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ORIGINAL ARTICLE

The relationship between renal functions and thrombolysis in myocardial infarction frame count in patients with slow coronary flow

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Abstract We investigated the relationship between renal function and coronary thrombolysis in myocardial infarction frame count (TFC) in patients with slow coronary flow (SCF). The patient group was composed of 34 patients with SCF. The control group was made up of 34 well-matched individuals who have normal SCF in their coronary arteries. The coronary flow rates of all subjects were documented by TFC. Glomerular filtration rate (GFR) and corrected GFR (cGFR) were calculated by creatinine clearance according to the Cockcroft-Gault formula. There is no difference in the gender or age of the groups. Blood urea nitrogen and creatinine were significantly higher in the SCF group compared the control group (blood urea nitrogen: 17 ± 6 mg/dL *vs.* 14 ± 4 mg/dL, $p = 0.04$ and creatine: 0.9 ± 0.1 mg/dL *vs.* 0.7 ± 0.1 mg/dL, $p = 0.01$). GFR and cGFR were significantly different between the groups (GFR: 92 ± 28 mL/min *vs.* 112 ± 27 mL/min, $p = 0.004$ and cGFR: 77 ± 22 mL/min/1.73 m^2 *vs.* 96 ± 24 mL/min/1.73 m^2, $p = 0.007$). There was a negative correlation between GFR/cGFR and TFC in all coronary arteries. This study shows that impaired renal function is associated with SCF. Patients with SCF have worse renal function compared with patients without SCF.

Introduction

Slow coronary flow (SCF) is defined as late opasification at the epicardial coronary arteries without stenosis, as shown by coronary angiography [1,2]. According to selective coronary angiography, SCF appears to have approximately a 1% frequency [3]. The endothelium plays a critical role in

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determining coronary blood flow and providing vascular tone. However, the etiology of SCF is unknown. Several studies have shown that resting microvascular resistance and flow-mediated dilatation (FMD) are deteriorated in SCF patients [4—6]. Other potential causes of SCF are small vessel disease, diffuse atherosclerosis, platelet dysfunction, microvascular dysfunction, and vasomotor dysfunction [1,7]. Studies showed that end-stage renal disease is associated with endothelial dysfunction [8—13].

The purpose of this study was to investigate the relationship between renal functions and thrombolysis in myocardial infarction frame count (TFC) in patients with and without SCF.

Methods

Study population

The study population was taken from a series of 1,881 consecutive patients who underwent coronary angiography in our unit between 2008 and 2010 because of the presence of typical angina or angina-like symptoms. Out of the 1,881 patients, 34 patients who had angiographically normal coronary arteries with SCF were enrolled in our study as well as 34 consecutive age- and sex-matched controls with angiographically normal coronary arteries and no SCF. Normal coronary arteries were defined as coronary arteries without any obstructive or nonobstructive lesions in the left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX), and right coronary artery (RCA). Coronary angiograms were analyzed by two expert cardiologists who were blinded to the patients' data. Patients with a history of coronary artery disease, heart failure, uncontrolled hypertension, and systemic disorders were excluded from the study. We determined the presence of diabetes mellitus by looking for a history of antidiabetic drug therapy or by a fasting glucose level greater than 126 mg/dL. Hypertension was diagnosed as blood pressure greater than 140/90 mmHg or use of antihypertensive therapy. Hyperlipidemia was defined as total cholesterol above 200 mg/dL or low-density lipoprotein cholesterol above 130 mg/dL or a history of statin use. Patients who had been smoking before the study were accepted and listed as smokers. Approval was obtained from the local ethics committee and informed consent was obtained from all patients

Coronary angiography

Coronary angiography was performed using Judkin's techniques. Coronary arteries were visualized in left and right oblique planes with cranial and caudal angles at a speed of 30 frames/s. An injection of 5—8 mL of contrast medium (Iopromide; Ultravist-370 Schering AG, Berlin, Germany) was given manually at each position. Coronary blood flow was quantified by two independent observers who were blinded to the clinical data. Coronary flow rates of all subjects were documented by TFC. The TFC for each coronary artery was determined according to a distal marking point specific for the coronary artery of interest [14]. Diagnosis of SCF was established as previously described [15].

Biochemical measurements

Blood samples were drawn from an antecubital vein before coronary angiography after a 12-hour overnight fast. Blood urea nitrogen (BUN), creatinine, and other biochemical parameters were determined by standard methods. Glomerular filtration rate (GFR) was measured by creatinine clearance according to the Cockcroft-Gault [16] formula. The corrected GFR (cGFR) was calculated using the Cockcroft-Gault formula adjusted for body surface area [17].

Statistical analysis

All statistical analyses were performed using SPSS for Windows version 15 (SPSS Inc., Chicago, IL, USA). Values for continuous variables were expressed as mean $\pm$ standard deviation and categorical variables were written as a percentage. Continuous data were compared using the "Student *t* test" or "Mann-Whitney *U* test" and categorical data via the "chi-squared test" or "Fisher's Exact test." The associations between TFC and renal parameters were determined by the Pearson or Spearman correlation test. Statistical significance was defined as $p < 0.05$.

Results

There were no differences between patients with and without SCF in gender (24 male *vs.* 19 male, $p = 0.14$) and age (56 ± 11 years *vs.* 53 ± 9 years, $p = 0.22$). The risk factors for coronary artery disease were similar between the groups (Table 1). In the SCF group, TFC in LAD, LCX, and RCA was significantly higher than the normal coronary artery group. The renal function parameters were significantly different between the two groups. Patients with SCF have higher BUN and creatinine and lower GFR and cGFR (Table 2). There was a negative correlation between GFR and LAD TFC ($r = -0.28$; $p = 0.02$), LCX TFC ($r = -0.30$; $p = 0.01$), and RCA TFC ($r = -0.28$; $p = 0.02$). Also, there was negative correlation between cGFR and LAD TFC ($r = -0.29$; $p = 0.05$), LCX TFC ($r = -0.33$; $p = 0.03$), and RCA TFC ($r = -0.35$; $p = 0.02$).

Discussion

In the present study, we found that BUN, creatinine, GFR, and cGFR are significantly different between patients with and without SCF. There is a negative correlation between the GFR/cGFR and TFC of each epicardial coronary artery.

TFC is a widely used method for the evaluation of coronary blood flow. It also gives important information about microvascular function and dysfunction in patients with microvascular angina [18—20]. FMD is a simple method that is used to evaluate endothelial function [21]. In the study by Sezgin et al. [6], it was found that brachial artery FMD is impaired in patients with SCF and observed that there is an important relationship between FMD and TFC. In previous studies, it has been reported that nitric oxide (NO) is an important regulator of coronary circulation [22—24]. In the study by Sezgin et al. [25], it was found that NO

Table 1 Demographic and clinical characteristics of participants with slow coronary flow and normal coronary flow[a]

Variables	Slow coronary flow ($n = 34$)	Normal coronary flow ($n = 34$)	p
Age, yr	56 ± 11	53 ± 9	0.22
Male	24 (70)	19 (55)	0.14
CAD risk factors			
Hypertension	18 (53)	20 (59)	0.63
Hyperlipidemia	9 (26)	13 (38)	0.31
Diabetes	6 (18)	4 (12)	0.50
Smoking	10 (29)	6 (18)	0.26
Family history	9 (26)	6 (18)	0.39
Laboratory findings			
Fasting glucose (mg/dL)	100 ± 34	101 ± 14	0.95
Total cholesterol (mg/dL)	206 ± 33	199 ± 36	0.45
LDL-cholesterol (mg/dL)	131 ± 27	130 ± 30	0.95
HDL-cholesterol (mg/dL)	42 ± 10	40 ± 10	0.44
Triglycerides (mg/dL)	171 ± 97	143 ± 55	0.20
Medications			
Aspirin	29 (85)	25 (74)	0.37
ACEI/ARB	19 (56)	18 (53)	0.80
Beta blockers	7 (21)	4 (12)	0.51
Calcium antagonists	5 (15)	8 (24)	0.54
Nitrates	3 (9)	3 (9)	1
Statin	11 (32)	6 (18)	0.26
TIMI frame counts			
LAD	40.8 ± 8.7	25.6 ± 4.3	0.001
LCX	31.0 ± 7.9	18.4 ± 3.5	0.001
RCA	26.3 ± 5.4	15.6 ± 1.9	0.001
Mean	29 ± 6	18 ± 3	0.001

[a] Data are presented as n(%) or mean ± standard deviation.
ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; CAD = coronary artery disease; HDL = high-density lipoprotein; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LDL = low-density lipoprotein; RCA = right coronary artery; TIMI = thrombolysis in myocardial infarction.

Table 2 Renal parameters of participants with slow coronary flow and normal coronary flow[a]

Variables	Slow coronary flow ($n = 34$)	Normal coronary flow ($n = 34$)	p
BUN (mg/dL)	17 ± 6	14 ± 4	0.04
Creatinine (mg/dL)	0.90 ± 0.19	0.79 ± 0.16	0.01
GFR (mL/min)	92 ± 28	112 ± 27	0.004
cGFR (mL/min/1.73 m^2)	77 ± 22	96 ± 24	0.007

[a] Data are presented as mean ± standard deviation.
BUN = blood urea nitrogen; cGFR = corrected glomerular filtration rate; GFR = glomerular filtration rate.

levels are significantly lower in SCF patients than in normal coronary artery patients and that NO is inversely correlated with TFC.

Several studies have shown that there is a relationship between coronary TFC and the previously determined parameters of endothelial dysfunction in SCF patients [26—30]. The deterioration of NO activity has been reported to have an important impact on the renal functions of both healthy and sick individuals because endothelial dysfunction develops before significant vascular disease [10]. It has been demonstrated that there is endothelial dysfunction in the patients who have end-stage renal disease [9]. Kielstein et al. [11] have found higher levels of asymmetric dimethylarginine in patients who have end stage renal disease and atherosclerotic vascular disease than in those who do not have vascular disease. Zoccali et al. [9] have found that plasma asymmetric dimethylarginine concentrations are a strong and independent predictor of overall mortality and cardiovascular outcome in hemodialysis patients. Iliescu et al. [12] showed that microcirculation disorders have an important role in the development of renal disease in pigs. Astrup et al. [13] demonstrated a significant relationship between endothelial dysfunction and GFR in

patients who have diabetic nephropathy. In another study, Erzen et al. [31] found an important relationship between brachial FMD and GFR. Similarly, we found a significant correlation between GFR and TFC in three coronary arteries in SCF patients.

Our results demonstrate that renal parameters are significantly different between patients with and without SCF. Also, there is a negative correlation between GFR and TFC. However, further studies are needed both to evaluate renal function differences in patients with SCF and to investigate whether these differences depend on endothelial dysfunction.

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