

Predictive Value of Fasting Blood Sugar for Non-Diabetic Individuals Suffering from Severe Coronary Disease

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Abstract: *This study was designed to determine if high fasting blood sugar (FBS) level is an independent predictor of severe coronary lesions in patients with coronary artery disease (CAD). In this study, 34 patients who had symptoms of chest discomfort and who underwent coronary angiography were enrolled. FBS was determined from blood samples and the extent of coronary artery lesions was analyzed according to Gensini score. We examined the relationships among diabetes, FBS and coronary artery severity. Diabetes and FBS were significantly and positively related to Gensini score. Diabetes, but not FBS, was independently correlated with the occurrence of a Gensini score >41. However, FBS was significantly associated with Gensini score >41 in non-diabetic patients. Hyperglycemia is an independent predictor of severe CAD in non-diabetic patients. Clinicians should be aware of this and should carry out appropriate early interventions.*

Keywords: Fasting blood sugar, coronary artery disease, Gensini score, Diabetes mellitus

1. Introduction

Diabetes mellitus (DM) is known to be a major risk factor for coronary artery disease (CAD), which is the main cause of death in diabetic patients. Diabetic patients have more extensive, diffuse, calcified, and severe coronary artery lesions compared with non-diabetic patients [1], which is closely related to the poor prognosis of DM. Coronary artery lesions can also be detected in the pre-diabetic state, including in patients with impaired fasting glucose (IFG) and impaired glucose tolerance [2,3]. There is thus a need to identify the early signs of atherosclerosis in patients with DM and pre-DM, to allow early interventions to treat the atherosclerotic process. Glycosylated hemoglobin (HbA1c) level is an indicator of the average blood glucose concentration over the past 3 months. Recent studies demonstrated that high HbA1c levels could predict the prevalence and complexity of CAD in patients with not only DM, but also those with pre-DM [4-6]. However, the HbA1c level may be affected by multiple factors including anemia, pregnancy, hypertriglyceridemia, and chronic liver disease [7], which might have a marked impact on the predictive value of HbA1c for CAD. Fasting blood glucose (FBS) is a cheap and convenient measure of glucometabolism, and could thus be a good candidate or a beneficial addition to HbA1c for screening for severe coronary artery lesions in patients with DM or pre-DM. Growing evidence suggests that hyperglycemia in non-diabetic patients is closely related to the presence and severity of CAD [8-11], raising the possibility that high FBS level might be a useful predictor of serious coronary lesions. However, the value of FBS as an independent predictor of serious coronary lesions currently remains unclear [4, 6, 12]. This study aimed to investigate the significance of FBS for predicting a Gensini score >41, as a marker of coronary artery lesion severity, in hospitalized patients undergoing coronary angiography.

2. Patients and Methods

The study population was selected from patients with symptoms of chest discomfort who underwent coronary angiography at Falluja teaching hospital from November 2018 to January 2019. Patients were diagnosed with CAD if they had at least one significant stenosis (>50%) of the arterial lumen in any of the major coronary arteries, including the left main coronary artery, left anterior descending artery, left circumflex coronary artery, and right coronary artery, or in the main branches of the vascular system.¹³ The present study did not include patients with coronary artery spasm, angina, valvular heart disease, systemic inflammatory disease, autoimmune disorders, neoplastic disease, or severe hepatic or renal dysfunction. A total of 34 patients were included in this study. The study protocol was approved by the of The Fallujah Teaching Hospital, and informed written consent was obtained from each patient.

All blood samples were collected during hospital stay after an overnight fast (12 hours) for measurement of FBS, total cholesterol, and total triglycerides. Diabetes was defined as a FBS ≥ 7.0 mmol/L, a history of diabetes, or current treatment with hypoglycemic medications. Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, a history of hypertension, or current treatment with antihypertensive medications. Hyperlipidemia was defined as a fasting total cholesterol concentration ≥ 6.21 mmol/L or total triglycerides ≥ 2.26 mmol/L, a history of hyperlipidemia, or the use of lipid-lowering medications. Smoking status was determined from the patient's medical history.

Selective coronary angiography was performed using the standard Judkin's technique, by filming multiple views of each blood vessel. Coronary angiograms were analyzed by two experienced interventional physicians blinded to the clinical characteristics of the patients. The severity of

coronary artery stenosis was assessed using the Gensini scoring system, as described previously [13].

The Gensini score was calculated by assigning a severity score to each coronary narrowing on the basis of the degree of luminal stenosis and its geographic importance. Decreases in luminal diameter of 25%, 50%, 75%, 90%, 99%, and total occlusion were given scores of 1, 2, 4, 8, 16, and 32, respectively. The score was then multiplied by a factor symbolizing the functional significance of the lesion in the coronary arterial tree, e.g. 5 for the left main coronary artery, 2.5 for the proximal left anterior descending artery or left circumflex coronary artery, 1.5 for the mid-left anterior descending artery, and 1 for the right coronary artery or the distal left anterior descending artery [13,14]. On the basis of the calculated Gensini scores, the subjects were divided into two subgroups: low and intermediate Gensini score (≤ 41 , n=20) and high Gensini score (>41 , n=14) [13].

Statistical analysis

Statistical analyses were performed using SPSS Statistics program version 21. Quantitative data are shown as mean \pm standard deviation and were compared by Student's t-test when the data were normally distributed. Categorical data were expressed as number of cases (n) and percentage (%), and compared by chi-square test. Relationships among DM, FBG, and coronary artery severity were investigated by Pearson's correlation analysis. Logistic regression analyses were performed to evaluate the relationship between FBG and a Gensini score >41 .

3. Results

A total of (34) patients were included in this study, with mean age of (55.4 \pm 10.9) years and 23 (67.6%) of them were men. The percentages of patients with smoking, DM, hypertension, and hyperlipidemia were 55.9%, 32.4%, 58.8%, and 32.4%, respectively. The demographic and clinical characteristics of the patients classified according to Gensini score are shown in table (1). There were no significant differences between the groups in terms of age, gender, smoking history, blood pressure, or blood lipids. However, patients with a high Gensini score were more likely to have a history of DM and more likely to have a higher FBG.

Table 1: Clinical characteristics based on Gensini score

Variable	Low and intermediate GS (≤ 41 , n=20)	High GS (>41 , n=14)	P value
Age (year)	55.8 \pm 11.8	50.0 \pm 10.0	0.143
Male (n, %)	13 (65%)	10 (71%)	0.301
Smoking (n, %)	8 (40%)	8 (57%)	0.529
Diabetes (n, %)	3 (15%)	9 (64%)	0.009
Hypertension (n, %)	10 (50%)	9 (64%)	0.646
Hyperlipidemia (n, %)	7 (35%)	6 (43%)	0.909
FBS (mmol/L)	5.5 \pm 1.2	7.1 \pm 1.8	0.003

GS: Gensini score, FBS: Fasting blood sugar.

Gensini score was positively correlated with DM (r = 0.525, P<0.001) and FBS (r = 0.309, P=0.015). There was no significant correlation between Gensini score and age, gender, smoking, hypertension, or hyperlipidemia. However, Gensini score was significantly related to FBS in nondiabetic patients (r =0.391, P=0.014).

We evaluated the value of FBS for predicting a high Gensini score, as a marker of CAD severity, by multivariate logistic regression analysis. Multiple logistic regression identified DM (odds ratio [OR] = 10.390, 95% confidence interval [CI] 2.096–41.121, P<0.005), but not FBS (OR=1.131, 95% CI 0.925–1.157, P=0.856), as an independent correlate of high Gensini score (Table 2). The power of the logistic regression analysis was 73.5%.

Table 2: Independent predictors of Gensini score >41 in multivariate logistic regression analysis

Variable	OR, 95% CI	P value
Age	1.754 (0.835–1.325)	0.518
Sex	1.728 (0.875–2.971)	0.892
Smoking	0.979 (0.421–2.856)	0.876
Diabetes	10.390 (2.096–41.121)	0.005
Hypertension	1.085 (0.685–2.751)	0.546
Hyperlipidemia	0.969 (0.205–4.373)	0.897
FBS	1.131 (0.925–1.157)	0.856

GS:Gensini score, FBS: Fasting blood sugar.

The predictive value of FBS for high Gensini score in nondiabetic patients was further explored by conducting multivariate logistic regression analysis based on traditional risk factors impacting on high Gensini score. There was a significant association between FBS and high Gensini score (OR=5.131, 95% CI 1.583–19.543, P=0.005) when confounding factors including age, gender, smoking, hypertension, and hyperlipidemia were analyzed in the logistic regression model (Table 3). The power of the logistic regression analysis was 71.3%.

Table 3: Independent predictors of Gensini score >41 in non-diabetic patients according to multivariate logistic regression analysis

Variable	OR, 95% CI	P value
Age	1.373 (0.875–1.985)	0.375
Sex	1.595 (0.329–5.753)	0.985
Smoking	1.564 (1.758–7.152)	0.877
Hypertension	2.787 (1.564–6.758)	0.099
Hyperlipidemia	1.486 (1.589–4.446)	0.689
FBS	5.131 (1.583–19.543)	0.005

GS: Gensini score, FBS: Fasting blood sugar

4. Discussion

This study demonstrated that hyperglycemia was closely linked to the complexity of CAD in non-diabetic patients, and that non-manipulated FBS could independently predict severe CAD in these patients. DM is an important risk

factor for, and indeed is often considered to be equivalent to, coronary heart disease. Compared with non-diabetic patients, patients with DM tend to have more inflammatory infiltration (macrophages and T lymphocytes), larger necrotic core size, and more diffuse atherosclerosis in the coronary lesions [15]. A systematic review by Ford et al [16] revealed that IFG increased the relative risk of cardiovascular disease by about 1.12 to 1.37 times, indicating that IFG could moderately increase the risk of cardiovascular disease. In the current study, we demonstrated that DM and high FBS were positively related to the severity of coronary artery stenosis, in line with the results of previous reports [8,11]. Basic research supports an important role for hyperglycemia in the progression of atherosclerosis. Hyperglycemia might accelerate atherosclerosis by inducing endothelial cell dysfunction, reducing nitric oxide bioavailability, promoting a vasoconstrictive or prothrombotic state, and boosting nuclear factor- β expression [17]. The extent and severity of CAD can be evaluated using the Synergy between percutaneous coronary intervention with Taxus and cardiac surgery (SYNTAX) score [18] or the Gensini score [13]. These scores, together with several clinical variables, can predict the likelihood of fatal and non-fatal cardiovascular events in patients with CAD. Yang et al [12] demonstrated that SYNTAX scores were higher in subjects with type 2 DM or IFG compared with those with normal FBS. In a study by Karakoyun et al [4], high FBS and a SYNTAX score >22 were significantly correlated in patients with type 2 DM, while a further study found that either DM or IFG could predict a SYNTAX score >22 [12]. However, no association between fasting glucose levels and SYNTAX score >22 was found in nondiabetic patients in a study by Arbel et al [6]. Notably, in terms of artery stenosis, the Gensini score starts at 25% occlusion while the SYNTAX score only begins at 50%, suggesting that the Gensini score might be a more sensitive parameter than SYNTAX score for detecting early atherosclerotic coronary artery lesions. Although previous studies demonstrated that hyperglycemia was positively related to Gensini score in non-diabetic patients [8,11] whether hyperglycemia was closely correlated with high Gensini score in these patients remained unknown. Using the Gensini rather than the SYNTAX scoring system, we found that high FBS in non-diabetic patients could predict the presence of severe coronary lesions, indicated by a Gensini score >41 . However, further larger studies are needed to explain the discrepancies among the above studies and to determine the predictive role of FBS for severe coronary lesions. Importantly, this study showed that both DM and high FBS were closely linked to the extent and severity of CAD. However, FBS did not predict the severity of coronary lesions in patients with DM. This could be because FBS may be influenced by antidiabetic drugs in patients with DM, while FBS in non-diabetic patients is not manipulated by hypoglycemic agents. These results thus support different predictive values for FBS in terms of coronary lesion severity between diabetic and nondiabetic patients. This study had several limitations. First, it was a cross-sectional study and lacked long-term follow-up data. Second, the number of patients was relatively small because of funding limitations, which might have limited its statistical power. Third, all patients

in our study population underwent coronary angiography, which might have introduced selection bias.

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