

Editorial / Editöryal Yorum

Left ventricular remodeling impacts coronary flow reserve in diabetic patients: what is the mechanism?

Diyabetli hastalarda sol ventrikül yeniden şekillenmesi koroner akım rezervini etkilemektedir: Mekanizması nedir?

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In the absence of epicardial coronary artery stenosis, assessment of coronary flow reserve (CFR) helps to identify microvascular function. Transthoracic echocardiography has been shown to provide accurate measurement of CFR. It has several advantages including its non-invasive nature, wider availability, lower cost, and lack of radiation exposure, when compared with other modalities like invasive intracoronary measurements, positron emission tomography and magnetic resonance imaging.

It has been well established in previous studies that CFR is depressed in patients with diabetes, and that this is significantly related to prognosis, even in the absence of significant coronary artery disease.^[1] Vasomotor function is impaired in patients with type 2 diabetes, due to decreased bioavailability of endothelium-dependent nitric oxide.^[2] Also, secretion of vasoconstrictor mediators like endothelin-1 and angiotensin-II are increased. Moreover, wall thickening of intramural arterioles and reduced capillary vessel density have been reported in patients with diabetes.^[3] Many people with diabetes have also hypertension, obesity, and metabolic syndrome, each of which may contribute to impaired CFR.^[4] All these factors may lead to myocardial ischemia and adverse cardiovascular events in this patient population. In the study by Yuksel Kalkan and colleagues^[5] in this issue of the

journal, the authors report that in addition to impaired CFR in patients with diabetes compared to normal controls, impairment of CFR also differs according to the degree of left ventricular remodeling. In diabetic patients with concentric left ventricular hypertrophy, CFR was lowest compared with other patterns of left ventricular remodeling. This preliminary observation in diabetic patients could provoke other pathophysiological mechanisms underlying impaired CFR.

Four different patterns of ventricle adaptation can be recognized based on the relationship between left ventricle mass and relative wall thickness: (1) concentric left ventricular hypertrophy (increased mass and wall thickness), (2) eccentric hypertrophy (increased mass, normal relative wall thickness), (3) concentric remodeling (normal mass, increased relative wall thickness) and (4) normal left ventricular geometry. Concentric hypertrophy is known to be associated with high arterial pressure. In the study by Yuksel Kalkan et al., systolic and diastolic blood pressures were not different between patients with different left ventricular adaptations. However, HbA1C levels were significantly higher in the group with concentric hypertrophy. It was reported almost two decades ago that hyperglycemia and hyperinsulinemia may promote concentric changes in the left ventricle, even in normotensive patients.^[6] Even though data was not



presented in the study, one may assume that diabetes duration may also have an impact on left ventricular adaptation. In this sense, poorly-controlled diabetes could lead to concentric hypertrophy, and eventually worse CFR.

Left ventricular mass index was another parameter that was significantly related to CFR in the present study. An inverse relation was also demonstrated in diabetic patients in previous studies. In a study by Galderisi and colleagues diabetic and hypertensive patients had higher left ventricular mass index, relative wall thickness and lower CFR compared to controls.^[7] However; left ventricular mass index, and not relative wall thickness, was the main predictor of reduced CFR. Interestingly, in an older paper, patients with hypertension were studied and it was found that CFR was reduced to the greatest extent in those patients with concentric remodeling, and only left ventricular wall thickness had a linear relationship with CFR^[8]. Yuksel Kalkan et al. reported that not only left ventricular mass index, but also left ventricular geometry, has an impact on CFR in diabetic patients with normal blood pressure. Hypertension and diabetes may induce similar adaptational changes in left ventricular geometry. However, different findings related to the effect of these changes on CFR between patients with diabetes and hypertension suggest that there may be specific mechanisms related to each disease.

Authors reported that E/A ratio, as an index for left ventricular diastolic function, was related to reduced CFR. However, the relation was not significant in multivariate analysis. Galderisi and colleagues have nicely shown that not E/A, but mitral annular Em/Am (obtained by tissue Doppler imaging) was significantly related to reduced CFR in patients with hypertension.^[9] Since it is well known that concentric hypertrophy may lead to impaired relaxation of the left ventricle, comprehensive analysis of the left ventricular diastolic function in diabetic patients with different patterns of left ventricular geometry would be very helpful in identifying the mechanism of reduced CFR in those patients.

One of the major limitations of the present study is that absence of significant epicardial coronary artery stenosis was not demonstrated by coronary angiogra-

phy. Instead, clinical variables were used. Even mild coronary artery disease may lead to reduced CFR in patients with left ventricular concentric hypertrophy.

Data presented by Yuksel Kalkan et al. needs to be confirmed in further studies with an attempt to provide information on the mechanism of reduced CFR in the subset of diabetic patients with left ventricular concentric hypertrophy. Also, we need information on the follow-up of these patients, and the impact of concentric hypertrophy and low CFR on their prognoses.

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