Early Failure of the Diabetic Heart

That diabetes is a risk factor for congestive heart failure has been established for decades, but knowledge of the pathophysiology and treatment of heart failure in diabetes is limited. The prevalence of diabetes in different surveys and clinical trials of heart failure ranges from 10 to >30% (1). In the community setting, data from the Framingham Heart Study have shown an increased incidence of congestive heart failure in diabetic subjects irrespective of coronary heart disease and hypertension (2). The relative impact of diabetes on developing heart failure was found to be greater in women. In the Studies of Left Ventricular Dysfunction (SOLVD) Trials and Registry, diabetes was found to be an independent risk factor for mortality and morbidity in both symptomatic and asymptomatic heart failure (3). A common finding in diabetic patients enrolled in clinical trials of myocardial infarction is a discrepancy between left ventricular systolic function and heart failure symptoms (4,5). Despite similar left ventricular systolic function, patients with diabetes have more pronounced heart failure symptoms, use more diuretics, and have an adverse prognosis compared with those without diabetes. One putative explanation for this discrepancy is diastolic dysfunction of the left ventricle.

In overt heart failure, diastolic dysfunction often coexists with systolic dysfunction as a consequence of ischemic heart disease. However, as described in the article by Poirier et al. (6) in this issue of *Diabetes Care*, diastolic dysfunction is a frequent finding in many studies of cardiac function in type 2 diabetic subjects without symptoms and signs of heart disease. Most of these studies did not angiographically exclude coronary artery disease, which implies that preclinical atherosclerosis as a contributory cause of diastolic dysfunction is a potential source of bias. Diastolic dysfunction independent of ischemic heart disease is presumably due to diabetic cardiomyopathy (7).

Previous studies estimating the prevalence of diastolic filling abnormalities in diabetic subjects have used measurements of transmitral Doppler flow velocity and have categorized the patients into groups of impaired relaxation or restrictive impairment. The intermediary stage between the two groups has not been thoroughly investigated. This stage is characterized by a normal ventricular relaxation at the expense of an increased left atrial filling pressure, resulting in a pseudonormalized pattern of diastolic filling. This stage cannot be distinguished from the normal pattern by standard transmitral flow measures. The pseudonormal ventricular filling pattern is always a pathological phenomenon, whereas impaired relaxation is also a feature of aging. To unmask pseudonormal ventricular filling patterns and thereby allow estimation of the true prevalence of diastolic dysfunction in healthy type 2 diabetic men, Poirier et al. (6) performed a study using conventional assessment of transmitral Doppler flow velocity as well as measurements of pulmonary venous flow and transmitral flow after Vasalva maneuver. The latter method decreases filling pressures and consequently unmasks the underlying impaired relaxation. The main finding of this study is a very high prevalence of diastolic dysfunction in men with well-controlled type 2 diabetes and no clinically detectable heart disease. Among the 46 patients studied, 60% had diastolic filling abnormalities, 32% had impaired relaxation, and 28% had a pseudonormalized filling pattern.

The prognostic impact of isolated diastolic dysfunction in patients with diabetes is unknown, but in hypertensive patients, diastolic dysfunction has been shown to be a predictor of morbidity (symptoms of heart failure) (8). Likewise, information on the prognostic impact of diastolic dysfunction in clinical heart failure in the diabetic subgroup is lacking. In patients with clinical heart failure in the Vasodilator Heart Failure Trial, prognosis was better in patients with normal ejection fraction compared with those with low ejection fraction (9). In patients with heart failure and systolic dysfunction, a restrictive filling pattern has been shown to have an independent prognostic impact (10). In the setting of acute myocardial infarction, measures of left ventricular diastolic function have prognostic value on in-hospital heart failure and mortality (11).

The findings of Poirier et al. (6) are important and should encourage future research in this field. Because myocardial stiffness increases with age, the results obtained by Poirier et al. could to some extent be confounded by an effect of aging. Therefore, the results should be confirmed in a larger cohort including women and a control group of subjects without diabetes. Moreover, new investigations could apply the relatively new echocardiographic techniques of color M-mode and tissue Doppler, which may provide a more accurate estimate of left ventricular relaxation, since these methods appear to be insensitive to the effects of preload compensation (12). Also, prospective studies of the prognostic impact of both early isolated diastolic filling abnormalities and concomitant abnormalities with systolic dysfunction in patients with diabetes are needed. When considering early diastolic dysfunction as a potential marker of evolving heart disease, echocardiographic screening with assessment of diastolic function could be relevant in diabetic patients. However, documentation of a beneficial effect of interventions to improve diastolic dysfunction and prevent progression in heart disease in these patients is mandatory before a screening procedure is recommendable. Putative ways of improving diastolic dysfunction are exercise (13) or, pharmacologically, the use of β-blockers and calcium antagonists (14), but the evidence to substantiate these methods is insufficient. Previous studies on the effect of glycemic control on diastolic function have shown conflicting results; Poirier et al. were not able to show a correlation between indexes of glycemic control and diastolic filling abnormalities in the group of well-controlled type 2 diabetic subjects. Nevertheless, it seems worthwhile to study the effect of strict metabolic control on diastolic function more thoroughly with the above-mentioned new and more sensitive echocardiographic modalities. While knowledge on treatment of diastolic dysfunction is sparse, it is important to emphasize that in the high-risk group of diabetic patients with overt heart failure, aggressive anticongestive treatment including ACE inhibitors (15) and β-blockers (16) is highly warranted.

In conclusion, diastolic filling abnormalities in type 2 diabetic subjects without clinical evidence of heart disease appear to

be common and suggest the presence of early subclinical alterations in cardiac function. The prognostic importance of this subclinical dysfunction and the possibilities for intervention are not fully known, and further studies are warranted before introducing general early echocardiographic screening in patients with diabetes. The growing impact of diabetes and congestive heart failure on public health should stimulate pathophysiological and clinical research on the incipient alterations in cardiac function in diabetes.

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