

CORRESPONDENCE

Letters to the Editor

A New Era in the Natural History of Dilated Cardiomyopathy

I read with interest the paper by McNamara et al. (1), which supports the findings of our previous report of a logistic model that identifies factors associated with restoration of normal ventricular function in this patient population (2). As we noted in that paper, which indeed references the marked improvement in left ventricular function observed in the placebo group of the IMAC (Intervention in Myocarditis and Acute Cardiomyopathy) trial, we have entered a new era in the natural history of dilated cardiomyopathy in which restoration of normal ventricular function may be anticipated in a significant number of patients. This demands that we better identify those patients who are likely to recover normal ventricular function. Identification of those who have a high probability of recovery will allow early implementation of more aggressive therapies in those who are not likely to recover, and will point towards interventions that may augment the factors found to be associated with restoration of normal ventricular function.

In particular, our report identified progressive increases in QRS duration, male gender, ischemic etiology of heart failure, and a history of diabetes mellitus as factors that decrease the probability of recovery. The probability of recovery increased with increasing systolic blood pressure at the time of initial diagnosis. Indeed, the report by McNamara et al. (1) is in agreement with 3 of these factors. They also find that female gender and increasing blood pressure are associated with recovery of ventricular function. Electrocardiographic QRS duration is known to correlate highly with ventricular chamber size, and therefore, it is not surprising that they find end-diastolic dimension to be a significant correlate with ventricular recovery. The cohort in their study did not strictly match that in our study, being focused on those with recent-onset cardiomyopathy. They specifically excluded patients with ischemic heart disease and diabetes, and therefore, our data provide insight into different etiologies of cardiomyopathy and the important comorbidity of diabetes. In addition, the average time to recovery of left ventricular function in our study was 40.3 ± 4.7 months, providing total patient-years equivalent to that in the study by McNamara et al. (1), even though our cohort size was smaller. Our data show that recovery can be a slow process, and it would be interesting to see how the factors they identify influence recovery over longer periods of time.

The recognition that patients with dilated cardiomyopathy can recover normal ventricular function raises important questions. Importantly, it is unknown whether return to normal ventricular function represents a true recovery from the cardiomyopathic process or is in fact a "remission" with persistence of normal function dependent on continued medical therapy. Indeed, we have reported a small series of patients who have "relapsed" with discontinuation of medical therapy (3). Should the current Amer-

ican Heart Association/American College of Cardiology classification of heart failure stage include a new category designating those who have returned to normal cardiac function? As we continue to understand this new era in the natural history of cardiomyopathy, we are challenged to address these and other issues.

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doi:10.1016/j.jacc.2011.09.070

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Reply

We certainly agree that several of the same factors appear to predict recovery in both the IMAC2 (Intervention in Myocarditis and Acute Cardiomyopathy 2) trial (1) and the cohort reported by Dr. Binkley and his colleagues (2). Indeed, consistent with the Ohio State report, in unpublished data from IMAC2, subjects with a left bundle branch block (LBBB) at presentation had a significantly lower left ventricular ejection fraction (LVEF) at 6 months (with LBBB, mean LVEF: 0.38 ± 0.12 ; no LBBB: 0.41 ± 0.12 , $p = 0.04$) and a trend toward less improvement in LVEF (with LBBB, change in LVEF from entry to 6 months: 0.14 ± 0.14 ; no LBBB: 0.18 ± 0.12 , $p = 0.07$). Although only 19% of IMAC2 subjects had LBBB at presentation, 54% had evidence of dyssynchrony by speckle tracking imaging despite a narrow QRS (3). This declined to 12% by 6 months, and the restoration of synchrony may indeed have played a role in subsequent myocardial recovery.

As suggested, QRS duration may also be a surrogate for remodeling. The finding in IMAC2 that greater remodeling (as defined by left ventricular end-diastolic diameter [LVEDD]) predicts less recovery has also been reported by Simon et al. (4) for a cohort of subjects on LV assist device support, and indeed was previously evident in the first IMAC trial (5). LVEDD appears to be a consistent clinical tool for predicting myocardial recovery. Whether the impact of QRS duration on myocardial recovery

reflects an association with remodeling or a primary role of dyssynchrony itself remains to be determined.

The consistency of these clinical characteristics for predicting recovery, in particular gender, QRS duration, and the degree of remodeling (LVEDD), does support the concept of a “recovery score” advocated by the Ohio State group. If prospectively validated, this would be of great assistance to clinicians in the management of subjects with recent-onset cardiomyopathy. We thank Dr. Binkley for his insightful comments.

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doi:10.1016/j.jacc.2011.10.889

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Angiotensin-Converting Enzyme Inhibitors Can Increase the Transvalvular Gradient Among Patients With Aortic Stenosis

We read with interest the study of Herrmann et al. (1) that examined the longitudinal left ventricular (LV) function, degree of myocardial fibrosis, hemodynamic distinctions, and clinical outcomes of symptomatic patients attributed to isolated aortic stenosis

(AS). The patients were grouped and analyzed according to aortic valve area, transvalvular gradient, and left ventricular ejection fraction (LVEF); all patients with severe AS, regardless of transvalvular gradient, underwent aortic valve replacement.

We respectfully point out that the proportion of patients on medical therapy with angiotensin-converting enzyme (ACE) inhibitors, aldosterone antagonists, beta-blockers, and/or statins at baseline and on follow-up 9 months later was not reported. This information is important because these medications can potentially affect the outcomes being evaluated. We would like to focus our comments regarding ACE inhibitor use, specifically.

The preoperative use of ACE inhibitors can potentially affect the outcome of the study by altering 2 factors considered for patient assignment: transvalvular gradient and LVEF. Since resistance in a series is additive, ACE inhibitors will decrease systemic vascular resistance through arterial vasodilation, which in turn may increase the transvalvular gradient (2). These agents are also established reverse remodeling agents and can improve the LVEF of patients with systolic dysfunction with long-term use. Although previously thought to be a contraindication for patients with AS because of the theoretical concern for hypotension, decreased coronary perfusion, and renal insufficiency, several prospective studies suggest that medical therapy with ACE inhibitors may be safe (2,3). Dalsgaard et al. (4) recently demonstrated with a small randomized controlled trial that the use oftrandolapril among patients with severe AS did not cause adverse outcomes or symptomatic hypotension. Over 8 weeks of follow-up, treatment withtrandolapril led to a decrease in LV end-systolic volume and N-terminal pro-B-type natriuretic peptide, suggesting beneficial effect of ACE-induced LV unloading (4). The study of Herrmann et al. (1) also showed that the sickest patient subgroups (i.e., those with low-gradient severe symptomatic AS, regardless of ejection fraction) have the highest systemic vascular resistance and relatively preserved blood pressure. It is plausible that medical therapy with ACE inhibitors could potentially be used as a bridge to aortic valve surgery.

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doi:10.1016/j.jacc.2011.10.892

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