

Noninvasive Mapping of Electrical Dyssynchrony in Heart Failure and Cardiac Resynchronization Therapy



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KEYWORDS

• Electrocardiographic imaging • LBBB • Heart failure • CRT • LV activation mapping • RV pacing

KEY POINTS

- Causes for diverse effects of cardiac resynchronization therapy (CRT) are poorly understood.
- Because CRT is an electrical treatment of an electrical disorder, attention to the electrical substrate and its interaction with pacing may be important. In support, electrocardiogram (ECG) features (morphology and duration) affect CRT outcomes; however, the surface ECG reports rudimentary electrical data.
- Noninvasive electrocardiographic imaging provides high-resolution, single-beat ventricular mapping, which reveals significant heterogeneity of left ventricle (LV) activation in patients with heart failure with wide QRS duration (≥ 120 milliseconds), coupled to unpredictable LV activation in response to biventricular pacing. Complex electrophysiologic barriers sometimes impede wave front propagation, and are not always related to scar. Several of these complex electrical characteristics, not decipherable from the 12-lead ECG, are linked to CRT effect.
- CRT response may be improved by candidate selection and LV lead placement directed by electrical evaluation on an individual basis.

INTRODUCTION

Cardiac resynchronization therapy (CRT) improves survival in patients with heart failure showing prolonged QRS duration.¹ The rationale underlying this therapy is that a prolonged QRS duration indicates late left ventricle (LV) activation, leading to intra-LV (septal vs lateral wall) and inter-ventricular (LV vs right ventricle [RV]) dyssynchrony, to trigger adverse molecular remodeling and compromise mechanical function. Biventricular pacing is used to electrically resynchronize the

ventricles. However, the persistence of a ~30% incidence of nonresponse over a decade of CRT practice, despite many attempts to ameliorate this condition by using measures of mechanical assessment,² indicates that current selection methods and/or pacing techniques are imperfect.

Limitations of the Surface QRS from the 12-Lead Electrocardiogram

Although CRT is intended to improve mechanical function, it is essentially an electrical therapy

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directed toward an electrical disorder, with transduced hemodynamic effects. Thus, candidate selection still depends on the electrical measure of the QRS. This electrical measure has recently been refined. For instance, QRS duration is only a reflection on the body surface of the total duration of ventricular activation and not a reliable marker of LV activation. Logically, patients with only RV delay should not benefit, and this has been confirmed in recent trials. Patients with right bundle branch block (RBBB) did not benefit from CRT.³ In contrast, those candidates with left bundle branch block (LBBB) and wider QRS (eg, >150 milliseconds) have greater LV activation delay (eg, >95 milliseconds), and should derive greater benefit from CRT.^{4,5} This finding too was supported by trial data and incorporated into guidelines. Nevertheless, not all patients with LBBB and QRS greater than 150 milliseconds gain benefit, and uncertainty remains about CRT outcomes for patients with QRS duration between 120 and 150 milliseconds.⁶ Thus, current criteria, although showing the importance of electrical parameters, remain insufficient, which may reflect the limitations of the surface QRS.

Noninvasive Biventricular Electrical Mapping

More precise characterization of electrical substrate and also of responses to pacing may be fundamental to understanding CRT effect. This characterization is integral to candidate selection, deployment of pacing electrodes, and programming, but represents a line of inquiry that has been underexamined. It has been explored recently with a validated technique for detailed noninvasive electrical mapping of ventricular activation (electrocardiographic imaging [ECGI⁷]). This technique has shown that both substrate and its reaction to pacing are highly patient specific, and a one-size-fits-all strategy applied to any group of potential CRT candidates yields diverse responses.

Electrocardiographic Imaging Methodology

ECGI provides noninvasive high-resolution electrical mapping of cardiac excitation on the epicardial surface. ECGI images epicardial potentials, electrograms, isochrones (activation sequences), and repolarization patterns from body-surface electrocardiographic measurements. The system has been validated extensively both experimentally and in humans by comparison with direct epicardial mapping during open-heart surgery and with catheter mapping. Reconstruction accuracy superior to 10 mm was consistently obtained in humans. ECGI may therefore be used as a noninvasive

imaging modality for evaluation of human ventricle cardiac activation under differing conditions. The methodology has been detailed previously.^{7,8} ECGI acquires more than 200 channels of body-surface electrocardiograms (ECGs) using a multielectrode vest. Epicardial geometry and body-surface electrode positions are registered simultaneously by a thoracic computed tomography scan. The body-surface potential data and the geometry data are processed with algorithms developed to compute epicardial potentials over the entire epicardium, from which epicardial electrograms (typically 600 over the heart surface), isochrones, and repolarization patterns are constructed. All images are obtained during a single beat.

REDEFINING LEFT BUNDLE BRANCH BLOCK

QRS duration is tightly correlated with time to terminal LV activation in LBBB (but not in RBBB).⁴ This interval (qLV) sums 2 separate components: transeptal activation time and LV free wall activation time. Patients with LBBB by definition have delayed LV activation, conceived as a delay in transeptal transit of ventricular activation initiated by the right bundle branch (RBB; intact RBB conduction is responsible for rapid initial forces) (Fig. 1). Electrocardiographic mapping investigations of LBBB based on criteria used in the main CRT trials (QRS duration more than 120 milliseconds; RsR' in lead V₆ and rS/QS in V₁ or V₂) showed large variability in LV delay. Although RBB conduction and RV activation were well preserved, transeptal conduction could be rapid or delayed, and the following LV activation patterns were remarkably variable.^{9,10}

In contrast, when applying more strict ECG criteria to the definition of the LBBB (eg, broad notched or slurred R wave in leads I, aVL, V₅, and V₆; and R peak time >60 milliseconds in leads V₅ and V₆), detailed electrical mapping revealed a fairly homogeneous pattern of the ventricular activation (Fig. 2). This pattern was characterized by a unique RV breakthrough, presence of lines of conduction delay, a laterobasal latest activated area, and a consistent delay of more than 50 milliseconds between the mean activation time of the two ventricles. These features have been shown to be associated with an increased probability of response. ECGI may therefore help to refine the LBBB definition and thus the selection reliability for CRT.

Features of Left Ventricle Activation Influencing Candidate Selection

In one study, a U-shaped LV activation pattern (ie, forced by an anterior conduction barrier), which

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