Nonischaemic heart failure and diabetes mellitus

Daniel M. Shindler

Robert Wood Johnson Medical School, UMDNJ, 1 Gloucester Court, 08816 East Brunswick, USA

This editorial refers to "Impact of diabetes mellitus on long-term survival in patients with congestive heart failure" by de Groote et al. on page 656

Knowledge about the impact of diabetes mellitus on prognosis in patients with heart failure continues to grow. As reported in this issue, de Groote et al. used coronary angiography to stratify diabetics with systolic heart failure into ischaemic and nonischaemic aetiologies. The hypothesis tested was that diabetic status may be used as a prognostic indicator in heart failure patients. The study also sought to analyse the impact of diabetes on survival according to the aetiology of heart failure.

Although diabetic heart failure patients in the study had a significantly higher cardiovascular mortality rate, the finding was not as conclusive as in previous studies. Multivariate analysis of the combined ischaemic and nonischaemic study population did not show diabetes as an independent predictor of cardiovascular mortality. Importantly, in this study only 45% of the patients were classified as ischaemic. When the 45% with ischaemic aetiology were analysed separately, the results were again consistent with previously published findings. Diabetes mellitus was indeed an independent predictor of increased cardiovascular mortality in patients with heart failure of ischaemic aetiology.

The study surprisingly finds opposite prognostic implications in diabetics with heart failure of nonischaemic aetiology. In the comparatively large nonischaemic cohort of this study, diabetes was actually associated with decreased cardiovascular mortality. The reasons for this finding are unclear and for now should be interpreted with caution.

The prognostic importance of diabetes in patients with ischaemic heart disease was demonstrated in the well-known Framingham publications. However, heart failure of nonischaemic aetiology in diabetics was not the subject of the reports. For example, in the course of follow-up of the Framingham patients, 414 men and 195 women survived an initial myocardial infarction. In this group, 55 men and 37 women had diabetes. Excessive early mortality among diabetics who had myocardial infarctions resulted in the small numbers of patients available for follow-up analysis. The time to recurrent myocardial infarction or fatal coronary event was significantly shorter in female Framingham diabetics compared to female nondiabetics. Pertinent to the present discussion, female diabetics were found to be significantly more likely to develop heart failure. These were all patients with ischaemic heart disease.

Large prospective clinical heart failure trials have enrolled patients with both ischaemic and nonischaemic aetiologies. The premise has been that treatment of heart failure would be the same regardless of the underlying aetiology. A recent literature review concluded that apart from the use of digitalis, which must be prudent in postinfarction cardiomyopathy or in patients with ventricular arrhythmias, the treatment of cardiac failure differs little with respect to its ischaemic or nonischaemic aetiology. Such was the case in the Studies of Left Ventricular Dysfunction (SOLVD) Trials and Registry. SOLVD entry criteria allowed enrolment based on angiographic, echocardiographic, or nuclear ejection fraction. Ischaemic and nonischaemic aetiologies were included. Initial analysis of this large group of patients to determine the prognostic importance of diabetes combined ischaemic and nonischaemic aetiologies. This analysis showed conclusively that diabetes was a powerful independent predictor of all-cause mortality, hospitalisation for congestive heart failure, all-cause hospitalisation, and the combined endpoint of death or hospitalisation for congestive heart failure. By including this large number of diabetics in the analysis, it was possible to determine that diabetes was an independent predictor of the endpoints listed above, irrespective of ACE inhibitor treatment, in all aetiologies combined.

The SOLVD data were subsequently reanalysed to determine the relative prognostic impact of diabetes in ischaemic compared with nonischaemic aetiology. Once again, diabetes was strongly associated with an increased risk for all-cause mortality in the ischaemic aetiology group. However, this was not the case in those with...
nonischaemic aetiology. There was no association between diabetes and mortality risk in those with nonischaemic cardiomyopathy. The number of diabetics in the nonischaemic cohorts in this second SOLVD analysis was necessarily smaller, but similar to the number studied in this issue by de Groote, and the findings in both studies are consistent.

The effect of aetiology was also recently studied in patients with advanced heart failure enrolled in the BEST trial. Once again, diabetes conferred an increased risk for adverse cardiovascular events in patients with ischaemic aetiology. In contrast, in patients with nonischaemic aetiology, diabetes was not a predictor for all-cause death or cardiovascular death.

These unexpected findings in diabetics with heart failure of nonischaemic aetiology should actually help refine heart failure treatment. Pharmacologic treatment strategies may also differ. For example, the altered glycaemic state may eventually be approached differently in the ischaemic and nonischaemic heart failure patient. Metabolic goals, such as reducing myocardial free fatty acid accumulation and improving myocardial glucose utilisation with β-blockers, may have different priority in the two groups. Treatment initiation of heart failure may consist of different drug sequences and combinations in the two groups. Therapeutic intervention for associated disorders such as hypertension may also vary with aetiology. Tight blood pressure control has been shown to confer a 56% reduction in risk of heart failure in diabetics. Thiazide versus loop-diuretic use and β-blocker dosing already tend to differ in diabetics with heart failure who have normal coronary angiograms compared to diabetics with ischaemic heart disease.

Unfortunately, the above findings do not offer a single obvious explanation for the divergent prognostic importance of diabetes in heart failure. The findings also need to be confirmed by prospective studies. In the meantime, one should avoid extrapolating ominous prognostic implications in diabetics with ischaemic aetiology to diabetics with heart failure of nonischaemic aetiology.

The prevalence of both diabetes and heart failure continues to rise at an alarming rate around the world. No one is suggesting the existence of “good” diabetes that protects patients from the complications of nonischaemic heart failure. ACC/AHA guidelines state that it may be useful to define the presence, anatomic characteristics, and functional significance of coronary disease in selected patients with systolic heart failure. In light of the de Groote study, this may be especially important in the diabetic with heart failure.

References