High prevalence of abnormal glucose regulation in patients presenting for routine coronary angiography

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ABSTRACT

Abnormal glucose metabolism is a known risk factor for coronary artery disease (CAD) and is frequently unrecognised even in patients with acute coronary syndrome. Patients with stable coronary symptoms frequently have multiple risk factors and may have no assessment of glucose regulation. The purpose of this study was to assess the prevalence of impaired glucose tolerance (IGT) and diabetes mellitus (DM) in a group of patients with stable symptoms presenting for coronary angiography.

A modified oral glucose tolerance test (OGTT) was performed on 182 unselected patients undergoing elective angiography. Patients with known DM were excluded. Demographic data including cardiovascular risk factors, body mass index (BMI), and history of CAD were recorded.

In all, 182 patients with a mean age of 62.1 years (±10.7 years) were studied. Indications for angiography were suspected angina. By WHO criteria an abnormal two-hour glucose was present in 49% of individuals, with 10.4% of these patients having overt DM. An abnormal two-hour glucose was seen in 63.2% of patients with significant CAD compared with 40.3% with normal or insignificant disease (p=0.004); 48.9% of patients with IGT or DM had normal fasting plasma glucose (FPG). In 78% of patients, BMI was over 25kg/m^2.

In this high risk population with multiple risk factors for CAD, previously undetected IGT and overt DM are very common. Almost two-thirds of patients with significant CAD had abnormal glucose regulation. The use of an FPG test alone may miss a significant number of patients with unrecognised glucose intolerance.

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KEY WORDS

diabetes mellitus; coronary artery disease; abnormal glucose regulation; oral glucose tolerance test; impaired fasting glucose

Introduction

Type 2 diabetes mellitus (DM) and impaired glucose regulation are known risk factors for coronary artery disease[1] and are frequently unrecognised even in patients with acute coronary syndrome. Patients with stable coronary symptoms frequently have multiple risk factors and may have no assessment of glucose regulation.

Even with elevated blood glucose levels still below the current threshold for DM there is an apparent increased risk of coronary artery disease (CAD).[2–4] Unfortunately, a large proportion of adults meeting the diagnostic criteria for diabetes do, however, remain undiagnosed and this has been shown in the recent Glucose Tolerance in Patients with Acute MI (GAMI) study.[5] It has been suggested that an oral glucose tolerance test (OGTT) should be part of the evaluation of overall cardiac risk in patients with CAD.[6,7]

The use of the OGTT with a two-hour plasma glucose assessment in the diagnosis of DM has been a debated topic. The American Diabetes Association[8] favours the use of the fasting plasma glucose (FPG) in the diagnosis of DM whereas the World Health Organization (WHO) endorses the use of the OGTT in clinical practice.[9] Many studies have questioned the preference of the FPG test over the two-hour plasma glucose in diagnosing diabetes.[10–12] The impaired glucose tolerance (IGT) category has been associated with cardiovascular events and cardiovascular disease mortality,[13–21] whereas the association between impaired fasting glucose (IFG) and cardiovascular disease is not as strong.[14–19]

The main objectives of our study were: to determine the prevalence of abnormal glucose metabolism in patients presenting for elective coronary angiography; to evaluate if there was a relationship between the presence of significant CAD and abnormal glucose regulation; and to determine if an FPG was sufficient to diagnose abnormal glucose regulation or whether a two-hour plasma glucose after a glucose challenge was a more sensitive marker. As a secondary aim, the relationship between body mass index (BMI) and abnormal glucose metabolism and BMI and significant CAD was also investigated.

Methods

This was a prospective observational study performed in a single tertiary referral cardiology centre. A total of 182 unselected patients undergoing elective cardiac catheterisation were included in the study. Only patients without a diagnosis of DM were

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Table 1. Patient demographics demonstrating the age, gender, risk factor profiles and current medications. Comparisons are made between those with significant CAD and those with insignificant or no CAD

	All n=182	Coronary artery disease (CAD) n=68	Normal/ insignificant CAD n=114	P-value
Age: years, mean [SD]	62.1 [10.7]	65.3 [9.8]	60.9 [10.9]	0.009
Gender: male, n (%)	111 (61%)	47 (69.1%)	64 (56.1%)	0.083
Risk factors:				
BMI: kg/m^2, mean [SD]	29.0 [5.3]	28.6 [4.6]	29.3 [5.7]	0.389
Cholesterol: mmol/L, mean [SD]	4.7 [1.04]	4.5 [1.1]	4.84 [1.0]	0.066
LDL: mmol/L, mean [SD]	2.3 [1.0]	2.4 [1.0]	2.4 [1.1]	0.728
Positive family history, n (%)	83 (45.6%)	30 (44.1%)	53 (46.5%)	0.756
Current smoker, n (%)	29 (15.9%)	9 (13.2%)	20 (17.5%)	0.698
Hypertension, n (%)	109 (59.9%)	46 (67.6%)	63 (55.3%)	0.099
Medication:				
Aspirin, n (%)	147 (80.8%)	62 (91.2%)	85 (74.6%)	0.006
Beta blocker, n (%)	94 (51.6%)	44 (64.7%)	50 (43.9%)	0.006
Statin, n (%)	114 (62.6%)	53 (77.9%)	61 (53.5%)	0.001

included; patients with known DM were excluded. This study was compiled with the recommendations of the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was obtained from all patients prior to participation in the study.

Demographic data collected included age, gender, cardiovascular risk factors including BMI, family history of premature CAD (a first degree relative <55 years in men and <65 years in women with CAD), smoking history, history of hypertension (BP >140/90mmHg) and hyperlipidaemia. Patients were considered to have hyperlipidaemia if the fasting total cholesterol was >5mmol/L, LDL cholesterol was ≥3mmol/L, or if they were taking medication for hypercholesterolaemia according to European Society of Cardiology guidelines.[22] Angiograms were reported by one of three cardiologists who were blinded to the results of glucose status of the patient.

Prior to angiography an FPG and lipid profile (total-, LDL-, HDL-cholesterol and triglycerides) were performed on each patient. After angiography each patient received a 75g oral glucose load and had a plasma glucose measured two hours later. Patients were divided into four categories depending on the results of the OGTT according to WHO guidelines:[9] *Normal:* FPG <6.1mmol/L and a two-hour glucose <7.8mmol/L; *IFG:* FPG between ≥6.1 but <7.0 and a two-hour glucose <7.8mmol/L; *IGT:* two-hour plasma glucose ≥7.8 but <11.0mmol/L; *Diabetes mellitus:* FPG ≥7.0mmol/L and/or a two-hour ≥11.1mmol/L.

Coronary angiography results were classified as normal, insignificant CAD (one or more stenosis <70%) and significant CAD (stenosis of ≥70% in one or more coronary arteries).

The classification was dichotomised to normal/insignificant CAD and significant CAD for some analyses to ease the interpretation of results.

BMI was recorded and classified into six categories according to WHO classification:[22] *Underweight:* BMI <18.5kg/m^2; *Normal weight:* BMI 18.5–24.9kg/m^2; *Pre-obese:* BMI 25.0–29.9kg/m^2; *Class I obesity:* BMI 30.0–34.9kg/m^2; *Class II obesity:* BMI 35.0–39.9kg/m^2; *Class III obesity:* BMI ≥40kg/m^2.

Statistical analysis. Data were cleaned and analysed using SPSS version 13.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics, univariate and multivariate analysis were performed for each variable. Data are expressed as mean ± standard deviations (SD) when normally distributed. Relationships for fasting glucose levels and two-hour glucose levels were performed using Pearson's correlation (fasting glucose, two-hour glucose, cholesterol, LDL, BMI and age) or Spearman's (LDL). The independent Student's t-test or Kruskal–Wallis test was performed for categorical data. A p-value of <0.05 was considered statistically significant.

The multivariate linear regression model was used to determine which variables influenced the two-hour plasma glucose results. The variables included in the model were those associated with a two-hour plasma glucose with a p-value <0.20 at univariate analysis. These variables were entered into the model and checked for colinearity. Continuous variables included were age, BMI, fasting glucose level and LDL. Dummy variables were created for hypertension, aspirin and beta blocker medication and the presence of significant (>70% stenosis) coronary artery disease at angiography. Gender was also included although there was no association with the two-hour plasma glucose result.

Results

In all, 182 patients without a prior history of DM were enrolled in the study. All patients recruited were presenting for elective day case cardiac catheterisation for suspected coronary artery disease. All patients were Caucasian. The mean (±SD) age was 62.1 years (±10.7) and 61% were male.

Demographic and baseline risk factor profiles for all patients by

Figure 1. The percentage of patients presenting for elective coronary angiogram with previously undiagnosed abnormal glucose regulation. Groups are divided into: normal or insignificant coronary artery disease (CAD), CAD, and the total patient cohort. Results compare the abnormal glucose regulation in the fasting plasma glucose and 2-hour plasma glucose from the OGTT

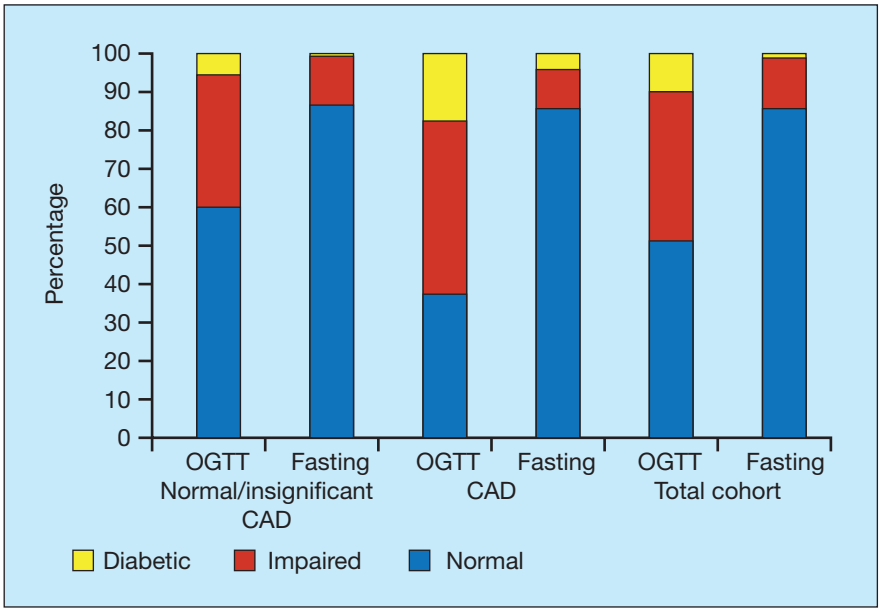


Table 2. Patients with significant coronary artery disease (CAD) and those with normal/insignificant CAD: results showing the mean fasting plasma glucose (FPG) and 2-hour glucose, and the percentage of those with abnormal FPG and 2-hour glucose

	Coronary artery disease n=68	Normal/ insignificant CAD n=114	P-value
Fasting glucose, mean [SD]	5.5 [0.8]	5.3 [0.6]	0.025
2-hr plasma glucose, mean [SD]	8.7 [2.4]	7.5 [2.1]	0.001
Abnormal fasting glucose, n (%)	30 (44.1%)	36 (31.6%)	0.032
Abnormal 2-hr plasma glucose, n (%)	43 (63.2%)	46 (40.3%)	0.004
Abnormal fasting glucose and 2-hr plasma glucose, n (%)	25 (36.8%)	21 (18.4%)	0.006

subgroup (normal/insignificant CAD and CAD) are presented in Table 1. A significantly higher percentage of patients with CAD were older and taking aspirin, beta blockers and statins; otherwise, no significant difference in patient demographics was demonstrated between the two groups.

Plasma glucose levels. From the total cohort of patients, new DM was diagnosed in 1.6% based on FPG levels and in 10.4% based on the two-hour post glucose challenge result. IFG was identified in 12.6% of patients compared to 38.5% with a two-hour IGT (Figure 1).

Relationship between CAD and abnormal glucose metabolism. Significant CAD was identified in 37% of patients. Of this group, 63.2% had an abnormal two-hour glucose compared to 40.3% with insignificant or no CAD (p=0.004).

The association between abnormal glucose metabolism and the presence of significant CAD was stronger for the two-hour post glucose challenge than the FPG; 17.6% had overt DM diagnosed after a glucose challenge compared with 4.4% with DM based on an FPG. More patients with CAD and impaired glucose regulation were identified based on the glucose challenge (Table 2).

Fasting glucose versus two-hour plasma glucose. On comparing the overlap of the FPG and the two-hour glucose, almost half (48.9%) of the patients with an abnormal two-hour glucose had normal fasting plasma glucose; 14.3% with an abnormal FPG had a normal two-hour result. Twenty individuals (10.9%) met both criteria, with an abnormal FPG and abnormal two-hour glucose.

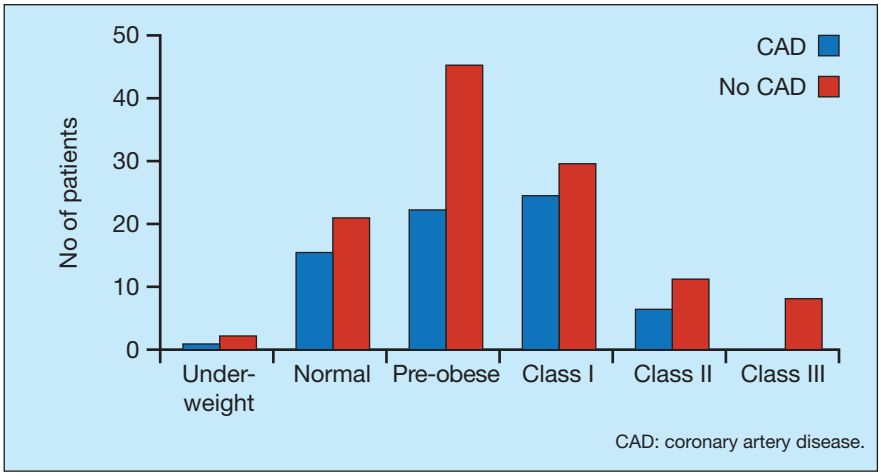
Multivariate analyses demonstrated that an abnormal two-hour glucose was associated with abnormal fasting plasma glucose (p=0.00, r=0.35), the absence of significant CAD (p=0.023, r= -0.17) and older age (p=0.003, r=0.21). There was no association between BMI, LDL, hypertension, aspirin and beta blocker use or gender.

Body mass index. The mean BMI was 29.1kg/m^2 and 78% of patients had a BMI of 25kg/m^2 or greater (Figure 2). There was a significant correlation between abnormal FPG and elevated BMI (p=0.018) but no correlation between an abnormal two-hour glucose and BMI was observed. There was no correlation between an elevated BMI and the presence of significant coronary artery disease(p=0.690).

Discussion

In this study we report a high prevalence of unrecognised DM and impaired glucose regulation in patients presenting for elective cardiac catheterisation for suspected CAD. Although the prevalence of IGT and DM was highest in patients

Figure 2. The body mass index distribution in the study population



with CAD, it was common even in those without significant CAD who presented for cardiac catheterisation in this study population.

Of the patients with significant CAD, 63.2% had evidence of abnormal glucose metabolism based on an OGTT (45.6% had IGT and 17.6% with DM). These results of an Irish population show higher rates of undiagnosed DM and IGT in patients with stable CAD than those seen in the Euro Heart Survey on diabetes and the heart, where 32% had IGT and 14% had DM on OGTT.[14] The higher average BMI in the Irish cohort (29kg/m^2 vs 27.5kg/m^2) may explain in part this difference in prevalence. This may also explain the high prevalence of IGT and DM in the patient group without CAD in this study.

This study has demonstrated that a significant number of patients presenting for angiography have previously unidentified impaired glucose metabolism. It suggests that all patients should receive a formal assessment of risk factors at this time regardless of the presence or absence of CAD. Attendance for angiography presents an opportunity to engage this group with risk factor management, with advice on smoking cessation, healthy diet and the importance of increased physical activity. In particularly high risk patients, referral to a formal lifestyle intervention programme may be appropriate. Such programmes, individualised and performed by skilled professionals, such as that used in the Finnish Diabetes Prevention Study, have shown compelling results.[23] However, there are limited resources available across Europe even for those with established CAD.[24] Lifestyle programmes should be an integral part of the health care system. All patients at high risk for DM and CAD should have access to comprehensive cardiac prevention programmes.[25]

Almost half of the patients in our study cohort would have remained undiagnosed without the use of a glucose challenge. Even higher rates of patients with normal FPG and an abnormal two-hour glucose were seen in the Euro Heart Survey.[14] Although the two-hour plasma glucose has been reported to be a more sensitive assay, the FPG is considered the test of choice because of convenience, reproducibility and cost.[26] The WHO recommends that the OGTT should be retained for clinical diagnosis in subjects with marginally raised FPG concentrations and as the main measurement for epidemiological studies.[9] Our data suggest that consideration should be given to performing an FPG in all patients presenting for cardiac catheterisation, and a subsequent OGTT performed if a raised FPG is identified.

Stress induced hyperglycaemia has been well documented after acute myocardial infarction.[27,28] In patients with stable symptoms undergoing cardiac catheterisation, studies have indicated the absence of any inflammatory response or stress response.[29,30] In this study, patients had stable symptoms and no history of recent myocardial infarction. All underwent elective angiography as a day case procedure without any major physiological stresses apart from any general anxiety associated with the procedure. Therefore, it is unlikely that stress induced hyperglycaemia was a contributory factor in this study.

In conclusion, in this high risk population with multiple risk factors for CAD, previously undetected impaired glucose regulation and overt DM was common. Almost two-thirds of patients with significant CAD had abnormal glucose results. Intensive lifestyle intervention programmes should be implemented in the management of all patients with impaired glucose regulation and with cardiovascular risk factors. The use of a fasting blood glucose test alone may miss a significant number of patients with unrecognised glucose intolerance. Ideally, patients with significant CAD should be screened for abnormal glucose regulation with an OGTT in order not to miss a large proportion of individuals with normal fasting glucose but IGT.

Declaration of interest

There are no conflicts of interest.

References

References are available at: www.practicaldiabetesinternational.

Key points

- There was a high prevalence of previously undiagnosed diabetes mellitus and impaired glucose regulation in patients presenting for elective coronary angiography. The high prevalence suggests that all these patients should receive a formal assessment of risk factors and appropriate advice on primary prevention of cardiovascular disease and diabetes mellitus
- A significantly higher number of patients with coronary artery disease had abnormal glucose regulation compared with patients with normal or insignificant coronary artery disease
- Almost half of the patients in the study cohort with abnormal glucose regulation would have remained undiagnosed without the use of an oral glucose challenge and assessment of a two-hour plasma glucose

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