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Diagnostic Value of Hemoglobin A1c and Fasting Plasma Glucose Levels in Coronary Artery Bypass Grafting Patients With Undiagnosed Diabetes Mellitus

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Background. **Early detection, diagnosis, and treatment of diabetes are of utmost importance in preventing diabetic complications and improving short- and long-term outcomes in patients undergoing coronary artery bypass grafting surgery. The aim of this study was to evaluate the ability of preoperative hemoglobin A1c (HbA_{1c}) measurement, either alone or in combination with fasting plasma glucose (FPG), to detect glycometabolic disturbances among patients undergoing elective on-pump coronary surgery.**

Methods. **A total of 166 patients who underwent elective isolated on-pump coronary surgery were included. Hemoglobin A1c and 8-hour FPG measurements were obtained by venous blood sampling on the day before the operation. After 1 month, an oral glucose tolerance test was performed in all discharged patients without known diabetes. The sensitivity and specificity for the diagnosis of diabetes were analyzed for FPG, HbA_{1c}, and for the combined use of HbA_{1c} and FPG, in reference to the tolerance test results.**

Results. **Sixty percent of patients without known diabetes were diagnosed as diabetes or prediabetes with glucose tolerance test. Compared with either test alone, combined use of FPG and HbA_{1c} had higher sensitivity and specificity. Positive predictive values for FPG, HbA_{1c}, and combined use of these two factors were 83.6%, 94%, and 97%, respectively. The combined use had a sensitivity and specificity of 84.4% and 94.1%, respectively.**

Conclusions. **Fasting plasma glucose alone does not seem sufficient for diagnosing approximately half of the patients with dysglycemia. Our results suggest that the use of FPG and HbA_{1c} measurements in combination may be a useful strategy to preoperatively identify coronary patients with unknown diabetes.**

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Diabetes mellitus (DM) has long been recognized as an independent risk factor for the development of coronary artery disease (CAD) [1]. The prevalence of CAD in patients with type 2 diabetes ranges between 13% and 43% [1], and 20% to 30% of patients undergoing coronary artery bypass grafting (CABG) have DM [2]. Type 2 diabetes is often asymptomatic in its early stages and can remain undetected for several years before it is diagnosed. Studies have shown that half of the subjects with type 2 diabetes, which is the most common type of DM, are not aware of their condition [3]. Among patients with CAD referred to a cardiologist, the incidence of newly diagnosed glycometabolic disturbances ranges between 51% and 58% [4]. In the undiagnosed diabetic population, asymptomatic hyperglycemia has been reported to predict increased risk of cardiovascular death and morbidity and mortality after cardiac surgery [5]. Therefore, early detection, diagnosis, and treatment of type 2 DM are of utmost importance to prevent diabetic complications, and to improve short- and long-term outcomes in patients undergoing CABG [6].

The most widely used tests for the diagnosis of DM include fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT) [3]. A multitude of reports have indicated that up to 50% of patients with DM who were diagnosed by OGTT criteria would have been missed by FPG criteria [7]. Despite being the diagnostic gold standard for DM, OGTT is costly, time-consuming, and labor intensive [3] and is also impractical for diabetes screening [6]. Therefore, an additional, simple, cost-effective, efficient, and patient-friendly method for detecting these diabetic subjects would be highly desirable. Another suggested measure for clinical screening of DM is hemoglobin A1c (HbA_{1c}) [6].

In this study, we have evaluated the sensitivity and specificity of HbA_{1c} and FPG in detecting type 2 DM. We have grouped the patients as diabetic (type 2) and nondiabetic according to the HbA_{1c} values. The definitive diabetes was diagnosed with HbA_{1c}, FPG, and both

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CAD = coronary artery disease
COPD = chronic obstructive pulmonary disease
CVA = cerebrovascular accident
CVD = cerebrovascular disease
DM = diabetes mellitus
FN = false negative
FP = false positive
FPG = fasting plasma glucose
HbA_{1c} = hemoglobin A1c fraction
HT = hypertension
IFG = impaired fasting glucose
IGT = impaired glucose tolerance
LMC = left main coronary
NPV = negative predictive value
OGTT = oral glucose tolerance test
PAD = peripheral artery disease
PG = plasma glucose
PPV = positive predictive value
TN = true negative
TP = true positive

HbA_{1c} and FPG, and the results have been compared with the OGTT study, which is the gold standard test for the time being [8].

Patients and Methods

Patients

Before the study procedures commenced, the study protocol was approved by our institutional ethics committee. An informed consent has been obtained from each patient. One hundred sixty-six consecutive patients who underwent elective isolated on-pump CABG surgery between October 2008 and January 2009 were included in the study. Patients who had an acute coronary syndrome, had ST-elevated or non-ST-elevated myocardial infarction, or had undergone invasive cardiologic interventions or any type of surgical or invasive medical intervention for noncardiac causes at least 3 months before cardiac surgery were excluded. Emergency interventions and combined procedures were also excluded, along with patients who underwent CABG on the beating heart.

Data Collection

All data were collected prospectively. Routine cardiac and medical screening was performed in all patients. For the diabetic patients, only FPG and HbA_{1c} measurements were made on the day after hospitalization. To verify the glycometabolic status of the patients without a history of diabetes, routine biochemical measurements, including HbA_{1c} and 8-hour FPG, were obtained by venous blood sampling on the day after hospitalization (the day before operation). One month after the operation, OGTT was performed in all discharged patients who did not have preexisting diabetes at the time of operation.

Study Groups

Patients were divided into three groups: patients with known DM (n = 54); patients without a preoperative history of diabetes who had a preoperative HbA_{1c} value between 4.80% and 5.90% (n = 44); and patients without a preoperative history of diabetes who had a preoperative HbA_{1c} of 6.1% or greater (n = 68). Fasting plasma glucose, HbA_{1c}, and OGTT were assessed in all surviving patients in the latter two groups at the end of the first month postoperatively. According to FPG and HbA_{1c} results, patients were diagnosed as diabetic or not diabetic. The sensitivity and specificity for the diagnosis of DM were analyzed for FPG, HbA_{1c}, and the combined use of HbA_{1c} and FPG, in reference to the OGTT results. Preoperative characteristics of the patient groups are outlined in Table 1.

Glycometabolic Status

Patients with a preoperative history of type 2 DM and taking antidiabetic medication (oral hypoglycemic agent or insulin) were considered diabetic. In patients without a history of type 2 DM preoperatively, classification of glycometabolic status was based on OGTT criteria established by the World Health Organization [8]. Diabetes was defined as FPG of 7.0 mmol/L or greater or OGTT of 11.1 mmol/L or greater. Impaired fasting glucose (IFG) was defined as FPG from 5.6 mmol/L to 6.9 mmol/L or OGTT less than 11.1 mmol/L, and impaired glucose tolerance (IGT) was defined as OGTT of at least 7.8 mmol/L but less than 11.1 mmol/L [8]. In the analyses, the term *prediabetic* was used for patients with IFG and IGT, as has been used by other authors [9–11]. The HbA_{1c} values of 6.1% or greater were accepted as definitive DM. In the study, comparisons were made between the sensitivity and specificity of FPG of 7.0 mmol/L or greater, HbA_{1c} values of 6.1% or greater, or use of both tests together.

Plasma Glucose and Hemoglobin A1c Values

Plasma glucose values were measured with the Cobas Integra 400 Plus Gluc3 system (Glucose HK Gen 3; Roche Diagnostics, Indianapolis, IN) and the Roche Medical Kit (Alger; Roche Diagnostics). Reference range for normal plasma glucose was 80 to 120 mg/dL (4.44 to 6.67 mmol/L) in our laboratory. Hemoglobin A1c measurement was made using COBAS Integra 400 (Roche Diagnostics), and the reference range of our laboratory was 4.80% to 5.90%. Oral glucose tolerance test measurements were made after administering 75 g of glucose in 2 dL of water and detection of plasma glucose levels after 2 hours.

Statistical Analysis

The statistical analyses were carried out using the NCSS 2007 and PASS 2008 Statistical Software (NCSS, Kaysville, UT). Descriptive analyses are presented as mean ± standard deviation, median, and percentages (%), as appropriate. One-way analysis of variance and Tukey's honestly significant difference test were used to compare the variables with normal distribution. For the

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