

## Mitral annular calcification associated with impaired coronary microvascular function

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### Abstract

**Background:** Mitral annular calcification (MAC) has been shown to be associated with atherosclerosis, and is a predictor of cardiovascular events. Coronary flow reserve (CFR) determined by transthoracic echocardiography has been introduced as a reliable indicator for coronary microvascular function. In this study we sought to investigate CFR in patients with and without MAC.

**Methods:** Seventy patients (mean age,  $68.2 \pm 6.6$  years) who were free of coronary artery disease or diabetes mellitus were involved; 35 patients with MAC constituted the experimental group while 35 patients without MAC served as controls. Using transthoracic Doppler echocardiography coronary peak flow velocities were measured at baseline and after dipyridamole infusion. CFR was calculated as the ratio of hyperemic to baseline diastolic peak flow velocities.

**Results:** The clinical and demographic characteristics including age, sex, and traditional coronary risk factors did not differ between the groups ( $P > .05$ ). The mean value of CFR was significantly lower in participants with mitral annular calcification than it was in controls ( $2.25 \pm 0.41$  vs.  $2.64 \pm 0.57$ ;  $P < .0001$ ). Multivariable regression analysis identified MAC ( $\beta = -0.40$ ,  $P = .004$ ), smoking ( $\beta = -0.36$ ,  $P = .007$ ), and C-reactive protein levels ( $\beta = -0.28$ ,  $P = .04$ ) as the independent variables significantly associated with CFR.

**Conclusions:** Our results demonstrate that CFR is impaired in patients with mitral annular calcification suggesting that coronary microvascular-endothelial dysfunction, an early finding of atherosclerosis, is present in these patients.

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**Keywords:** Mitral annular calcification; Coronary flow reserve; Atherosclerosis

### 1. Introduction

Mitral annular calcification (MAC) is a chronic, degenerative process characterized by calcification of the surrounding fibrous support of the mitral valve. Patients with MAC have been shown to have higher prevalences of different forms of atherosclerotic cardiovascular disease including carotid stenosis, coronary artery disease (CAD), peripheral artery stenosis and aortic atheroma [1–4].

Coronary atherosclerosis, MAC, and aortic valve calcium represent similar etiologies and processes; fatty plaques grow,

and as the nutritional needs become insufficient, the fatty plaques degenerate into calcific deposits [5]. Based on these data, it is believed that atherosclerotic mechanisms are basically involved in the pathogenesis of MAC, and that presence of MAC is a manifestation of atherosclerosis.

Evaluation of coronary flow reserve (CFR) by pharmacological stress transthoracic Doppler echocardiography has been introduced as a reliable and reproducible indicator of coronary microvascular function. Demonstrating CFR non-invasively by transthoracic Doppler echocardiography has been shown to have a strong correlation with CFR obtained by intracoronary Doppler wire and positron emission tomography [6,7]. A decrease in CFR as an indicator of coronary microvascular dysfunction has been proved to be an early manifestation of atherosclerosis and coronary artery disease [8].

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Based on the preceding, we hypothesized that CFR might be impaired in patients with MAC. Therefore, we sought to evaluate CFR using transthoracic Doppler echocardiography in subjects with and without MAC and to determine factors associated with CFR.

## 2. Materials and methods

### 2.1. Study population

Seventy patients admitted to our outpatient cardiology clinic were enrolled in the study. The study group included 35 patients with MAC, and 35 age- and sex-matched control patients without MAC. The study complies with the declaration of Helsinki. All participants gave informed consent, and the institutional review board at Baskent University Hospital approved the research protocol.

The demographic and clinical data, including traditional risk factors for atherosclerosis (hypertension, smoking, dyslipidemia, family history of premature coronary artery disease) were noted. Patients were defined as hypertensive, if they had a diastolic pressure  $>90$  mmHg or a systolic pressure  $>140$  mmHg or if they were being treated with an antihypertensive medication; as dyslipidemic if they had a

total cholesterol level  $>200$  mg/dL, an LDL cholesterol level  $>130$  mg/dL, or a triglyceride level  $>150$  mg/dL or were on a lipid-lowering agent; and as smoker if they were using tobacco at present or quit  $\leq 2$  years.

CAD was defined as the presence of 1 of the following: typical angina, ST-segment or T-wave changes specific for myocardial ischemia, Q waves on echocardiogram, wall motion abnormality on echocardiography, a noninvasive stress test revealing ischemia or any perfusion abnormality, and history of a myocardial infarction/revascularization. Patients having unequivocal symptoms underwent a noninvasive stress test; treadmill exercise or myocardial perfusion scintigraphy, and those demonstrating a positive result were excluded.

Patients with CAD, diabetes mellitus, aortic stenosis, moderate–severe aortic or mitral regurgitation, rheumatic valvular disease, hypertrophic cardiomyopathy, uncontrolled hypertension prior to the study (systolic blood pressure  $\geq 160$  and diastolic blood pressure  $\geq 90$  mmHg), renal dysfunction, asthma or malignancy were excluded.

### 2.2. Echocardiographic examination

Using a commercially available system (the Acuson Sequoia C256, Mountain View, CA, USA), complete

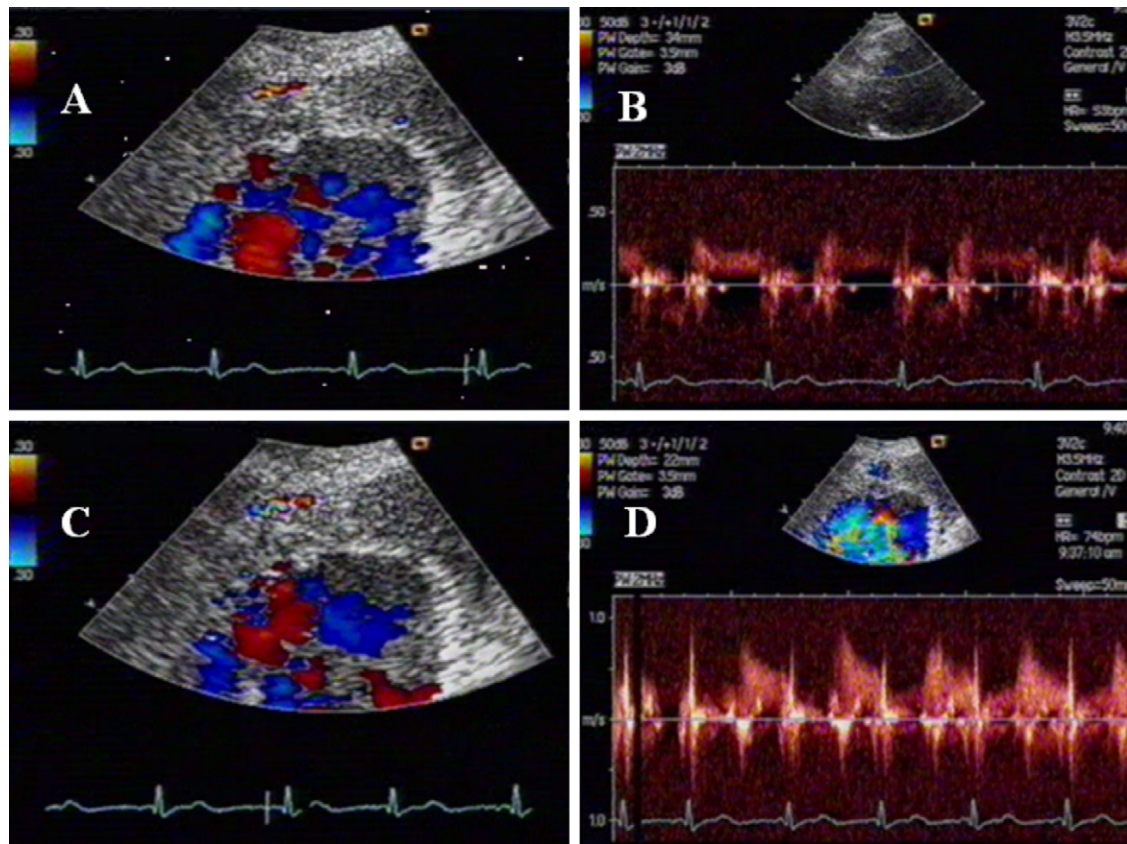


Fig. 1. Evaluation of coronary flow reserve. Mid to distal segment of the LAD coronary artery in color-coded transthoracic Doppler echocardiography; spectral Doppler coronary blood flow by sampling in mid to distal segment of the LAD. (A and B) At rest; (C and D) after diprydamole infusion at hyperemia.

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