Letter Regarding Article by Adamson et al, “Continuous Autonomic Assessment in Patients With Symptomatic Heart Failure: Prognostic Value of Heart Rate Variability Measured by an Implanted Cardiac Resynchronization Device”

To the Editor:

We read the article by Adamson et al with great interest. In a prospective manner, they have convincingly shown that (1) a measure of long-term heart rate variability (HRV), SDAAM, is a predictor of mortality and hospitalization in patients with congestive heart failure and (2) reductions in SDAAM precede clinical deterioration. Although we do not question the prognostic value of this measure, SDAAM is not simply a marker of the autonomic nervous system.

The closest conventional HRV measure to SDAAM (the standard deviation of a 5-minute atrial-atrial sensed interval) is SDANN (the standard deviation of a 5-minute mean normal RR interval). The spectral correlate of SDANN is the standard deviation of a 5-minute median atrial-atrial sensed clinical deterioration. Although we do not question the prognostic value of this measure, SDAAM is not simply a marker of the autonomic nervous system.

We have shown that SDANN and ULF are heavily influenced by ranges of physical activity. The poor prognosis observed with low SDANN may reflect a reduction in activity resulting from clinical deterioration. We have conducted 2 separate protocols to test this hypothesis. Both in patients with heart failure and in healthy control subjects, we showed that SDANN significantly increased from periods of enforced rest to those of scripted activity.

Equally compellingly, we demonstrated that SDANN and ULF could be generated equally by dual-chamber pacing driven completely by either sinus node activity or a mechanical activity sensor. Both of these studies indicate the major role of activity in inducing long-range measures of HRV. Therefore, an alternative conclusion, and perhaps a more cautious one, may be that measures of HRV that are heavily influenced by the range of physical activity of the patient are important prognostic markers. Indeed, the authors’ reported relationship between a decline in physical activity of the patient are important prognostic markers.

These minor caveats aside, we agree with the most important conclusion, and perhaps a more cautious one, may be that differences in activity certainly contribute to measures of large-scale heart rate variability. Therefore, an alternative conclusion, and perhaps a more cautious one, may be that measures of HRV that are heavily influenced by the range of physical activity of the patient are important prognostic markers. Indeed, the authors’ reported relationship between a decline in physical activity of the patient are important prognostic markers.

These minor caveats aside, we agree with the most important finding of Adamson et al: SDAAM is a prognostic marker in patients with congestive heart failure.

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Response

We sincerely appreciate the comments by Raj and colleagues concerning the role of activity in producing the ultralow- and very-low-frequency components of heart rate variability (HRV) spectral analysis. Unfortunately, it is difficult to speculate about the degree to which any component of short-term HRV correlates to the SDAAM measurement reported in our work. We agree that the effects of activity on cardiovascular function are primarily mediated through the autonomic nervous system, which should be reflected in long-term HRV. With this in mind, the SDAAM measurement certainly incorporated differences in activity; however, device-based activity measurements that use similar methods as reported by Raj and colleagues were less predictive than was SDAAM in our long-term follow-up with a large group of patients.

Device-based activity measurements had a maximum sensitivity of 50% corresponding to a 2.2 false positive per patient-year of follow-up when used to predict impending heart failure exacerbations as compared with SDAAM, which had a 70% sensitivity with 2.4 false positive rate per patient-year of follow-up. Patients in our study who had a heart failure hospitalization during follow-up were more likely to be NYHA class IV at the time of implantation and consistently had lower SDAAM measurements throughout follow-up, suggesting persistent sympathetic activation. It is not surprising, then, that this group of patients exhibited lower activity levels because their heart failure syndromes were much more symptomatic. It is possible that activity levels in these symptomatic patients were already at low levels, which made it difficult to detect a further decrease, thus influencing the predictive value of the measurement. We conclude, therefore, that differences in activity certainly contribute to SDAAM, but analysis of the A-A interval, in simple time-domain calculations, incorporates more information to detect alterations in cardiac autonomic control that precede decompensation in heart failure patients. The important addition of non-activity-based control system changes made the marker highly predictive and potentially clinically useful.

Disclosure

Alex Shih, who was a contributor to the original article, was unavailable to sign the Copyright Transfer Agreement and therefore does not appear as an author of this response.

Dr’s Abraham and Adamson have received research grants from, served on the speakers’ bureau of and/or received honoraria from, and consulted for and/or served on the advisory board of Medtronic Inc. Dr Smith has received a research grant from, has served on the speakers’ bureau of and/or received honoraria from, and has consulted for and/or served on an advisory board.
Karen Kleckner, Melissa Rhodes, and Dr Stadler are employed by Medtronic.

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