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Editorial

Impaired Cardiac Function in Metabolic Syndrome

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See articles by Crendal et al. on pages 320-324 and Tadic et al. on pages 325-331 of this issue.

Metabolic syndrome (MS) is defined as a cluster of risk factors leading to the development of cardiovascular disease and type 2 diabetes. These risk factors include abdominal obesity, hypertension, abnormal glucose metabolism, reduced high-density lipoprotein cholesterol, and elevated triglyceride levels. Coronary artery disease and heart failure are more frequent in individuals with metabolic syndrome.[1]

Similar to MS, patients with diabetes, even in the absence of coronary heart disease and hypertension, are at risk for the development of heart failure; the so-called "diabetic cardiomyopathy."[2,3] Multiple etiological factors are implicated in the development of heart failure in patients with MS and type 2 diabetes, including myocardial insulin resistance, oxidative stress, and altered substrate metabolism.[4]

Abnormal cardiac function secondary to MS and diabetes is frequently detected during clinical studies as impaired left ventricular (LV) diastolic function. LV diastolic dysfunction identified using tissue Doppler imaging (TDI) is present in approximately 40% of patients with diabetes.[5] Although there is a correlation between LV diastolic dysfunction and abnormal myocardial perfusion, abnormal diastolic function is often observed in patients with diabetes who have no overt epicardial coronary artery disease. Furthermore, in patients with MS, abnormal LV diastolic function is frequently observed independent of LV mass.[6] Despite being an intense area of research, the precise mechanism(s) by which MS or diabetes cause abnormal diastolic function (including insulin resistance) is unknown.

Abnormalities of systolic function, in the presence of preserved ejection fraction in patients with diabetes and MS have been demonstrated using advanced imaging techniques. TDI and 2-dimensional (2D) speckle tracking echocardiography (STE) have been shown to demonstrate abnormal longitudinal strain in up to 43% of asymptomatic patients with diabetes despite preserved LV ejection fraction.[7,8] Reduced systolic tissue velocities and strain rates have also been observed in patients with metabolic syndrome without hypertension.[9]

Two studies in this issue of the *Canadian Journal of Cardiology* have examined different aspects of ventricular function in patients with metabolic syndrome. Crendal et al.[10] have examined parameters of LV performance in patients with MS, with and without diabetes and compared their findings with observations from healthy control subjects. Previous studies by the same group demonstrated attenuated longitudinal strain rates attributable to systolic dysynchrony in patients with metabolic syndrome.[11] Results from the present study show that MS patients had higher LV mass, impaired diastolic function, and lower longitudinal systolic strain rates. Longitudinal LV dyssynchrony observed using STE and TDI was longer in patients with MS whether or not they had diabetes mellitus. The study identified correlations between dyssynchrony indices and LV mass, and the presence of abdominal obesity and the inflammatory markers, irrespective of whether the subjects had diabetes. Furthermore, abnormalities of LV dyssynchrony were observed in the absence of any diastolic dysfunction.

In the second study, Tadic et al.[12] examined the effects of metabolic syndrome on right heart mechanics and function using 2D and 3-D echocardiography. This group demonstrated that the right ventricle (RV) and right atrial longitudinal strain rates were decreased in patients with MS. RV ejection fraction (RVEF) determined using 3-D echocardiography was also decreased in MS subjects. Abnormalities of RV function were correlated with systolic blood pressure and abdominal obesity.

These novel methods of studying myocardial mechanics demonstrate abnormalities of left and right ventricular systolic function in asymptomatic patients with MS whether or not they have diabetes. Although hypertension is a common feature of MS, and was present in 64% of the patients,[10] LV dysynchrony was similar in patients with or without hypertension. Furthermore, systolic blood pressure correlated with RVEF and global RV longitudinal strain. The mechanism responsible for the abnormal LV and RV function in MS is unclear. The strong association seen by Crendal et al.[10] between abnormal LV mechanics and systemic inflammation/central adiposity suggest myocardial metabolic disturbances due to insulin resistance might result in

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impaired contractile function. However, although metabolic disturbances might play a role, it is also possible that microvascular abnormalities might reduce perfusion to the subendocardial myofibrils. The consistent finding that longitudinal, rather than circumferential shortening is impaired in MS suggests that the longitudinal fibres, which run in the subendocardium, are prone to myocardial ischemia and might be preferentially affected. Further research is required to clarify this.

The finding of impaired RVEF and longitudinal strain in the RV in patients with MS also raises the question as to the mechanism. However, although the difference met statistical significance, the RVEF difference between the control and MS group was only 3%, and the RVEF still fell within the normal range at 55% ± 4%. The significance of such a finding is unclear, as it still remains well within the range of normal values, and was not associated with RV dilatation. Like the LV dysynchrony indices, RVEF correlated significantly with systolic blood pressure and waist circumference. Whether the change in RV longitudinal function and RVEF occurred as a primary response to abnormalities of metabolism,[13] or occurred secondary to abnormal LV diastolic function and elevated left atrial filling pressures remains unclear. Furthermore, although the correlation was statistically significant, the r values of -0.27 to -0.35 suggest other factors contribute significantly to the changes observed.

Despite the use of advanced imaging techniques to demonstrate subtle abnormalities in LV and RV function, many questions remain unanswered from the 2 studies. For instance, do these abnormalities identify patients at particular risk for the development of heart failure? How do the changes demonstrated give mechanistic insight into potential therapeutic targets to prevent the development of heart failure? What magnitude change in strain or dyssynchrony, measured in the left and RV is clinically relevant? Finally, how do these measures guide clinical therapy for patients when identified? At present, treatment for patients with MS and type 2 diabetes with preserved LV ejection fraction remains empiric with blockade of the renin angiotensin system, and tight glycemic and optimal blood pressure control being the mainstay of therapy. Despite the use of TDI and 2D STE in the assessment of cardiac disease for at least 10 years, none of these techniques has made it into routine clinical practice. As a result, although these findings are of interest, further research—preclinical and clinical—is necessary to ascertain the clinical relevance of such measures and to assess how they might be used to guide therapeutic intervention for individuals with MS or type 2 diabetes.

Disclosures

The authors have no conflicts of interest to disclose.

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