Performance of HbA_{1c} and Fasting Plasma Glucose in Screening for Diabetes in Patients Undergoing Coronary Angiography

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OBJECTIVE—The performance of glycated hemoglobin (HbA_{1c}) and fasting plasma glucose (FPG) was compared in screening for diabetes by an oral glucose tolerance test (OGTT) in patients undergoing coronary angiography (CAG).

RESEARCH DESIGN AND METHODS—Patients without known diabetes admitted for CAG were eligible. OGTT and HbA_{1c} were assessed 2–4 weeks after hospital discharge. The performance of HbA_{1c} and FPG was evaluated by using receiver operating characteristic (ROC) analysis.

RESULTS—Diabetes was diagnosed in 83 of 400 patients (20.8%). The area under the ROC curve was higher for FPG than for HbA_{1c} (0.81 vs. 0.73, $P = 0.032$). We proposed a screening algorithm and validated it in another 170 patients. Overall, this algorithm reduced the number of OGTTs by 71.4% (sensitivity 74.4%, specificity 100%).

CONCLUSIONS—FPG performed better than HbA_{1c} in screening for diabetes in patients undergoing CAG. A screening algorithm might help to reduce the number of OGTTs.

Oral glucose tolerance test (OGTT) is recommended for abnormal glucose regulation screening in patients with coronary artery disease (CAD) (1). However, OGTT is not satisfactory as a routine test (2,3). Glycated hemoglobin (HbA_{1c}) has been adopted as a diagnostic criterion for diabetes (4), and HbA_{1c} testing has some advantages, such as requiring nonfasting samples and having less biological variability (3). On the other hand, the fasting plasma glucose (FPG) test is widely available and inexpensive (3). The performance of HbA_{1c} and FPG in screening for diabetes has only been reported in a limited number of patients with acute coronary disease (5,6). Doerr et al. (7) reported that the sensitivity of HbA_{1c} ≥6.5% for the detection of newly diagnosed diabetes (NDD) in patients undergoing coronary angiography (CAG) was only 16%. The present study aimed to compare the performance of HbA_{1c} and FPG in screening for diabetes, as determined by an OGTT, and to develop a screening algorithm for patients undergoing CAG.

RESEARCH DESIGN AND METHODS

This study was approved by the institutional review board of Taichung Veterans General Hospital, Taichung, Taiwan and was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent before undergoing any study-related procedures. Adult patients without known diabetes were eligible if they were admitted for CAG for suspected or known CAD. Patients with serum creatinine ≥250 μmmol/L, hemoglobin <10 g/dL, or history of blood transfusion within 3 months were excluded. CAD was defined as ≥50% stenosis of the lumen diameter in any coronary artery.

Two–four weeks after hospital discharge, a standard 75-g OGTT (8) was performed between 0800 and 1100 h after a 10–12-h overnight fast. Blood samples were collected at 0, 30, and 120 min for the measurements of HbA_{1c} and plasma glucose and insulin concentrations. The methods of laboratory measurements are provided in the Supplementary Materials and Methods.

Patient glucometabolic state was defined based on the results of the OGTT (4). Insulin resistance was calculated with the homeostasis model assessment of insulin resistance (HOMA-IR) (9). β-cell function was assessed with the homeostasis model assessment of β-cell function (HOMA-β) (9) and insulinogenic index (IGI) (10).

Statistical analyses were performed with SPSS version 10.0 (IBM, Chicago, IL) software. The performance of HbA_{1c} and FPG for detecting NDD was evaluated by receiver operating characteristic (ROC) analysis, and diagnostic accuracy was assessed with the area under the curve (AUC) (11). $P < 0.05$ was considered statistically significant.

RESULTS

From December 2009–September 2011, OGTT was conducted

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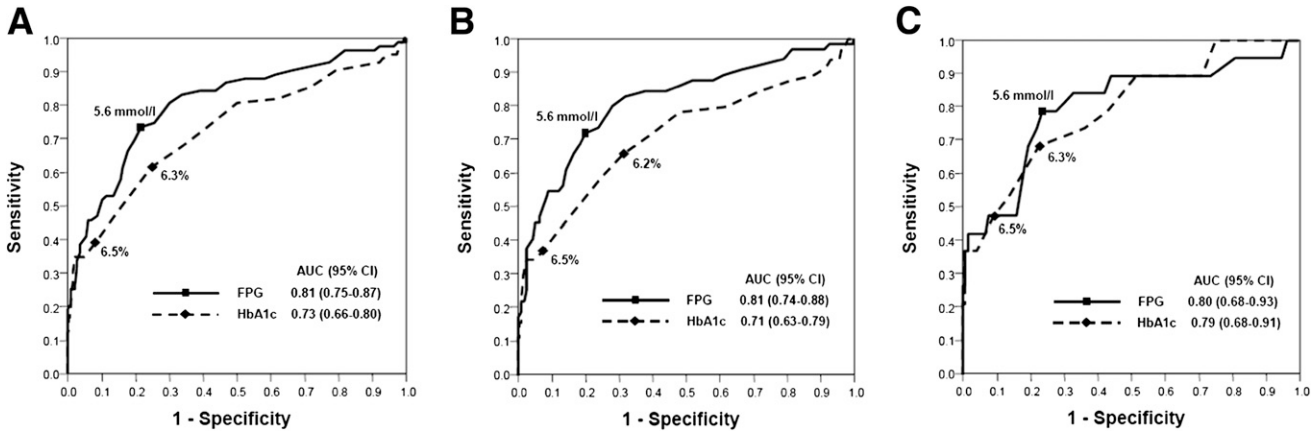

Figure 1—*ROC curve for HbA_{1c} and FPG to detect NDD in all patients* (A)*, patients with CAD* (B)*, and patients without CAD* (C)*. The optimal cutoff points for HbA_{1c} were 6.3%* (A)*, 6.2%* (B)*, and 6.3%* (C)*. The optimal cutoff point for FPG was consistently 5.6 mmol/L in all three groups.*

in 400 of 780 eligible patients (mean age 65 ± 13 years, male 75.9%, CAD 67.8%) (Supplementary Table 1). Figure 1 shows the ROC curves for HbA_{1c} and FPG to detect NDD. Overall, the AUC was higher for FPG than for HbA_{1c} (0.81 vs. 0.73, P = 0.032). The optimal cutoff point was 5.6 mmol/L for FPG and 6.3% for HbA_{1c}. In patients with CAD, the AUC was higher for FPG than for HbA_{1c} (0.81 vs. 0.71, P = 0.017), whereas the difference was not significant in patients without CAD (0.80 vs. 0.79, P = 0.881).

Patients were divided into different groups according to their FPG and HbA_{1c} levels (Supplementary Table 2). Patients with FPG 5.6–6.9 mmol/L were more insulin resistant (HOMA-IR 2.4 ± 1.5 vs. 1.7 ± 1.2, $P < 0.001$) and had worse β-cell function (HOMA-β 74 ± 49 vs. 104 ± 70, $P < 0.001$; IGI 60 ± 57 vs. 104 ± 87, $P < 0.001$) than those with FPG <5.6 mmol/L. However, in patients with HbA_{1c} 5.7–6.4%, the HOMA-IR, HOMA-β, and IGI were not significantly different from those in patients with HbA_{1c} <5.7%.

Based on our findings, we proposed a screening algorithm (Supplementary Figure 1). Diabetes was diagnosed in patients with FPG ≥7.0 mmol/L. OGTT needs to be conducted in patients with FPG 5.6–6.9 mmol/L and may be waived in those with FPG <5.6 mmol/L. In this way, the number of OGTTs was reduced by 71.8%, and the sensitivity and specificity for detecting NDD was 73.5% and 100%, respectively.

This algorithm was tested in another 170 patients (mean age 62 ± 13 years, male 82.9%, CAD 67.1%) admitted for CAG between October 2011 and June 2012. Following this algorithm, an OGTT would be needed in 50 (29.4%) patients, and the sensitivity and specificity for detecting NDD was 76.5% and 100%, respectively.

CONCLUSIONS—We reported that the AUC was higher for FPG than for HbA_{1c} in detecting NDD in patients undergoing CAG, especially in those with CAD. A recent study comparing the performance of HbA_{1c} and fasting capillary glucose in screening for diabetes in a general Chinese population found a higher AUC for fasting capillary glucose than for HbA_{1c} (men 0.77 vs. 0.67, $P < 0.01$; women 0.75 vs. 0.67, $P < 0.01$) (12). These findings were in line with the present results and suggest that FPG is a better test than HbA_{1c} in screening for diabetes.

We observed that patients with FPG 5.6–6.9 mmol/L were more insulin resistant and had worse β-cell function than those with FPG <5.6 mmol/L. However, in patients with HbA_{1c} 5.7–6.4%, the indexes of insulin resistance and β-cell function were not significantly different from those in patients with HbA_{1c} <5.7%. Some studies reported that β-cell function progressively declined with the increase in either FPG or 2-h postchallenge glycemia (13,14). In contrast, the relationship between HbA_{1c} and β-cell function was reported to be highly nonlinear (15). These results suggest that a higher-than-normal FPG might be a better index of insulin resistance and β-cell dysfunction than a higher-than-normal HbA_{1c}.

There are some limitations in this study. First, only 51.3% of eligible patients participated. Second, we did not conduct a second OGTT to confirm the diagnosis, and the poor reproducibility of OGTT (3) may confound the results. Third, the efficacy of the screening algorithm has not been tested in another independent cohort.

In summary, we reported that the FPG test performed better than HbA_{1c} in screening for diabetes in patients undergoing CAG. We proposed a screening algorithm, and its efficacy and practicability need further investigation.

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