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LETTERS TO THE EDITOR

Dual-Chamber Pacing in Dilated Cardiomyopathy: Insufficient Sample Size, Heterogeneous Population and Inappropriate End Point May Lead to Erroneous Conclusions

We read with great interest the report by Gold et al. (1) in the October issue of the Journal, which concluded discouraging the "routine use of pacemaker implantation with short atrioventricular (AV) delay as a primary treatment of heart failure in patients without standard arrhythmic indications." However, it is our opinion that such strong conclusions cannot be drawn on the basis of a small number of patients (9 of 12 subjects were able to complete randomization and follow-up) from the heterogenous population selected (given that 67% of patients had coronary artery disease) and that most patients (83%) were in New York Heart Association functional class III. Unfortunately, no information on the extent and severity of the coronary artery disease were presented nor on the investigation of stunned or hibernating myocardium or the presence of concomitant disease (i.e., diabetes, chronic obstructive pulmonary disease). This information would be of great interest in view of the results of this study (1). Thus, the patient population selected by Gold et al. profoundly differs from that of Hochleitner et al. (2) or ours (3), which included mainly patients with severe end-stage heart failure as documented by the use of intravenous inotropes. Moreover, in both series the population was consistently homogenous with regard to etiology in that Hochleitner et al. (2) described patients with idiopathic dilated cardiomyopathy, and we (3) have included two patients with severe coronary artery disease.

Another surprising finding was the left ventricular ejection fraction during VVI and VDD pacing, as reported in Figure 3 of Gold et al. (1). In light of the prevalent underlying etiology of their study (coronary artery disease), the lack of major improvement in such a short period of pacing is not surprising. In addition, questionable data were presented because apparently results from only 8 of 12 patients were plotted (Figure 3 [1]). Furthermore, the data plotted demonstrated substantial improvement in left ventricular ejection fraction when patients were paced in VDD mode, which was >15% in some patients (e.g., the second patient in Figure 3 whose left ventricular ejection fraction changed from ~22% to 26% (i.e., an 18% improvement). However, Gold et al. did not extensively comment on this point but only briefly reported that "There was not significant improvement in ejection fraction with short AV delay pacing because the mean ejection fraction was 18 ± 4% in VVI mode and 16 ± 6% in VDD mode. Moreover, no patient had an improvement >5% with VDD pacing compared with VVI control pacing." Because modification of left ventricular ejection fraction was one end point of the study, we would appreciate further insights into the data discrepancies and some pathophysiologic explanation for the worsening of the left ventricular ejection fraction during VDD compared with VVI stimulation.

Moreover, the methodology for assessing changes in cardiac output by thermodilution during different AV delays seems to be not the most appropriate. Gold et al. correctly discussed the limitation of this technique and mentioned in their methods the need to minimize the effects of hemodynamic drift, the cumulative effects of pacing and fluid infusion for cardiac output determinations on the results, but all these problems continued to persist even when the order of pacing was varied. In fact, by study design they required that cardiac output at each AV delay should be evaluated in triplicate at least or more if drift in baseline occured, which could expose a very sick heart to consistent liquid overloading in a crucial recovery phase after the implantation. In addition, because 10 to 15 min of steady state before and after any measurement was required, this implies an acute study duration of at least 1 h. In our experience, a subtle spontaneous drift with continuous undulations of the baseline (sometimes considerably large) occurs as a result of intrinsic autonomic tone variability the hemodynamic consequences of which are further dramatically influenced by long duration of the study period and liquid infusion. Furthermore, the large interindividual variability, as recently demonstrated by Nishimura et al. (4), implies that analysis of cumulative data (e.g., cardiac output or left ventricular ejection fraction) rather than individual data could be considerably misleading. Finally, many recent data indicate that the use of a single AV delay is not appropriate and that it is necessary to tailor the AV delay and pacing site to maximize the benefit of pacing in each patient (5).

In conclusion, we as "believers" in pacing as additional therapy for congestive heart failure, at least in a subset of patients, accept the conclusion of Leinbach (6) to not close the door to "everyone," and we welcome prospective studies to identify subsets of patients who can potentially benefit from such a cheap and widely available therapy as pacing.

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Reply

Our study (1) was designed to test the hypothesis that dual-chamber pacing with a short atrioventricular (AV) delay improves acute hemodynamic variables and causes sustained clinical benefit in patients with advanced chronic congestive heart failure. As such, to our knowledge this was the first prospective, double-blind, randomized study of pacing in this patient population. The motivation for our study was the previously described anecdotal and uncontrolled reports of the favor-

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