Left ventricular diastolic (dys)function in type 2 diabetes: time for a critical reappraisal

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Over the next two decades, the incidence of both type 2 diabetes and congestive heart failure should increase to epidemic levels [1]. Patients with diabetes are characterized by an increased likelihood of heart failure, largely reflecting the contribution of diabetes to coronary artery disease and its association with hypertension [2]. Patients with unexplained idiopathic dilated cardiomyopathy were found to be 75% more likely to have diabetes than age matched controls [3]. In the meantime, the existence of a specific diabetic heart disease or cardiomyopathy, referring to ventricular dysfunction in diabetic subjects in the absence of hypertension, coronary atherosclerosis, or any other known cardiac disease, has remained controversial [4]. Left ventricular (LV) remodeling in type 2 diabetes, includes increased LV mass, wall thicknesses and arterial stiffness and reduced LV systolic chamber and myocardial function [5]. LV mass and wall thickness increase with worsening glucose intolerance [6]. Diabetes mellitus, especially with worse glycaemic control, is independently associated with abnormal LV relaxation, similar to the well-known impaired relaxation associated with hypertension [7]. The noninvasive assessment of diastolic dysfunction mainly relies on Doppler studies of transmitral inflow, measuring mitral inflow velocities, deceleration time, and isovolumic relaxation time, and assessing flow patterns. As diastolic function worsens, early diastolic LV filling (E wave) is reduced (delayed relaxation pattern). However, as left atrial pressure increases, the E wave returns to normal, producing a mitral pattern indistinguishable from normal (pseudonormal). The development of a restrictive filling pattern reflects a high left atrial pressure associated with an increased risk of heart failure and cardiovascular complications [8]. New techniques such as mitral annulus velocity by tissue Doppler imaging (TDI) and flow propagation velocity are relatively preload-independent measurements of diastolic function [9]. Changes in diastolic function have been widely described in diabetic patients without evidence of heart disease caused by other factors [10]. Diastolic inflow patterns have been reported as frequently abnormal, reflecting underlying abnormalities in relaxation and/or reduced myocardial compliance. In well-controlled type 2 diabetic patients who had no evidence of diabetic complications or overt systolic dysfunction, LV diastolic dysfunction was found in 60% of cases: 28% had a pseudonormal pattern of ventricular filling and 32% had impaired relaxation [11]. Similar results have been found in young type I diabetic patients without known cardiac disease [12]. The exact prevalence of LV diastolic dysfunction in diabetic patients remains however a matter of debate, depending on populations, definitions and the methods used, varying from 30% [13] to 75% [14]. More recent studies using less load-dependent parameters have shown that in diabetic patients with normal or comparable diastolic function, myocardial diastolic TDI velocities were significantly decreased [15]. In a subsequent study, the same group found that myocardial diastolic function (Em) was independently predicted by age, hypertension, insulin and metformin treatment [16]. However, not all studies demonstrated the presence of diastolic dysfunction assessed using transmitral flow-derived parameters in both type 1 [17] and type 2 [18] diabetic patients.

In the current issue of the D&M, Cosson et al. [19], using a combined Doppler echocardiographic approach (TDI and flow propagation) did not find any significant difference with regard to LV morphology (including LVM) or diastolic function parameters in type 2 diabetic normotensive patients, with normal LVEF and absence of microvascular complication. The main
limitation of this study, as well as in previous reports [11–18, 20], is the lack of statistical power to draw a definite conclusion from exposed-controls design studies, whereas epidemiological approaches underline the presence of both LV remodeling and some degree of ventricular dysfunction in diabetic populations [5–7,10]. Case–control studies are however useful to raise new hypotheses in this complex topic. Recent works using mainly strain rate imaging, suggest the presence of some degree of subclinical systolic LV impairment [15]. In addition, quantitative myocardial contrast echography has been proposed to demonstrate impaired transmural myocardial blood flow reserve in diabetic patients, but not related to LV function, raising the possibility that, although cardiac microangiopathy and subclinical diabetic cardiomyopathy may coexist, microvascular disease may not be the predominant causative factor in diabetic cardiomyopathy [20].

Is diabetic cardiomyopathy a distinct clinical entity? Diastolic and/or systolic dysfunction are related to pathogenic cellular (reticulum calcium overload, mitochondrial abnormalities and energetic metabolism dysfunction), molecular and microcirculation alterations that accompany diabetes mellitus [3]. The magnitude of left ventricular hypertrophy (LVH) depends on the magnitude and duration of hyperinsulinaemia. The extent of systolic dysfunction may depend more on the magnitude and duration of hyperglycaemia and the presence or absence of insulin. Diastolic abnormalities may occur as a consequence of either LVH or hyperglycaemia. Thus, LVH and diastolic abnormalities are observed most commonly and earlier than systolic abnormalities. Hypertension, dyslipidemia and atherosclerosis, common in diabetic patients, further compromise cardiac status. Currently, no specific therapeutic strategies can be recommended, but management of risk factors should be reinforced.

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A. Cohen*
S. Ederhy
F. Boccara
Cardiology Department, Saint-Antoine University and Medical School, Assistance Publique-Hôpitaux de Paris and Université Pierre-et-Marie-Curie, 184, rue du Faubourg-Saint-Antoine, 75571 Paris cedex 12, France

E-mail address: ariel.cohen@sat.aphp.fr (A. Cohen).

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*Corresponding author.