EDITORIAL COMMENT

Understanding the Impact of Abnormal Cardiac Activation on Cardiac Function*

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Poor exercise tolerance is both a symptom of left ventricular (LV) dysfunction and a predictor of reduced survival in patients with known cardiac dysfunction (1). Yet, poor exercise capacity in patients with reduced LV systolic function is not predicted by level of ejection fraction. Identification of other markers of reduced exercise capacity and, ultimately, reduced survival has been actively researched in recent years. Factors such as left bundle branch block (LBBB) (2) and underlying coronary artery disease (CAD) (3,4) have been shown to predict reduced survival among patients with congestive heart failure. Recently, reports suggest that indices measuring the isovolumic time in the cardiac cycle may contribute to the assessment of overall cardiac function (5,6). In this issue of the Journal, Duncan et al. (7) have demonstrated that total isovolumic time (t-IVT) at rest (defined as 60 – [total ejection time + total filling time], i.e. the time during the cardiac cycle when the ventricle is neither ejecting nor filling) is an independent predictor of exercise tolerance. These findings extend the observations from their previous report associating prolonged t-IVT with reduced cardiac output during dobutamine stress (6).

Because LBBB significantly affects isovolumic time and impairs stress induced decreases in t-IVT (6), these investigators sought to determine whether this index can independently predict functional capacity. Ultimately, a simple resting echo-Doppler measurement might be a practical way to estimate the severity of functional limitations in patients with dilated cardiomyopathy.

Duncan et al. (7) studied 111 patients with dilated cardiomyopathy (DCM), including patients with and without LBBB and CAD. The data were collected in patients with DCM undergoing clinically indicated cardiopulmonary exercise testing over a three-year period who had also undergone routine resting echocardiography within two months of the exercise testing. All had LV dysfunction with an ejection fraction <40%. Despite similar degrees of LV dysfunction and mitral insufficiency, patients with LBBB, CAD, or both had reduced peak exercise capacity (VO2\text{max}) compared with patients with LV dysfunction but no CAD or LBBB. The t-IVT, CAD, LBBB, the Tei index, and QRS duration were found to be univariate predictors of % predicted peak VO2 but in multivariate analysis, only t-IVT and CAD were independent predictors, with LBBB, QRS duration, and Tei index all subsumed by the impact of t-IVT. The t-IVT and CAD were combined to explain 57% of the total variance in percent predicted peak VO2 (7). These findings demonstrate that t-IVT, a relatively simple echo-Doppler measure, has independent predictive value in determining exercise capacity in addition to the presence of LBBB and CAD.

However, CAD also predicted reduced VO2\text{max} without alteration in t-IVT and without LBBB, thus supporting additional unmeasured explanations for reduction in exercise capacity with CAD. The notion that CAD prolongs t-IVT with exercise was not tested here, although stress testing with dobutamine has been shown to influence t-IVT (6).

Why does t-IVT predict poor exercise performance? Left bundle branch block markedly increases t-IVT in the cardiac cycle by producing abnormal activation and dispersion of the timing of local systole and diastole. The effective mechanical functioning of the ventricle is thereby altered by the disordered activation and can be measured by the t-IVT. Other studies have demonstrated that t-IVT is reduced after three months of atrio-biventricular pacing in patients with dilated cardiomyopathy (8).

This report highlights the pioneering work undertaken by these authors in investigating the timing of cardiac activation and clinical implications for LV dysfunction and exercise tolerance. They have effectively pursued the use of echo-Doppler methods as refined timing-measurement tools to elucidate mechanisms of ventricular dysfunction. This time-domain analysis of LV function using echo-Doppler measurements at rest predicts maximal exercise tolerance in patients with poor LV function. These results help explain why therapeutic approaches targeting systolic function (e.g., inotropic stimulation) may have limited value in some patients. Based on their body of work, including the present study, they recommend that measurement of t-IVT be incorporated into the standard echocardiographic assessment of patients with dilated cardiomyopathy.

How do new measurements, even simple ones, become integrated into standard examinations? The adoption of new clinical practices may be slow and is dependent on both evidence and opinion. The mere demonstration of an association of a new measure with a given clinical feature or outcome is not enough. The new measurements must have proven value for clinical decision-making. Demonstrating that a new measurement has value beyond an existing standard set of mea-
measurements requires convincing, such as evidence-supported documentation through peer-reviewed presentations and publications. Such promotion must also be repeated in a variety of forums to maximize audience awareness. In addition, new techniques should ideally be simple to perform and understand. The establishment of practice guidelines by independent, authoritarian organizations may provide endorsement but also will not guarantee widespread adoption. Eventually, practitioners must be convinced that the alterations to longstanding procedures are warranted.

In the case of t-IVT, prospective studies will be needed to verify these initial findings. The potential relevance of this measurement to the increasingly common decision to recommend biventricular pacing in patients with DCM and LBBB may be the most practical topic for the next round of research. Future studies of DCM and biventricular pacing should consider incorporating this measure when assessing the impact of therapies for DCM, particularly those with LBBB.

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REFERENCES