The constellation of metabolic abnormalities comprising central obesity, raised triglycerides (TG), reduced high-density lipoprotein (HDL) cholesterol, raised blood pressure (BP) and raised fasting plasma glucose is referred to as the metabolic syndrome (MS).  

In the past decade several panels of experts have attempted to provide a definition of the diagnostic criteria for the MS. The World Health Organization (WHO) published the first definition in 1998, which was soon modified by the European Group for the Study of Insulin Resistance. In 2001, the National Cholesterol Education Program Adult Treatment Panel III (NCEP: ATP III) issued its definition. Subsequently, the American College of Endocrinology released a position statement on the MS. Each of these definitions used differing sets of criteria that led to confusing and inconsistent estimations of the MS prevalence in diverse populations.

In response to this controversy, the International Diabetes Federation (IDF) proposed a single unifying definition in 2005.

The International Diabetes Federation (IDF) introduced a new definition of the metabolic syndrome (MS) that emphasises ethnic-specific cut-offs for waist circumference (WC).

To compare MS prevalence rates using the National Cholesterol Education Program Adult Treatment Panel III (NCEP: ATP III) and IDF definitions.

Anthropometric data, fasting biochemical variables and MS prevalence rates were measured in 40 black patients with established coronary artery disease (CAD). Glucose metabolism was assessed using the oral glucose tolerance test (OGTT), and insulin-mediated glucose disposal (M-value) was evaluated using the hyperinsulinaemic euglycaemic clamp technique.

Based on the NCEP: ATP III definition, MS prevalence was 60% and using the IDF definition, it was 57.5%. The two definitions similarly classified ~83% of patients as being MS positive or MS negative. Lower WC cut-offs in the IDF definition classified greater numbers of men and women as having WC as a risk factor – IDF v. NCEP: ATP III men 57.6% v. 36.4%; women 100% v. 71.4%. Impaired glucose tolerance (IGT) was found in 12 of the 40 patients (30%) and diabetes mellitus (DM) in 8 (20%). Mean M-value was reduced in IGT and DM groups compared with the normal group, significantly so in the DM group (p = 0.01).

NCEP: ATP III and IDF definitions both generated similar MS prevalence estimates. The two definitions similarly identified the presence or absence of the MS in the majority of patients. The IDF definition classified greater numbers of men and women as having WC as a risk factor. There was a high prevalence of previously undiagnosed IGT and DM in our South African black patients with established CAD.
definition is central obesity, as assessed by waist circumference (WC). It varies from the earlier NCEP: ATP III definition in that it incorporates specific WC cut-offs for men and women in different ethnic groups. The levels of the other criteria are as described by the NCEP: ATP III definition, which was updated in 2004 to include the diagnostic glucose concentration (≥ 5.6 mmol/l) above which persons have either impaired fasting glucose (IFG) or diabetes mellitus (DM).

Much interest is currently being focused on the striking global increase in the prevalence of the MS. Figures taken from studies using the older definitions indicated that prevalence rates varied widely among different populations. Japan had the lowest prevalence of 6%, followed by 11% in Finland, 27% in Mexico, 32% in India. Prevalence was higher in the USA, where rates of 34% and 39% were reported for black and white Americans, respectively. In Africa, an even higher prevalence rate of 43% was found in black Zimbabweans, and we recently reported the highest rate of 60% in a clinical study of 40 urbanised South African blacks with established coronary artery disease (CAD).

The multiple risk factors of obesity, atherogenic dyslipidaemia, hypertension and hyperglycaemia that relate to CAD are also components of the MS. The clinical importance of the MS is, therefore, that it helps to identify individuals at high risk of developing CAD, abnormal glucose tolerance and subsequent DM.

The new IDF definition standardises the criteria for the diagnosis of the MS and offers an opportunity for a fresh assessment of the syndrome. Limited data are available comparing the impact of the IDF-defined, ethnic-specific criteria with the previous definitions, and as yet no comparisons have been made in sub-Saharan African populations.

The aim of this study was to compare the IDF and NCEP: ATP III criteria for the MS among urbanised black South Africans with CAD. Other objectives were to compare the two definitions in terms of their different gender-associated WC cut-offs, and the ability of both definitions to identify the presence or absence of the MS. An additional aim was to assess the prevalence of abnormal glucose metabolism in our patients, who had no previously diagnosed DM.

**Methods**

**Patients**

The study was conducted between January 2003 and June 2006. Most of the patients who were initially excluded were HIV positive (N = 10), and based on the other exclusion criteria described below, a final cohort of 40 patients (33 men and 7 women) with documented CAD were included in the study. All of the patients had had a coronary angiogram performed in the preceding 24 months and they had significant CAD, which was defined as more than 50% lesions in one or more major coronary arteries. An oral glucose tolerance test (OGTT) and a hyperinsulinaemic euglycaemic clamp were performed on all patients at least 3 months after angiography or a previous myocardial infarction. Patients who had a dominant risk factor such as severe hypercholesterolaemia or who smoked more than 20 cigarettes per day were excluded, because the other CAD risk factors would have been overshadowed.

The study design involved the performance of the hyperinsulinaemic euglycaemic clamp technique, which could not have been done on diabetics, and therefore patients with previously diagnosed DM were excluded. Patients with severe hypertension were also excluded. However, the majority of patients with CAD who participated in the study (95%) had previously diagnosed moderate hypertension and were taking antihypertensive medication. Other exclusion criteria were overt liver, renal or thyroid disease because these conditions might affect insulin sensitivity. Almost half of the patients were either unemployed or pensioners. Most of the remainder were labourers and domestic workers, and a few were executives. All the patients gave written informed consent to participate in the study, which was approved by the Human Research Ethics Committee of the University of the Witwatersrand.

**Design**

Four weeks before starting the study, lipid-lowering medications such as statins and fibrates were discontinued. Other drugs that might alter lipid levels and/or insulin resistance, such as thiazide diuretics, beta-blockers or steroids were stopped 3 days before testing began. The night before the test, patients were asked to refrain from smoking and to fast for 12 hours.

On the first day of the study each patient underwent a structured examination, which included an interview. Height, weight, WC and hip measurements were taken, and a fasting venipuncture and OGTT were done. Height and weight were measured to the nearest 0.5 cm and 0.1 kg, respectively. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. WC was determined to the nearest 0.1 cm using a measuring tape positioned at the midpoint between the lowest rib and the iliac crest, and hips were measured at the largest gluteal circumference. These measurements were used to calculate the waist:hip ratio (WHR). Questionnaires were used to obtain information on demographic variables, medical history, medication use, dietary habits, physical activity, and smoking status. On the second occasion, after an overnight fast, the hyperinsulinaemic euglycaemic clamp technique was performed.
Metabolic studies

Diagnosis of the MS was based on two definitions. The NCEP: ATP III definition requires any three or more of the following risk factors: (i) WC ≥ 102 cm in men or ≥ 88 cm in women; (ii) TG ≥ 1.7 mmol/l; (iii) HDL cholesterol < 1.03 mmol/l in men or < 1.29 mmol/l in women; (iv) BP ≥ 130/85 mmHg or use of antihypertensive medication; and (v) fasting blood glucose ≥ 5.6 mmol/l. In addition, we included patients with impaired glucose tolerance (IGT) or frank DM on OGTT (i.e. 2-hour post-load glucose), even if the fasting glucose was < 5.6 mmol/l.

The IDF definition requires: (i) WC ≥ 94 cm in men or ≥ 80 cm in women plus any two or more of the following risk factors: (ii) TG ≥ 1.7 mmol/l or specific treatment for this abnormality; (iii) HDL cholesterol < 1.03 mmol/l in men or < 1.29 mmol/l in women or specific treatment for this abnormality; (iv) BP ≥ 130/85 mmHg or treatment of previously diagnosed hypertension; and (v) fasting blood glucose ≥ 5.6 mmol/l or previously diagnosed DM. As recommended by the IDF, European WC cut-offs were used until specific data are available for sub-Saharan Africans.6

Oral glucose tolerance test (OGTT)

A standard OGTT (75 g glucose) was performed as described by the WHO,4 and glucose concentrations were measured at baseline and at 2 hours post-load. IGT and DM were defined according to the criteria adopted by the American Diabetes Association (ADA).17 Normal glucose tolerance was defined as a fasting glucose level < 5.6 mmol/l and a 2-hour post-load glucose level < 7.8 mmol/l. Patients were classified as having IGT if the fasting plasma glucose concentration was ≥ 5.6 mmol/l but < 7.0 mmol/l, or the 2-hour post-load glucose concentration was ≥ 7.8 mmol/l but < 11.1 mmol/l. DM was diagnosed if the fasting plasma glucose value was ≥ 7.0 mmol/l or the 2-hour post-load glucose value was ≥ 11.1 mmol/l.

Hyperinsulinaemic euglycaemic clamp technique

Peripheral tissue sensitivity to exogenous insulin was measured using the hyperinsulinaemic euglycaemic clamp technique.18 Briefly, an intravenous catheter was inserted by venipuncture for the infusion of glucose and insulin. A second catheter was inserted into a dorsal hand or wrist vein and the hand was enclosed in an electric heat pad, which was warmed to approximately 70°C to ‘arterialise’ the blood obtained for all the samples. Three blood samples were drawn at 10-minute intervals to assess the basal glucose concentration. Thereafter, the glucose concentration was measured and the exogenous 10% dextrose infusion rate was adjusted at 10-minute intervals as calculated by a computerised algorithm based on the negative feedback principle.21 The glucose concentration was clamped at 5.1 mmol/l and a continuous infusion of insulin (40 mU/m²/min; Actrapid, Novo Nordisk, Denmark) was performed for 120 minutes. Steady-state glucose requirements were determined during the last 30 minutes of the study. Under these steady-state conditions of euglycaemia, the glucose infusion rate equalled glucose uptake by all the tissues in the body and was, therefore, a measure of tissue sensitivity to exogenous insulin. Insulin-mediated glucose disposal (M-value) was expressed as mg/kg/min with a value above 5.0 mg/kg/min considered normal.21

Laboratory determinations

Blood glucose, TG, total cholesterol (TC) and HDL cholesterol concentrations were determined by automated enzymatic methods, using a Hitachi Modular analyser and reagents were supplied by Roche Diagnostics GmbH, Mannheim, Germany. Calculation of LDL cholesterol values was based on the Friedewald equation.22

Statistical analysis

Data analysis was performed using the GB-STAT program (Dynamic Microsystems, Inc., Silver Spring, MD, USA), with a value of p < 0.05 considered significant. Student’s t-test and the Mann-Whitney U-test were used to analyse parametric and non-parametric data, respectively. Results are expressed as mean ± standard deviation (SD) or as proportion (%), where appropriate. The frequencies of values above and below the different WC cut-offs were compared using the chi-square test and Fisher’s exact test.

Results

Metabolic studies

Table I summarises the anthropometric measurements, fasting biochemical variables, and clinical characteristics of all the patients and the groups of men and women. In the men, mean age, BMI and WC were lower, and WHR was higher than in the group of women. The mean TG level was also higher in men, while mean TC, HDL cholesterol, LDL cholesterol and glucose concentrations were all lower than in the women, but not significantly so (all p > 0.05). Most of the men (94%) and all of the women had been previously diagnosed with hypertension and were taking antihypertensive medication. Almost half of the men smoked more than 20 cigarettes per day, but none of the women smoked.

Prevalence estimates of the MS based on the two definitions are shown in Table II. Prevalence of the MS was 60% based on the NCEP: ATP III definition, and 57.5% based on the IDF definition. If the original 2001 NCEP: ATP III definition had been applied, which used a fasting glucose cut-off level of 6.1 mmol/l, the
The prevalence of the MS would have been somewhat lower, namely 52.5%. In men, the prevalence was also slightly higher using the NCEP: ATP III definition (54.5% v. 51.5%) and in women, prevalence estimates were identical for both definitions (85.7%).

Table III presents a comparison of the different gender-associated WC cut-offs listed in the two definitions. Lower cut-offs in the IDF definition classified greater numbers of men and women as having WC as a criterion for the MS – IDF v. NCEP: ATP III for men = 57.6% v. 36.4% and for women = 100% v. 71.4%. There were no significant differences in the proportions of men or women above and below the various WC cut-offs for the two definitions – men: p = 0.14 and women: p = 0.45. The two definitions similarly identified 82.5% of the patients as being either MS-positive or MS-negative. Agreement among the men was 78.8% and 100% among the women.

OGGT and hyperinsulinaemic euglycaemic clamp technique

Among the 40 patients, none of whom had known DM before the study, half (N = 20) had abnormal glucose regulation. When classified according to the 2-hour post-load glucose concentration, 12 of the 40 patients had IGT (30%) and 8 had DM (20%). Eight of the 12 patients with IGT (66.7%) had a normal fasting glucose concentration (< 5.6 mmol/l) and a 2-hour post-load glucose concentration ≥ 7.8 mmol/l. Two patients had a fasting glucose concentration ≥ 5.6 mmol/l and a 2-hour post-load glucose concentration < 7.8 mmol/l, while the remaining 2 patients had a fasting glucose concentration ≥ 5.6 mmol/l and a 2-hour post-load glucose concentration ≥ 7.8 mmol/l. The mean M-value was reduced in both the IGT and DM groups compared with the normal group, significantly so in the DM group (p = 0.01). Although the M-value was lower in patients with MS compared with those without MS (mean ± SD = 4.2 ± 0.4 v. 6.4 ± 1.0), the difference was not significant (p = 0.07).

Discussion

To the best of our knowledge, this is the first clinical study comparing the new IDF and the older NCEP: ATP III definitions in a small group of urbanised South African black patients with CAD. The main findings that arose from our study were that both definitions generated similar prevalence estimates of the MS and the two definitions similarly identified the presence or absence of the MS in more than 80% of patients. We also found that lower WC cut-offs in the IDF definition resulted in a greater number of men and women being classified as having an elevated WC as a criterion for the MS. In addition, half of the patients studied had previously undiagnosed IGT or DM.

Recently, we reported a prevalence of MS of 60% in these patients using the 2004 NCEP: ATP III definition. If the original 2001 NCEP: ATP III definition had been applied, which used a fasting glucose cut-off level of 6.1 mmol/l, the prevalence of the MS would have been somewhat lower, namely...
52.5%. The rate based on the IDF definition in this study was 57.5%. This figure exceeds the IDF-defined rates documented in other ethnic groups such as the Chinese (46.3%),23 Arabs (45.5%),24 Mexicans (42.6%),25 and European populations in Austria (45.5%)26 and Greece (43.4%).27 In these studies, estimates of MS prevalence were all higher than those based on the NCEP: ATP III definition. This trend is the opposite of our result, which showed a similar or slightly lower rate, using the IDF definition. The reason for this discrepancy lies in the application of the criteria listed in the two definitions. The NCEP: ATP III definition makes an elevated WC one of five equally weighted criteria and allows a combination of any three or more risk factors. In contrast, the IDF definition requires the presence of obesity as defined by ethnic-specific WC cut-offs plus two or more risk factors. In our study, some patients who complied with the IDF-defined WC cut-offs were not diagnosed as being MS-positive because they did not have two or more of the other risk factors.

The main point of difference between the IDF and NCEP: ATP III definitions is the various ethnic-specific WC cut-offs for men and women. In its recent publication the IDF6 recommends that WC cut-offs currently designated for Europeans should be used for sub-Saharan Africans. Although these measurements are not necessarily appropriate for this ethnic group, we have applied them to our patients until more specific data become available. There are also ethnic differences in lipid profiles. Traditionally, rural black South Africans have tended to have lower TC and higher HDL cholesterol levels than whites, but with urbanisation and the adoption of a Western lifestyle, their lipid profiles are becoming more atherogenic.28 Since lower WC cut-offs are listed for both genders in the IDF definition, it could be expected that a greater number of men and women would be classified as having an elevated WC as a risk factor for the MS. Indeed, more than half of the men (57.6%) and all of the women (100%) had an elevated WC. Interestingly, both the IDF and the NCEP: ATP III definitions classified more women than men as having an elevated WC. This risk factor, therefore, contributed substantially to the higher overall MS prevalence in the women included in our study. A similar finding has been reported in other ethnic groups, notably the Chinese,23 Arabs,24 and Koreans.29

An important reason for comparing the two definitions in our study was to see if the new IDF criteria were better than the older NCEP: ATP III criteria at identifying patients with the MS. We found that the two definitions similarly identified the presence or absence of the MS in ~83% of the patients. This high overlap is not surprising considering the fact that both definitions use the same five components, and that four of the five criteria (TG, HDL cholesterol, BP and glucose) are defined almost identically. There are, however, a couple of noteworthy differences. The IDF definition allows for the treatment of hypertriglyceridaemia, a low concentration of HDL cholesterol, and hypertension to be counted as being MS-positive. Furthermore, under the IDF definition, patients who have previously diagnosed DM are automatically considered to have hyperglycaemia even if their fasting glucose level is < 5.6 mmol/l. The increased risk for CAD, however, is already present at modestly increased levels of blood glucose that are actually below the threshold for the diagnosis of DM.30 In our study we found that half

| Table III. Comparison of different gender-associated waist circumference cut-offs of the NCEP: ATP III and IDF definitions for the metabolic syndrome in 40 black patients with coronary artery disease |
|--------------------------------------------------|-----------------|-----------------|
| Waist circumference (cm) (mean ± SD) | Men (N = 33) | Women (N = 7) |
| NCEP: ATP III definition | | |
| Men (%) | | |
| > 102 cm (N = 12) | 36.4 | - |
| < 102 cm (N = 21) | 63.6 | - |
| Women (%) | | |
| > 88 cm (N = 5) | - | 71.4 |
| < 88 cm (N = 2) | - | 28.6 |
| IDF definition | | |
| Men (%) | | |
| > 94 cm (N = 19) | 57.6 | - |
| < 94 cm (N = 14) | 42.4 | - |
| Women (%) | | |
| > 80 cm (N = 7) | - | 100.0 |
| < 80 cm (N = 0) | - | 0 |

NCEP: ATP III = National Cholesterol Education Program Adult Treatment Panel III; IDF = International Diabetes Federation.
of the patients had abnormal glucose regulation, despite the exclusion of previously diagnosed DM. This high prevalence was revealed by the OGTT when, according to the 2-hour post-load glucose concentration, 30% of the 40 patients had IGT and 20% had DM. Our results were similar to those reported recently for IGT (28%) and DM (24%) by Kernan et al.12 in the USA. Compared with the Euro Heart Survey (EHS)13 of patients with CAD across Europe, our figure of 20% for DM was also similar to their 18%, and for IGT it was slightly lower than the 36.5% quoted in the EHS.12

Major limitations of our study warrant consideration. We did not include a control group without CAD because this study focused on the MS specifically in patients with established CAD. However, our group is currently participating in another larger study, the ‘Heart of Soweto Study,’17 which is investigating the emergence of CAD in the black African community and it includes a control group recruited from the same population as the patients. The relatively small sample size, particularly the low number of women, hindered the wider extrapolation of our results, which may have been skewed somewhat by the exclusion of patients with DM. Our study is, however, the first to compare the new IDF and NCEP: ATP III criteria for the MS in urbanised black South Africans with CAD.

In conclusion, our finding that both definitions generated similar prevalence estimates of the MS implies that the predicted risk of developing CAD, DM and other adverse events based on the new IDF definition is likely to be similar to that observed with the NCEP: ATP III definition. Regardless of which definition is used, the high prevalence rate indicates that large numbers of black South Africans have the MS. Increasing recognition of the MS in this ethnic group is, therefore, an important initial step in addressing the metabolic problems associated with the syndrome.

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