blood pressure patterns and cardiovascular risk factors in rural and urban Gambian communities. *J Hum Hypertens*. 2000;14:489–496.
16. Unwin N, Setel P, Rashid S, et al. Noncommunicable diseases in sub-Saharan Africa: where do they feature in the health research agenda? *Bull World Health Organ*. 2001;79: 947–953.
17. Rose GA, Blackburn H, Gillum RF, Prineas RJ. *Cardiovascular Survey Methods*. Monograph Series 56. Geneva: World Health Organization; 1982.
18. Groen JJ, Hilleboe HE, Speransky J, Morris JN, for the WHO Expert Committee. Hypertension and coronary heart disease: classification and criteria for epidemiological studies. First report of the expert committee on Cardiovascular Diseases and Hypertension. *World Health Organ Tech Rep Ser*. 1959;168: 6–28.
19. Selzer A, Cohn K. On the interpretation of the exercise test. *Circulation*. 1978;58(2):193–195.
20. Schoen FJ. Ischemic heart disease. In: Cotran RS, Kumar V, Robbins SL, eds. *Robbins Pathologic Basis of Disease*. 5th ed. Philadelphia, Pa: WB Saunders; 1995:523–582.
21. Rowlands DJ. *Understanding the Electrocardiogram: Section 2: Morphological Abnormalities in Ischemic Heart Disease and Exercise Stress Testing*. Alderley Park, Macclesfield, Cheshire, England: Imperial Chemical Industries PLC Pharmaceutical Division; 1982:198–211.
22. Bruce RA. Exercise testing of patients with coronary heart disease: principles and normal standards for evaluation. *Ann Clin Res*. 1971;3:323–332.
23. Bray GA. Definition, measurement, and classification of the syndromes of obesity. *Int J Obes*. 1978;2:99–112.
24. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18:499–502.
25. Executive Committee of the Hypertension Society of Southern Africa. Guidelines for the management of hypertension at primary healthcare level. *S Afr Med J*. 1995;85: 1321–1325.
26. A SEMDSA Consensus Document in association with DESSA, ADSA. Type II diabetes mellitus clinical guidelines at primary healthcare level [review]. *S Afr Med J*. 1997; 87:493–512. (Erratum in: *S Afr Med J*. 1997; 87: 915.)
27. Walsh JB. Hypertensive retinopathy. Description, classification, and prognosis. *Ophthalmology*. 1982;89:1127–1131.
28. South African Medical Association and Lipid and Atherosclerosis Society of Southern Africa Working Group. Diagnosis, management and prevention of the common dyslipidemias in South Africa: clinical guideline, 2000. *S Afr Med J*. 2000;90:164–178.
29. Leeder S, Raymond S, Greenberg H, Lui H, Esson K. *A Race Against Time. The Challenge of Cardiovascular Disease in Developing Countries*. New York, NY: Columbia University; 2004.
30. Yach D, Hawkes C. *Toward a WHO Long-Term Strategy for Prevention and Control of Leading Chronic Diseases*. Geneva: World Health Organization; 2004.

31. Steyn K, Gaziano TA, Bradshaw D, Laubscher R, Fourie JM. Hypertension in South African adults: results from the Demographic and Health Survey, 1998. *J Hypertens*. 2001;19: 1717–1725.
32. Steyn K, Sliwa K, Hawken S, et al, for the INTERHEART Investigators in Africa. Risk factors associated with myocardial infarction in Africa: the INTERHEART Africa Study. *Circulation*. 2005;112(23):3554–3561.

AUTHOR CONTRIBUTIONS

Design concept of study: Loock, Steyn
Acquisition of data: Loock, Becker
Data analysis interpretation: Loock, Steyn, Becker, Fourie
Manuscript draft: Loock, Steyn, Fourie
Statistical expertise: Loock, Becker
Acquisition of funding: Loock
Administrative, technical, or material assistance: Loock, Fourie
Supervision: Steyn, Becker