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Correlation between endothelial dysfunction in normal coronary patients with slow flow and aortic ectasia: The first report

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Abstract

Background: *Slow coronary flow (SCF) is slow dye progression in the coronary arteries during selective angiography, but there is no such study about greater visceral vessels. Studies have suggested that flow-mediated dilation (FMD) is impaired in SCF. Endothelial function can be assessed by FMD in the brachial artery as ischemia-induced vasodilation. Since inflammation is an underlying pathology in the inflammation of visceral vessels and probably SCF, we studied the correlation of aortic ectasia and SCF by means of FMD.*

Methods: *Patients with normal coronary arteries and SCF formed the case group, and patients with normal coronary arteries and normal coronary flow formed the control group. We measured the diameter of the patients' brachial artery at rest, after inflation of a sphygmomanometer on the forearm [endothelial-dependent vasodilation (EDV)], and after use of sublingual nitrate (endothelial-independent vasodilation) by sonography. We also measured the diameter of the aorta using sonography before administration of sublingual nitrate. Endothelial dysfunction was defined as EDV significantly less than standard EDV.*

Results: *There were insignificant differences between age, gender, and frequency of cardiac risk factors within the case and control groups, but diabetes mellitus was significantly different between the two groups. The diameter of the aorta was insignificantly different between the case and control groups. The response of the brachial artery to the cuff test and sublingual nitrate were insignificantly different between the case and control groups. Endothelial dysfunction based on cuff test and sublingual nitrate administration was significantly more common in men than women, as the p values for cuff and sublingual nitrate were 0.033 and 0.051, respectively.*

Conclusions: *It seems that there is no correlation between SCFP and aortic ectasia.* (Cardiol J 2009; 16, 2: 146–150)

Key words: endothelial dysfunction, slow coronary flow, aortic ectasia, flow mediated dilation

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Introduction

Slow coronary flow phenomenon (SCFP), which was first described in 1972 as the detection of slow dye progression in the coronary arteries during selective coronary angiography [1], is reported in approximately 1% of patients undergoing coronary angiography [2]. Its exact pathophysiological mechanism is unclear; however, increased flow resistance due to some small vessel involvement, increased microvascular tone [1, 3–5], platelet dysfunction [6], early demonstration of diffuse atherosclerosis [7], inflammation [8], and an imbalance of vasoactive substances [9–11] have been suggested as underlying mechanisms. Furthermore, several recent studies have observed that coronary flow reserve (which reflects coronary microvascular function) [12], resting microvascular resistance [13], and flow-mediated dilation (a simple and non-invasive method for determining endothelial function) were impaired in patients with SCFP [14]; however, all of these studies suffered from the major limitation of a small sample size.

Endothelial function of coronary arteries can be assessed by flow-mediated vasodilation (FMD) in the brachial artery [15]. During the1990s, a noninvasive technique was developed to facilitate the repetitive measurement of endothelium-dependent function by measuring brachial artery flow-mediated vasodilation [16]. In this method, transient ischemia in the forearm leads to a local increase in blood flow, which in turn provokes the endothelium to release nitric oxide with subsequent vasodilation. This vasodilation can be imaged and quantified as an index of vasomotor function [17].

Despite the studied correlation of lesser vessels (especially coronary arteries) with SCFP, there is no study concerning the correlation between SCFP and the diameter of greater visceral vessels like the aorta. Considering inflammation as an underlying pathology in both inflammatory conditions of visceral vessels and probably SCFP, we studied the correlation of aortic ectasia and SCFP. The purpose of the present study is to evaluate endothelial function in patients with SCFP by means of FMD and to compare the diameter of their aorta with normal coronary persons and SCFP.

Methods

Study population

This case-control study was conducted in the "Tehran Heart Centre" (Tehran University of Medical Sciences) between January 2006 and December 2006. We obtained the patients' data from the angiography databank of the hospital. Patients who underwent coronary angiography due to anginal chest pain but whose angiography showed no significant coronary stenosis were entered into this study. The patients who had undergone thrombolysis or percutaneous coronary intervention at time of admission, had received any kind of antihypertensive or vasoactive therapy within 24 hours before sonography, or had moderate to severe valvular heart disease or muscle bridge in angiography were excluded from the study. Inclusion criteria for the case group were epicardial normal coronary and SCFP in elective angiography (n = 45). On the other hand, patients with normal coronary angiography and normal coronary flow (n = 81) were assigned to the control group. According to corrected thrombolysis in myocardial infarction (TIMI) frame count, SCFP was defined as more than 2 standard deviations of frame count (TIMI 2) from the normal published range for that particular vessel [18]. A single experienced cardiologist reviewed all the patients' angiography and calculated the frame count. Normal coronary artery was defined as no stenosis even at < 50% of the diameter of the coronary artery. Every subject read and signed an "informed consent" form, approved by the Ethics Committee of Tehran Heart Centre, before entrance to the study.

Procedure technique

All case and control subjects underwent sonography by a single experienced sonographer, blind to the angiographic results, the day after angiography. Sonography technique for measurement of FMD was according to "guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery" [17]. The sonographer first measured the diameter of patient's brachial artery at rest and recorded it as a baseline value (GE LOGIQ 5 Expert Doppler sonography machine with linear 10 MHz transducer, United States). Thereafter, he placed the cuff of a sphygmomanometer on the patient's forearm and inflated it for 5 minutes. Within 2 minutes after deflation of the cuff, he recorded the percentage of increased diameter of the brachial artery [endothelial-dependent flow-mediated vasodilation (EDFV)]. When the diameter of the brachial artery returned to baseline, the sonographer applied 2 puffs of sublingual nitrate spray (Nitromint, Egis Pharmaceuticals Ltd., Hungary) and recorded the percentage of increased diameter of the brachial artery (endothelial-independent flow-mediated vasodilation). If EDFV in each subject was significantly less than its

Table 1. Patient characteristics.

Characteristic	Control (n = 81)	Case (n = 45)	P
Clinical data			
Mean age (years)	54.17 ± 8.79	54.20 ± 9.67	0.987
Gender			
Male	35 (43.2%)	20 (44.4%)	0.893
Female	46 (56.8%)	25 (55.6%)	
Diabetes mellitus	16 (19.8%)	2 (4.4%)	0.019
Hypertension	22 (27.2%)	11 (24.4%)	0.740
Smoking	16 (20.0%)	5 (11.9%)	0.260
Biochemical data (mean)			
Triglyceride	167 ± 75.2	203.3 ± 151.9	0.142
Cholesterol	191.5 ± 38.9	193.7 ± 44.8	0.776
LDL cholesterol	111.6 ± 34	109.6 ± 35.5	0.770
HDL cholesterol	45.57 ± 11.3	45.3 ± 11.06	0.906
Platelet	216493 ± 54953	200311 ± 44340	0.093
Hemoglobin	13.95 ± 1.6	14.5 ± 1.4	0.068
Urea	32.1 ± 9.5	33.1 ± 7.9	0.546
Creatinine	1.00 ± 0.26	1.04 ± 0.21	0.329

LDL — low density lipoprotein; HDL — high density lipoprotein

standard reference, it was considered as endothelia dysfunction. In addition, the sonographer measured and recorded maximal transverse diameter of all the patients' abdominal aorta (GE LOGIQ 5 Expert Doppler sonography machine with curved linear 3 MHz probe, United States) before administration of sublingual nitrate.

We compared the patients' age, gender, smoking habit (according to CDC definition [19], hematological indices (red and white blood cell count, platelet count, and hemoglobin concentration), lipid profile — triglyceride, cholesterol, high density lipoprotein and low density lipoprotein, according to the updated Framingham guidance [20], fasting blood sugar (levels, diabetes mellitus (according to American Diabetes Association Guidelines [21]), hypertension (according to according to Joint National Committee sixth report [22]), serum level of blood urea and creatinine, and diameter of aorta between the case and control groups.

The study was approved by the local bioethical committee and all patients gave their informed consent.

Statistical analysis

We used the independent two-sample T test to compare the mean differences of the variables mentioned above. We also applied the χ^2 test to investigate the correlation of SCFP with age, gender, diabetes mellitus, hypertension, smoking habit, and coronary diameter. Uni- and multivariate regression analysis was used to investigate the correlation of frame count and FMD with endothelial dysfunction and other variables. All statistical calculations were done with SPSS v. 13. A P value < 0.05 was considered significant.

Results

Patients' characteristics are shown in Table 1. There were no significant differences between mean age, gender distribution, and frequency of cardiac risk factors within the case and control groups, but, as can be seen, diabetes mellitus (DM) was significantly different between those two groups.

Table 2 shows the correlation of the diameter of the aorta with slow coronary flow phenomenon. As can be seen seen, there is no significant difference between case and control groups regarding the diameter of the aorta.

Table 3 shows the response of brachial artery to the administration of cuff and sublingual glyceryl trinitrate (TNG). It is clear that the responses of brachial arteries to both cuff test and administration of sublingual TNG were insignificantly different between the case and control groups. After application of uni- and multivariate regression to investigate the correlation of endothelial dysfunction with frame count, neither frame count nor mean

Table 2. Correlation of diameter of aorta with presence of slow coronary flow phenomenon.

Variable	Case (n = 45)	Control (n = 79)*	P
Size of aorta [cm]	15.22 ± 2.15	15.18 ± 2.48	0.92

*2 missing data, thus there are 79 patients instead of 81 patients

Table 3. Response of brachial artery to administration of cuff and sublingual nitrate for detection of endothelial dysfunction through flow-mediated dilation.

Variable	Case (n = 45)	Control (n = 81)	P
Cuff-based	0.89 ± 0.44	0.67 ± 0.54	0.164
Nitrate-based	0.96 ± 0.58	0.90 ± 0.63	0.545

frame count in any coronary vessel showed any relationship with endothelial dysfunction. After adjustment for age, gender, smoking habit, hypertension, diabetes mellitus, dyslipidemia, and level of serum creatinine, the p value for this correlation was 0.839. We found that endothelial dysfunction based on cuff and TNG administration was significantly more common in men than in women, as the p values for cuff and TNG were 0.033 and 0.051, respectively.

Discussion

Slow flow coronary phenomenon is sometimes considered as a new category of coronary disease with unknown etiology and indefinite outcome [23]. Several surveys have investigated the relationship between SCFP and endothelial dysfunction as a probable etiology. In the present study we tried to ascertain whether there is a relationship between the diameter of the aorta and SCFP. Analysis showed that there were no significant differences between the patients' mean age, gender distribution, and presence of heart disease risk factors in the case and control groups. A study by Beltrame and colleagues also indicated that there was no difference between these characteristics within the case and control groups [5]. In addition, Erdogan et al. [12] reported no significant difference between coronary risk factors in normal coronary and SCFP patients. Fineschi et al. [13] verified the same result. Sezgin et al. [14] emphasized the same finding, and Yigit et al. [24] concluded that the above-mentioned factors had no significant difference within normal coronary and SCFP patients.

On the other hand, DM was significantly more common in the control (healthy) group, but since analysis of the covariance for omission of the confounding effect of DM resulted in insignificant p values, we could conclude that the reverse frequency of DM in healthy people did not affect the correlation between endothelial dysfunction and slow coronary flow phenomenon [25].

We found an insignificant difference between the case and control patients' aorta diameters. Therefore, if there is any aneurysm or dilation in the aorta we can assign it to other underlying reasons.

Conclusions

It seems that there is no correlation between slow flow phenomenon and diameter of aorta.

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