Predicting left ventricular dyssynchrony: Can nuclear cardiology bring us closer “In Sync”?

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Multiple imaging modalities including baseline electrocardiography and echocardiography have been investigated for independent prediction of left ventricular mechanical dyssynchrony (LVMD). This cardiac finding is extremely important given the impact that it has both on worsening of cardiac status as well as treatment focus. Cardiac resynchronization therapy (CRT) is a Class I indication for patients with advanced heart failure and the following criteria: severely depressed left ventricular ejection fraction ($\leq 35\%$), left bundle branch block (LBBB) with wide QRS duration on electrocardiogram (≥ 150 ms), and New York Heart Association (NYHA) class II, III, or IV symptoms.¹ Although improvement in functional status and quality of life is seen in many patients, it has been reported that up to 30% of patients who meet AHA/ACC guidelines for implantation of CRT fail to respond.^{2–5} However, what is missing from the patient profile above is confirmation of LVMD. It has been observed that patients demonstrating LVMD are more likely to respond favorably to CRT suggesting that perhaps more refined criteria may be needed to predict which subset of patients will benefit from CRT.^{6,7} It has also been demonstrated that LVMD may exist in patients with right bundle branch block (RBBB) who may not fulfill the typical criteria for CRT implantation, but who may nevertheless, benefit from resynchronization.^{8,9} Prior studies have shown that LVMD can be accurately evaluated by gated single-photon emission computed

tomography (SPECT) myocardial perfusion imaging (MPI).^{10,11} However, the exact pathogenesis of LVMD remains poorly understood.

In this issue of the *Journal of Nuclear Cardiology*, Sillanmäki and colleagues bring us further “in sync” with the potential mechanisms responsible for LVMD.¹² The study authors investigated the relative contribution of QRS duration on electrocardiogram, left ventricular ejection fraction (LVEF), end-systolic and end-diastolic volumes as well as the presence of scar on abnormal phase bandwidth (PhaseBW). The study was conducted as a retrospective analysis of SPECT MPI data of 358 total patients with conduction abnormalities including 275 LBBB and 83 RBBB patients from three international sites (US, Italy, and Finland). Hospital and gender-specific normal values were obtained from 172 controls. LVMD was observed in 85% of LBBB patients and 40% of RBBB patients (as defined as abnormal phase bandwidth (BW) or phase standard deviation (SD)). In the authors’ multivariable model, left ventricular ejection fraction was independently associated with LVMD and explained 63% of variance seen in PhaseBW; moreover, EF had the highest AUC for ROC curve analysis of the variable analyzed (0.918, CI 95% 0.892 to 0.946). Surprisingly, QRS duration was not independently associated with LVMD. Additionally, analysis of patients with LBBB and without significant myocardial scar (as defined as sum rest score ≤ 8 on SPECT MPI) showed that a worsening EF was associated with increasing LVMD. In contrast, further stratification of patients by QRS duration within EF groups appeared not to impact LVMD.

One of the strengths of this study is that it attempts to address the knowledge gap surrounding the relationship of QRS duration and EF in LVMD in both LBBB and RBBB patients. Traditionally, this electrocardiographic finding has been used to support use of CRT for treatment. These findings suggest that a deeper dive might be needed to identify the truly predictive independent features. Also, the importance of myocardial

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scar is clear with its impact on ventricular remodeling and resulting LVMD. The authors should be commended for the rigorous approaches used to standardize interpretations and analysis at the individual sites. One concern for generalized use is the need to develop lab-specific normals for phase analysis parameters and a question remains of how standardized this can become. In addition, future investigation would be beneficial into the effect that gender has on both patients with normal and abnormal PhaseBW and PhaseSD.

The most recent data from the American Heart Association report that an estimated 6.2 million Americans are currently being treated for varying levels of heart failure.¹³ The more that we can elucidate the mechanisms of the underlying pathophysiology, the greater our chances to develop novel treatment plans to bring us better “in sync” with improved clinical outcomes.

Disclosures

Neither of the authors have any disclosures to report relevant to this publication.

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