Postprandial lipaemia, metabolic syndrome and LDL particle size in urbanised South African blacks with and without coronary artery disease

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Summary

Background: Postprandial lipaemia, characterised by a rise in triglycerides (TG) after eating, is associated with coronary artery disease (CAD) and metabolic syndrome (MetS). Small, dense, low-density lipoprotein (LDL) particles are implicated in atherogenesis. Little is known about postprandial lipaemia or small, dense LDL particles in urbanised black South Africans.

Aims: Assess postprandial lipaemia in black CAD patients with and without MetS and measure their fasting and postprandial lipid profiles and LDL particles.

Methods: Anthropometric data, biochemical variables and LDL particles were measured in 40 patients and 20 control subjects. Twenty three patients met International Diabetes Federation criteria for MetS and were subdivided according to fasting TG concentration either < or > 1.7 mmol/l. Postprandial lipaemia was assessed by an oral fat tolerance test (OFTT) and area under the curve (AUC).

Results: CAD patients with and without MetS had similar fasting lipid profiles, postprandial responses during OFTT and AUCs. MetS patients with fasting TG > 1.7 mmol/l had greater postprandial responses (P<0.001) and higher AUC (P<0.0001) than patients with TG < 1.7 mmol/l. AUC was higher in all patients than controls (P<0.03). The most significant correlation was between fasting TG and AUC (r=0.8703; P<0.0001). Small, dense LDL particles were present in 29 patients (72.5%) and 3 controls (15%) (p=0.0001).

Conclusions: Postprandial lipaemia was common in black CAD patients, including patients with MetS. Fasting TG concentration was the strongest determinant. Small, dense LDL particles were highly associated with CAD.

Introduction

The role of lipids and lipoproteins in the pathogenesis of atherosclerosis was first described by Gofman and Lindgren more than 50 years ago.¹ Subsequently, studies by Fraser² and Zilversmit³ in the 1970s led to the ‘postprandial theory of atherosclerosis’. This hypothesis proposed that atherosclerosis is a postprandial phenomenon that largely depends on the metabolic response to the ingestion of food. The number of meals consumed and the long duration of postprandial lipaemia lead to a continual fluctuation in the degree of lipaemia throughout the day.

Postprandial lipaemia is characterised by a marked increase in plasma levels of triglycerides (TG) and TG-rich lipoproteins. The resultant hyper-triglyceridaemic state is accompanied by a reduced concentration of high density lipoprotein (HDL) cholesterol and a raised level of low density lipoprotein cholesterol. These events are considered to be key features of the metabolic syndrome and to play a significant role in the promotion of atherosclerosis.

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lipoprotein (LDL) cholesterol. The structural protein constituents of these lipoproteins are classified as apolipoproteins. Apolipoprotein A-1 (apo A-1) and apolipoprotein B (apo B) are the main constituents of HDL and LDL, respectively. Lipoprotein (a) [Lp (a)] is composed of a LDL-like particle to which the lipoprotein (a)-specific apolipoprotein is bonded. The aggregation of abnormal levels of these lipoprotein abnormalities is a major risk for the development and progression of coronary artery disease (CAD).

Increased LDL cholesterol appears to be the primary CAD risk factor and it is thought that small, dense particles in the LDL subfraction are implicated in atherogenesis. Small, dense LDL particles are more susceptible to oxidation than large, buoyant LDL particles and they are retained to a higher degree in the arterial wall. Furthermore, small, dense LDL particles display reduced binding to LDL receptors and remain in the circulation for longer periods of time. These LDL particles are, therefore, subject to a greater degree of structural modification, which in turn, may increase their atherogenic potential.

Evidence is accumulating that many patients with established CAD also have postprandial abnormalities in lipid metabolism, and this relationship has been reported by several researchers. All of these studies showed that CAD patients had elevated TG concentrations as well as a prolonged postprandial response after a fatty meal. An enhanced TG rise postprandially also occurs in other conditions that are associated with an increased risk of vascular disease, such as obesity, hypertension, diabetes mellitus (DM) and the metabolic syndrome (MetS). In fact, postprandial lipaemia is now considered to be another characteristic feature of MetS. A further link between postprandial lipaemia and MetS is that an elevated fasting TG concentration is often simultaneously accompanied by abdominal obesity. These two risk factors, together with hypertension, low HDL cholesterol and raised plasma glucose concentrations, are diagnostic criteria for this syndrome.

Historically, CAD has been remarkably rare in black South Africans. However, with urbanisation and its associated epidemiological transition, the prevalence of CAD is increasing rapidly in urban areas. Indeed, whilst infectious diseases such as HIV, tuberculosis and malaria remain the leading cause of death in sub-Saharan Africa, cardiovascular disease is a close second. The INTERHEART study of risk factors associated with CAD in Africa showed that the traditional CAD risk factors, namely, cigarette smoking, hypertension, abdominal obesity and dyslipidaemia could explain 90% of CAD risk. Black Africans, however, tend to have fasting lipid profiles that are less atherogenic than whites, with lower total cholesterol (TC) and LDL cholesterol levels and higher HDL cholesterol concentrations. A recent South African survey reported an increase in cholesterol levels with urbanisation.

Relatively little is known, however, about the occurrence of postprandial lipaemia in urbanised black South Africans. The main aim of this study was to assess the postprandial response to an oral fat test in black patients with CAD, including a subset of patients who also had MetS. A group of control subjects without CAD was included in the study. An additional aim was to measure any quantitative differences in the fasting and postprandial lipid profiles, as well as LDL particle sizes, between these three groups.

**Methods**

**Patients and control subjects**

Black patients attending the Chris Hani Baragwanath Hospital in Soweto, one of the largest hospitals in the southern hemisphere, who underwent diagnostic coronary angiography to confirm or exclude CAD, were approached to participate in the study. Forty patients (33 men and 7 women) with documented CAD, of whom 23 patients (17 men and 6 women) also had MetS, agreed to take part.

Twenty control subjects (13 men and 7 women) who were matched with the patients for age, body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR) were also studied. Patients and control subjects were classified according to the number and extent of lesions in coronary arteries, which were verified by a coronary angiogram performed in the preceding 24 months. All of the patients had significant CAD, which was defined as more than 50% lesions in one or more major coronary arteries. None of the control subjects had evidence of coronary atherosclerosis on coronary angiography. Patients who had a previous myocardial infarction (MI) were at least three months post-MI before the study started. The majority of patients (95%) and control subjects (75%) had moderate hypertension and they were taking antihypertensive medication at the time of the study.

Patients who had a dominant risk factor such as severe hypercholesterolaemia or previously diagnosed DM were excluded from the study. Other exclusion criteria were HIV-positive status, overt liver, renal or thyroid disease and smoking...
more than 20 cigarettes per day. All participants gave written informed consent to take part in the study, which was approved by the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg, South Africa.

Definition of the metabolic syndrome

MetS was defined according to the International Diabetes Federation (IDF) definition, which requires: (1) WC > 94 cm in men or > 80 cm in women plus any two or more of the following risk factors: (2) TG > 1.7 mmol/l or specific treatment for this abnormality; (3) HDL cholesterol < 1.03 mmol/l in men or < 1.29 mmol/l in women or specific treatment for this abnormality; (4) blood pressure (BP) > 130/85 mmHg or treatment of previously diagnosed hypertension; and (5) 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.

Design

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

On the day of the study, each participant underwent a structured examination, which included an interview. Height, weight, WC and hip measurements, a fasting venipuncture and an oral fat tolerance test (OFTT) 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 WHR. Questionnaires were used to obtain information on demographic variables, medical history, medication use, dietary habits, physical activity and smoking status.

Oral fat tolerance test (OFTT)

After a 12-h overnight fast, an intravenous catheter was inserted into a forearm vein for blood sampling. The OFTT was performed as described by Patsch et al. with a slight modification of the fatty meal. Briefly, it consisted of cream, chocolate-flavoured syrup, sugar and powdered milk, which provided energy from fat (83.5%), carbohydrates (14%) and protein (2.5%). The meal was consumed within 20 min, after which the participants were instructed not to take anything orally, except water, for the subsequent eight hours. Lipid profiles comprising TC, HDL cholesterol, LDL cholesterol and TG concentrations were measured at baseline (defined as the value at 0 h) and at 2 h, 4 h, 6 h and 8 h post-load. In addition, fasting levels of apo A-1, apo B, Lp (a), free fatty acids (FFA), glucose and LDL particle sizes were measured.

Laboratory measurements

Serum concentrations of TC, HDL cholesterol, TG and plasma glucose were measured by enzymatic colorimetric methods using a Hitachi automated clinical analyser and reagents were supplied by Roche Diagnostics GmbH, Mannheim, Germany. Apo A-1, apo B and Lp (a) levels were measured with the same analyser using immunoturbidometric assays (Tina-quant, Roche Diagnostics, GmbH, Mannheim, Germany). Calculation of LDL cholesterol concentrations was based on the Friedewald equation. LDL subfractions were measured in serum by linear, polyacrylamide gel electrophoresis using a Quantimetrix Lipoprint System LDL Subfractions kit (Quantimetrix, CA, USA). The method resolves the LDL subfractions into profiles consisting primarily of large, buoyant particles or predominantly small, dense particles.

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. One-way analysis of variance (ANOVA) for repeated measures within a group or ANOVA for completely randomised measures between groups was used to assess any differences between the means of the variables, as appropriate. Comparison of two groups was done by the Student’s paired or unpaired \( t \)-test and the Mann–Whitney \( U \)-test or the Wilcoxon Signed-Rank test for parametric or non-parametric data, respectively. Results are expressed as mean ± SD or as proportion (%). The frequency of LDL profiles consisting of large or small LDL subfractions was compared using Fishers Exact test. Area under the curve (AUC) for serial measurements of TG concentrations at baseline and after the fat load was calculated using the trapezoid rule. Linear regression analysis and correlation coefficient calculations were
Table 1  Anthropometric measurements, fasting biochemical variables and clinical characteristics of the main study groups

<table>
<thead>
<tr>
<th></th>
<th>CAD patients with MetS (n=23)</th>
<th>CAD patients without MetS (n=17)</th>
<th>Control subjects (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.4 ± 9.0</td>
<td>53.7 ± 8.6</td>
<td>49.8 ± 9.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.7 ± 4.8c</td>
<td>24.9 ± 2.7a</td>
<td>29.1 ± 6.8</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>104 ± 7.2c,b</td>
<td>87.7 ± 6.7</td>
<td>93.5 ± 14.3</td>
</tr>
<tr>
<td>WHR</td>
<td>0.93 ± 0.05</td>
<td>0.91 ± 0.08</td>
<td>0.91 ± 0.07</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.34 ± 1.29</td>
<td>5.20 ± 0.91</td>
<td>4.63 ± 0.97</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.12 ± 0.25</td>
<td>1.23 ± 0.28</td>
<td>1.25 ± 0.47</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>3.37 ± 1.33</td>
<td>3.21 ± 0.89</td>
<td>2.89 ± 0.80</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.81 ± 0.91</td>
<td>1.63 ± 1.04</td>
<td>1.30 ± 0.40</td>
</tr>
<tr>
<td>Apo A-1 (mg/dl)</td>
<td>131 ± 36.5</td>
<td>135 ± 21.8</td>
<td>119 ± 37.8</td>
</tr>
<tr>
<td>Apo B (mg/dl)</td>
<td>103 ± 39.0</td>
<td>98.1 ± 25.1</td>
<td>82.9 ± 24.9</td>
</tr>
<tr>
<td>Lp(a) (mg/dl)</td>
<td>68.5 ± 35.2</td>
<td>50.3 ± 29.9</td>
<td>56.6 ± 37.7</td>
</tr>
<tr>
<td>FFA (mmol/l)</td>
<td>0.83 ± 0.28</td>
<td>0.90 ± 0.46</td>
<td>0.85 ± 0.30</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>5.37 ± 0.76b</td>
<td>5.02 ± 0.90</td>
<td>4.64 ± 0.83</td>
</tr>
<tr>
<td>On antihypertensive medication</td>
<td>22 (96%)</td>
<td>16 (94%)</td>
<td>15 (75%)</td>
</tr>
<tr>
<td>Cigarette smoker</td>
<td>7 (30%)</td>
<td>7 (41%)</td>
<td>2 (10%)</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD or %.

aP<0.02 for CAD patients without MetS vs. control subjects; bP<0.01 for CAD patients with MetS vs. control subjects; cP<0.0001 for CAD patients with MetS vs. CAD patients without MetS.

CAD: coronary artery disease; MetS: metabolic syndrome; WHR: waist-to-hip ratio; HDL: high density lipoprotein cholesterol; LDL: low density lipoprotein cholesterol; Apo: apolipoprotein; Lp: lipoprotein; FFA: free fatty acids.

performed to reveal any significant determinants of postprandial lipaemia (i.e. high AUC).

Results

Patients and control subjects

Patients (n=40) and control subjects (n=20) were matched for age (mean ± SD = 54.1 ± 8.8 vs. 49.8 ± 9.8 years), BMI (mean ± SD = 28.2 ± 4.9 vs. 29.1 ± 6.8 kg/m²), WC (mean ± SD = 96.8 ± 10.5 vs. 93.5 ± 14.3 cm) and WHR (mean ± SD = 0.92 ± 0.06 vs. 0.91 ± 0.07), all P>0.05.

Measurements of WC and the number of other risk factors for MetS were assessed according to the IDF definition. This allowed classification of the 40 patients into two groups. MetS was present in 23 patients (57.5%) and absent in 17 patients (42.5%). The group with MetS was further divided into patients who had a fasting TG concentration either ≥1.7 mmol/l (MetS +veTG, n=10) or <1.7 mmol/l (MetS −veTG, n=13). Three of the control subjects had MetS as defined, but they had no evidence of CAD on angiography and were, therefore, included in the study.

Fasting profiles of the main study groups

Table 1 summarises the anthropometric measurements, fasting biochemical variables and clinical characteristics of the groups of patients with and without MetS and the control subjects. Mean age and WHR were similar in all groups. Mean BMI was significantly higher in patients with MetS compared with those without MetS (P<0.0001), and lower in patients without MetS than in control subjects (P<0.02).

Fasting lipid profiles showed that patients with and without MetS had slightly elevated mean TC, LDL cholesterol and TG levels and lower HDL concentrations than the control subjects, but not significantly so. Mean apo A-1 and apo B levels were also slightly, but not significantly, higher in both patient groups than in control subjects. Mean Lp(a) levels were higher in patients with MetS and lower in patients without MetS compared with control subjects. Mean FFA concentrations were similar in all groups, while mean glucose concentrations were slightly higher in both patient groups compared with control subjects, significantly so in patients with MetS (P<0.01).

Most of the patients with MetS (96%) and without MetS (94%) and control subjects (75%) had moderate hypertension and were taking antihypertensive medication. Seven patients in each group and two control subjects smoked less than 20 cigarettes per day.

Postprandial lipid profiles of the main study groups

Lipid profiles of the patients with and without MetS and control subjects measured at baseline and
and denote difference P mmol/l.

Postprandial responses in patients with MetS and baseline TG $\geq$ or <1.7 mmol/l

Postprandial responses during the OFTT in patients with MetS and baseline TG concentration either $\geq$1.7 mmol/l (MetS +veTG) or <1.7 mmol/l (MetS −veTG), and control subjects are shown in Table 3 and presented graphically in Figure 1. Significant differences were found between the three groups before and after the fat load (ANOVA all P<0.0001). Mean TG concentrations were significantly increased in the MetS +veTG patients compared with the MetS −veTG patients, and also in the MetS +veTG patients compared with the control subjects at all time points (0 h P<0.0001; 2 h, 4 h, 6 h and 8 h P<0.0001). No significant differences were found between MetS −veTG patients and control subjects at any time point (P>0.05).

**Area under the curve**

Mean AUCs for TG were similar in patients with and without MetS (mean ± SD in mmol.h/l = 24.1 ± 12.2 and 25.7 ± 17.0, respectively). AUC in each MetS patient group was significantly higher than in the control subjects (mean ± SD of patients with and without MetS vs. control subjects in mmol.h/l = 24.1 ± 12.2 vs. 15.9 ± 6.1, P<0.02; and 25.7 ± 17.0 vs. 15.9 ± 6.1, P<0.04, respectively). In patients with MetS and baseline TG concentrations ≥1.7 mmol/l, AUC was significantly higher than in MetS patients whose baseline TG concentrations were <1.7 mmol/l (mean ± SD in mmol.h/l = 34.5 ± 10.5 vs. 16.2 ± 5.4, P<0.0001). AUC in the total patient group (n=40) was significantly higher than in the control subjects (mean ± SD in mmol.h/l = 24.8 ± 14.2 vs. 15.9 ± 6.1, P<0.03). A schematic presentation of AUCs in patients with CAD and control subjects is shown in Figure 2.

**Linear regression analysis**

Linear regression analysis of the total group of patients (n=40), in which AUC for TG was the dependent variable and age, BMI, WC, WHR, TC, HDL cholesterol, LDL cholesterol, fasting TG, apo A-1, apo B, Lp (a), FFA and glucose were the independent variables, revealed that only fasting TG, FFA and glucose correlated significantly with AUC. The highest correlation coefficient (r) was found for fasting TG (r=0.8703; P<0.0001), followed by FFA (r=0.4784; P<0.01) and glucose (r=0.4038; P<0.01) (Figure 3).

### Table 2 Lipid profiles of the main study groups measured at baseline and during the oral fat tolerance test

<table>
<thead>
<tr>
<th></th>
<th>CAD patients</th>
<th>CAD patients</th>
<th>Control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>with MetS</td>
<td>without MetS</td>
<td>(n=23)</td>
</tr>
<tr>
<td></td>
<td>(n=17)</td>
<td>(n=17)</td>
<td></td>
</tr>
<tr>
<td><strong>Total cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 h</td>
<td>5.34 ± 1.29a</td>
<td>5.20 ± 0.91b</td>
<td>4.63 ± 0.97c</td>
</tr>
<tr>
<td>2 h</td>
<td>5.12 ± 1.26</td>
<td>4.90 ± 0.89</td>
<td>4.17 ± 0.87</td>
</tr>
<tr>
<td>4 h</td>
<td>5.16 ± 1.29</td>
<td>4.97 ± 0.82</td>
<td>4.42 ± 0.93</td>
</tr>
<tr>
<td>6 h</td>
<td>5.17 ± 1.18</td>
<td>4.94 ± 0.82</td>
<td>4.34 ± 0.87</td>
</tr>
<tr>
<td>8 h</td>
<td>5.18 ± 1.13</td>
<td>5.02 ± 0.91</td>
<td>4.49 ± 0.97</td>
</tr>
<tr>
<td><strong>HDL cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 h</td>
<td>1.12 ± 0.25c</td>
<td>1.23 ± 0.28c</td>
<td>1.25 ± 0.47c</td>
</tr>
<tr>
<td>2 h</td>
<td>1.06 ± 0.25</td>
<td>1.12 ± 0.24</td>
<td>1.09 ± 0.29</td>
</tr>
<tr>
<td>4 h</td>
<td>1.02 ± 0.27</td>
<td>1.08 ± 0.24</td>
<td>1.08 ± 0.34</td>
</tr>
<tr>
<td>6 h</td>
<td>0.97 ± 0.26</td>
<td>1.01 ± 0.21</td>
<td>1.05 ± 0.33</td>
</tr>
<tr>
<td>8 h</td>
<td>1.00 ± 0.25</td>
<td>1.01 ± 0.21</td>
<td>1.08 ± 0.35</td>
</tr>
<tr>
<td><strong>LDL cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 h</td>
<td>3.37 ± 1.33c</td>
<td>3.21 ± 0.89c</td>
<td>2.89 ± 0.80c</td>
</tr>
<tr>
<td>2 h</td>
<td>3.00 ± 1.30</td>
<td>2.76 ± 0.92</td>
<td>2.49 ± 0.85</td>
</tr>
<tr>
<td>4 h</td>
<td>2.95 ± 1.46</td>
<td>2.67 ± 0.48</td>
<td>2.14 ± 0.84</td>
</tr>
<tr>
<td>6 h</td>
<td>2.87 ± 1.42</td>
<td>2.43 ± 0.58</td>
<td>2.23 ± 0.78</td>
</tr>
<tr>
<td>8 h</td>
<td>2.93 ± 1.26</td>
<td>2.52 ± 0.60</td>
<td>2.17 ± 0.79</td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 h</td>
<td>1.81 ± 0.91c</td>
<td>1.63 ± 1.04c</td>
<td>1.30 ± 0.40c</td>
</tr>
<tr>
<td>2 h</td>
<td>2.32 ± 0.97</td>
<td>2.27 ± 1.56</td>
<td>1.72 ± 0.72</td>
</tr>
<tr>
<td>4 h</td>
<td>3.23 ± 1.80</td>
<td>3.44 ± 2.34</td>
<td>2.14 ± 0.85</td>
</tr>
<tr>
<td>6 h</td>
<td>3.85 ± 1.99</td>
<td>4.37 ± 2.73</td>
<td>2.60 ± 1.01</td>
</tr>
<tr>
<td>8 h</td>
<td>3.54 ± 2.32</td>
<td>4.01 ± 3.41</td>
<td>2.29 ± 0.83</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. Results are presented in mmol/l.

P values were determined by repeated measures ANOVA and denote difference within each group.

° P<0.05; † P<0.001; ‡ P<0.0001.

CAD: coronary artery disease; MetS: metabolic syndrome; HDL: high density lipoprotein cholesterol; LDL: low density lipoprotein cholesterol;

0 h: baseline concentration; 2 h, 4 h, 6 h, 8 h: concentrations at 2, 4, 6 and 8 hours after the fat load.

During the OFTT are shown in Table 2. There were no significant differences in TC, HDL cholesterol, LDL cholesterol or TG levels between the three groups before or after the fat load (ANOVA all P>0.05). Within each group, however, small but significant changes from baseline were found in the lipid profiles (ANOVA P<0.05, P<0.001 and P<0.0001 in patients with MetS, patients without MetS and control subjects, respectively, for TC; and P<0.0001 in the three groups for HDL cholesterol, LDL cholesterol and TG). In all groups, mean concentrations of TC, HDL cholesterol and LDL cholesterol were significantly lower than baseline and TG levels were significantly higher than baseline at each time point during the OFTT.
LDL subfractions

LDL subfraction profiles consisting of predominantly small, dense LDL particles were found significantly more frequently in patients with CAD (n = 29, 72.5%) compared with controls (n = 3, 15.0%); Fishers Exact test: P = 0.0001. Patients with MetS (n = 17) and without MetS (n = 12) also had significantly more small, dense LDL particles than control subjects (Fishers Exact test: p = 0.0002 and p = 0.002, respectively).

Discussion

This study assessed the occurrence of postprandial lipaemia in urbanised South African black patients with CAD, some of whom also had MetS. Our results showed that CAD patients with and without MetS had similar fasting lipid profiles, postprandial responses during the OFTT and AUCs. We found that MetS patients with higher fasting TG concentrations had greater postprandial responses and higher AUCs than those with lower TG levels. In the total patient group, AUC was significantly higher than in the control subjects and the fasting TG concentration was the strongest determinant of postprandial lipaemia. Another interesting observation was that LDL subfractions consisting of predominantly small, dense LDL particles were present in more than 70% of our patients with CAD.

Table 3

Postprandial responses during the oral fat tolerance test in coronary artery disease patients with the metabolic syndrome and baseline triglyceride concentration either ≥1.7 mmol/l (MetS + veTG) or <1.7 mmol/l (MetS -veTG) and control subjects

<table>
<thead>
<tr>
<th>MetS +veTG</th>
<th>TG 0h (mmol/l)</th>
<th>TG 2h (mmol/l)</th>
<th>TG 4h (mmol/l)</th>
<th>TG 6h (mmol/l)</th>
<th>TG 8h (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG ≥1.7 mmol/l (n = 10)</td>
<td>2.62 ± 0.81a</td>
<td>3.12 ± 0.74b</td>
<td>4.73 ± 1.48b</td>
<td>5.41 ± 1.98b</td>
<td>5.38 ± 2.40b</td>
</tr>
<tr>
<td>MetS -veTG</td>
<td>TG &gt;1.7 mmol/l (n = 13)</td>
<td>1.18 ± 0.26</td>
<td>1.70 ± 0.61</td>
<td>2.08 ± 0.99</td>
<td>2.66 ± 0.88</td>
</tr>
<tr>
<td>Control subjects (n = 20)</td>
<td>1.30 ± 0.40</td>
<td>1.72 ± 0.72</td>
<td>2.18 ± 0.86</td>
<td>2.60 ± 1.01</td>
<td>2.29 ± 0.83</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

aP<0.0001 for MetS +veTG patients vs. MetS -veTG patients and control subjects at 0 h; bP<0.001 for MetS +veTG patients vs. MetS -veTG patients and control subjects at 2 h, 4 h, 6 h and 8 h.

MetS: metabolic syndrome; TG: triglycerides; 0 h: baseline concentration; 2 h, 4 h, 6 h, 8 h: concentrations at 2, 4, 6 and 8 hours after the fat load.
Fasting lipid profiles and postprandial responses to the oral fat load were similar in our patients with and without MetS. A possible explanation for this finding might be that because patients in both groups had established CAD, they exhibited some of the underlying features of CAD, such as atherogenic dyslipidaemia. The variables that differentiated the two groups were WC and BMI, with the MetS patients being more abdominally obese than those without MetS. A positive correlation between BMI and postprandial lipoaemia has been reported in some studies where an elevated BMI seemed to aggravate the postprandial response.28,29 In our study, however, there were no significant differences in postprandial magnitude during the OFTT or AUCs between patients with and without MetS, suggesting that obesity may not have been an additional factor in our patients. This finding agrees with a report by Kolovou et al.30 who concluded that obesity does not exacerbate the postprandial response.

Recent studies have indicated that an elevated fasting TG concentration is the main determinant of an exaggerated postprandial response.30–32 Since an enhanced TG rise postprandially also occurs in MetS,30–32 we divided a subset of our CAD patients with MetS into two groups according to their fasting TG concentrations and analysed their responses during the OFTT. We found that MetS patients with higher fasting TG concentrations (≥1.7 mmol/l) had significantly greater postprandial TG concentrations and higher AUCs than MetS patients whose fasting TG concentrations were below the cut-off point. This is in keeping with the results of a study in white patients with MetS30, although their AUCs above (28.2 mmol.h/l) and below (14.5 mmol.h/l) the 1.7 mmol/l cut-off point were lower than in our black MetS patients (34.5 mmol.h/l and 16.2 mmol.h/l). Taking the MetS patients as a whole, however, other studies in white MetS patients31,32 reported slightly higher AUCs (28.6 mmol.h/l and 27.0 mmol.h/l) than AUC (24.1 mmol.h/l) calculated in our black MetS patients. Interestingly, in a study by Patsch et al.9 AUC in white patients with CAD (24.0 mmol.h/l) was almost identical to AUC in our total group of black patients with CAD (24.8 mmol.h/l). AUC in our CAD patients was significantly higher than in the control subjects (15.9 mmol.h/l), and linear regression analysis confirmed that AUC correlated most significantly with the fasting TG concentrations.

As reported in previous studies of postprandial lipid metabolism in patients with CAD,9,33 we also noted that as TG concentrations increased in the OFTT, HDL cholesterol and LDL cholesterol levels decreased slightly, but significantly, from baseline. The mechanism proposed for this inverse relationship is that during the postprandial period, the exchange of core lipids is enhanced through the action of cholesteryl ester transfer protein.34 This process results in a reduction of circulating HDL cholesterol and LDL cholesterol as the TG-enriched HDL and LDL particles are subjected to lipolysis by hepatic lipase, ultimately forming small, dense particles.

There is a consistent relationship between increased fasting TG concentrations, elevated postprandial TG, and the presence of small, dense figures.
LDL particles. Several studies have found that the number of these particles is raised in CAD and they are present in 40%–50% of CAD patients. In our study, however, the relative proportion was somewhat higher with more than 70% of CAD patients having LDL subtraction profiles composed of predominantly small, dense LDL particles. There is some evidence that ethnic differences might influence LDL particle size. A study in a Mediterranean population revealed a low prevalence of small, dense LDL particles. Cho et al. reported that in Asia, Koreans had a higher concentration of small, dense particles than Western whites of Scottish origin. A study by Kral et al. found that white individuals have a greater preponderance of small, dense LDL particles than African-Americans, while another recent study reported that the level of these particles was remarkably lower in Afro-Caribbean men than either African-American or white men.

Our study was limited in certain aspects. Criteria for postprandial TG levels, similar to the diagnostic glucose cut-offs defined for the oral glucose tolerance test, have not been specified for the OFTT. This lack of standardisation has made it difficult to compare studies because researchers have used different meals containing variable amounts of fat, carbohydrate and protein. Furthermore, the length of studies and the time interval between blood sampling were not uniform. Some studies measured TG concentrations every hour and others (ourselves included) every two hours, or every three hours. Nevertheless, we have attempted to compare the results of our OFTT with studies that used a similar method. Performance of the OFTT is time-consuming and requires considerable laboratory resources; therefore, we studied a relatively small number of patients and control subjects. It was not our intention to recruit more male than female patients, but because CAD is more prevalent in males, the majority of participants in our study happened to be male. However, these limitations probably do not detract from the overall conclusions.

This study is, as far as we are aware, the first to contribute information about postprandial lipaemia in urbanised South African blacks with CAD. Despite relatively low fasting lipid levels, significant increases were demonstrated following a fat load. Prolonged exposure of the endothelium to TG-rich atherogenic remnant particles might be the reason why postprandial increases in TG account for greater CAD risk. Our results confirmed that the fasting TG concentration was the strongest determinant of postprandial lipaemia. Furthermore, we showed that a preponderance of small, dense LDL particles was highly associated with CAD in our black patients. Although their CAD prevalence is low at this stage, it is likely to increase rapidly among urban dwellers as they adopt a Western lifestyle.

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References