Diastolic Dysfunction and Heart Failure

I would like to congratulate Dr. Persson and colleagues for their recently published echocardiographic substudy of the CHARM (Candesartan in Heart Failure—Assessment of Reduction in Mortality and Morbidity)-Preserved trial (1). Their results emphasize the importance of an objective evaluation of diastolic function in determining prognosis of patients with heart failure and preserved systolic function. Interestingly, one-third of the patients in their study had no objective evidence of diastolic dysfunction, despite being enrolled in a study where they were presumed to have experienced heart failure. Furthermore, this group also had the best prognosis. The most likely explanation is that either 1) they were misclassified and did not have heart failure or 2) their heart failure was on the basis of a different mechanism altogether (i.e., they had neither diastolic nor systolic dysfunction), and whatever the underlying cause for their heart failure, it appears to be relatively benign. These possibilities illustrate the need for being more specific in how we assess and characterize patients with heart failure, particularly those with diastolic dysfunction. I believe the time has come for us to consider abandoning the “black box” term of “heart failure with preserved systolic function,” because this likely lumps together a number of different disease entities. Rather than trying to avoid classifying patients with diastolic dysfunction because of the current limitations in assessment, efforts would be better directed toward striving to improve the detailed assessment of diastolic function. The study by Persson et al. (1) is a first step toward that end. In the future, newer techniques such as tissue Doppler, strain-rate imaging, and speckle tracking may lead to better understanding of this disease process.

As the investigators pointed out, their study had a relatively small proportion of patients with mild diastolic dysfunction, and the prognosis of these patients was essentially the same as those with normal diastolic function. These findings are in contrast with a previously published study by Redfield et al. (2). One possible explanation is that Persson et al. (1) varied their ranges of normal E/A ratio by age group. Whereas the mean E/A ratio is known to decrease with advancing age, the rationale for considering this “normal” is unclear, as it is widely accepted that the decreasing E/A ratio with advancing age reflects impairment in left ventricular relaxation that occurs with aging. As such, just as we do not consider a mildly elevated systolic blood pressure as “normal” in an elderly individual just because the average systolic blood pressure of older subjects is higher, the decrease in E/A ratio seen in elderly patients should also not be considered “normal.” It is likely that were a standard E/A ratio used for all age groups, then the proportion of patients with mild diastolic dysfunction would be higher. It would be interesting to see if this approach would lead to increased differentiation among the 4 groups in the survival analysis.

REFERENCES


We thank Dr. Kolias for his congratulatory letter to us for our echocardiographic substudy in CHARM (Candesartan in Heart Failure—Assessment of Reduction in Mortality and Morbidity) Preserved—the CHARMES trial, recently published in *JACC* (1). His comments are appreciated, and we would agree with him that it is important to consider abandoning the “black box” term of “heart failure with preserved systolic function” and that efforts would be better directed toward striving to improve the detailed assessment of diastolic function. We have been able to reclassify the patients in CHARMES to respond to the relevant question posed by Dr. Kolias. In the revised analysis we have retrieved data for a conventional Doppler-echocardiographic evaluation of 181 of the 312 patients entered in the trial, thus not using the N-terminal part of the pro-B-type natriuretic peptide (NT-proBNP) to distinguish between normal and pseudonormal diastolic function. We have used a non–age-related classification of diastolic function following the current guideline from the Mayo Clinic (2). The present analysis is a secondary, post hoc analysis in a smaller subset; therefore, the results have to be interpreted with caution.

The results do show that the proportion of patients with normal diastolic function is similar to the previous results in CHARMES, with 1 out of 3 patients being normal (see Table 1). The proportion of patients with mild diastolic dysfunction is slightly higher, although the proportion with normal and mild diastolic dysfunction is not significantly different from the original CHARMES study (60% vs. 55%). We can still show a graded relationship between severity of diastolic dysfunction and outcome. The relative risk for moderate to severe diastolic versus mild diastolic dysfunction is approximately 2, both for the end point of cardiovascular death or readmission for heart failure (CV1) and for the combined end point of cardiovascular mortality, rehospitalization for heart failure, myocardial infarction, and stroke (CV2). The