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Relationship between hyperglycemia and coronary vascular resistance in non-diabetic patients

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Abstract

Background: Hyperglycemia upon hospital admission in patients with acute myocardial infarction is associated with the no-reflow phenomenon after successful reperfusion, and increased mortality. However, the mechanism underlying this phenomenon remains unclear. Therefore, the aim of this study was to characterize coronary hemodynamics in a homogenous group of non-diabetic patients without coronary artery disease.

Methods and Results: A total of 104 consecutive non-diabetic patients (mean age, 62±14 years) without coronary artery disease underwent Doppler flow study of the left anterior descending coronary artery. Vascular reactivity was examined by intra-coronary administration of papaverine, acetylcholine (Ach), and nitroglycerin using a Doppler guidewire. Coronary vascular resistance (CVR) was calculated as the mean arterial pressure divided by coronary blood flow (CBF). Baseline CVR was shown as CVR at control and minimal CVR was shown as CVR with papaverine administration. Fasting plasma glucose (FPG) level had a significant, positive correlation with baseline CVR and minimal CVR ($r=0.24$, $p<0.02$ and $r=0.21$, $p<0.05$, respectively). Hemoglobin A1c (HbA1c) also had a significant, positive correlation with baseline CVR and minimal CVR ($r=0.31$, $p<0.01$ and $r=0.32$, $p<0.01$, respectively). The percent change in CBF induced by Ach was inversely correlated with HbA1c but not with FPG ($r=0.22$, $p<0.05$ and $r=0.06$, $p=0.57$, respectively). By contrast, neither FPG nor HbA1c had significant correlation with coronary flow reserve to papaverine.

Conclusion: These data demonstrate that elevated glucose levels are associated with increases in baseline and minimal coronary vascular resistance. These changes may contribute to unfavorable coronary hemodynamics in non-diabetic patients without coronary heart disease.

Keywords: Coronary vascular resistance; FBS; HbA1; Hyperglycemia

1. Introduction

Hyperglycemia upon hospital admission in patients with acute myocardial infarction (AMI) is associated with the no-reflow phenomenon after successful reperfusion [1], resulting in larger infarct size and worse functional recovery. Further, hyperglycemia in patients with ST-segment elevation acute myocardial infarction is an important predictor of impaired epicardial flow before reperfusion therapy [2], and hyperglycemia in patients with AMI is associated with increased mortality [3–7]. However, the mechanisms underlying these adverse effects of hyperglycemia remain unknown. Therefore, the aim of this study was to characterize coronary hemodynamics in a

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Table 1
Clinical characteristics of the study patients.

Age (years)	62±14 (17–85)
Male gender	69 (66%)
Risk factors	
Hypertension	57 (55%)
Hyperlipidemia	35 (34%)
Smoker	27 (26%)
Laboratory data	
FPG (mg/dl)	94±8 (74–120)
HbAlc (%)	5.2±0.4 (4.1–6.3)
Total-cholesterol (mg/dl)	197±37 (114–314)
Triglycerides (mg/dl)	122±64 (40–368)
HDL–cholesterol (mg/dl)	57±15 (28–98)
LDL–cholesterol (mg/dl)	113±28 (53–211)

HDL: high density lipoprotein; LDL: low density lipoprotein; Values are mean±SD.

homogenous group of non-diabetic patients without coronary artery disease.

2. Methods

2.1. Study population

A total of 187 consecutive non-diabetic patients who had been referred for cardiac catheterization to exclude coronary artery disease were considered for enrollment in this study. Of these, 104 patients met the following inclusion criteria: 1) angiographically smooth arteries; 2) mild irregularities, <30% lumen diameter stenosis by visual assessment in any major conduit vessel; 3) proximal coronary arteries >2.0 mm in diameter; and 4) lacking a history of previous myocardial infarction, previous coronary revascularization, valvular heart disease, variant angina, cardiomyopathy, or myocarditis.

Patients meeting the following criteria were considered to have obvious diabetes and excluded: 1) previous diagnosis of diabetes, 2) current treatment by oral hypoglycemic agents or insulin, or 3) concentration of fasting plasma glucose (FPG) >126 mg/dl or hemoglobin A1c (HbA1c) >6.5% at admission [8].

Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a *priori* approval by the institution's human research committee.

2.2. Study protocol

Diagnostic coronary angiography was performed using a 6F Judkins catheter with a standard femoral percutaneous approach. Heparin (5000 units) was administered at the beginning of the procedure. Non-ionic contrast material was used for all patients. No nitroglycerin was given prior to the diagnostic procedure. Coronary blood flow (CBF) response to papaverine, acetylcholine (Ach), and nitroglycerin was studied according to previous reports [9,10]. After control coronary angiograms, interventions were performed as follows: 1) a 0.014-inch Doppler guidewire (Cardiometrics, Santa Anna, CA, USA) was introduced into the left anterior descending coronary artery; 2) after obtaining a stable Doppler signal, a bolus of papaverine (an endothelium-independent vasodilator in resistance coronary arteries) (12.5 mg/5 ml) was injected through a catheter; 3) infusion of Ach (an endothelium-dependent vasodilator in resistance and conduit coronary arteries) (0.5 ml/min) at a dose of 3 μg/min for 2 min was performed via the catheter [11,12,4] a bolus of nitroglycerin (an endothelium-independent vasodilator in conduit coronary arteries) (200 μg/5 ml) was administered. Drugs were infused with a minimum 5-min interval. Coronary arteriography was performed before and 2 min after each dose of Ach and after administration of nitroglycerin. Phasic CBF velocities, arterial blood pressure, and heart rate were monitored continuously and recorded. Measurements obtained during steady state conditions were used as control values for later analysis.

Doppler flow velocity spectra were analyzed on-line to determine time-averaged peak velocity. Volumetric CBF was determined from the formula: CBF = cross-sectional area × average peak velocity × 0.5 [13]. Coronary flow reserve to papaverine was calculated as the ratio of maximal CBF induced by papaverine to basal CBF, which was equivalent to

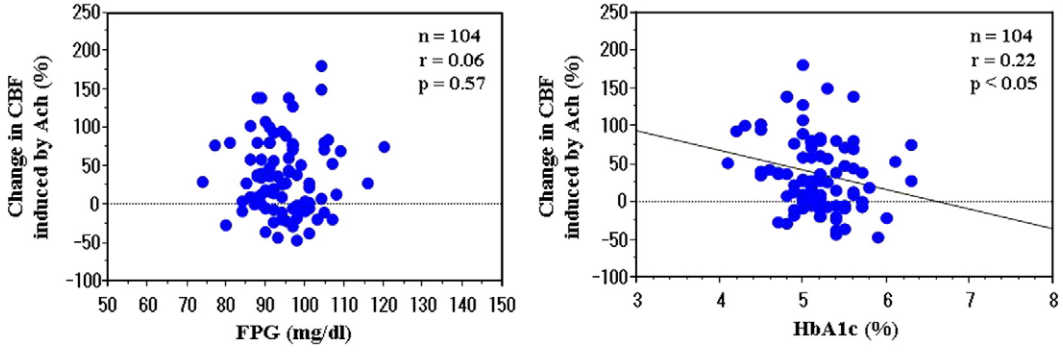

Fig. 1. Scattergram illustrating the correlation between percent change in CBF induced by Ach and FPG (left panel) and HbA1c (right panel).