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Noninvasive electrocardiographic imaging of cardiac resynchronization therapy in patients with heart failure

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Abstract

Cardiac resynchronization therapy (CRT) using biventricular (BiV) pacing has been developed to restore synchrony and improve cardiac performance in patients with heart failure. It has been clinically beneficial in 65% to 70% of patients. Being an electrical (pacing) approach, detailed electrical information during CRT is critical in understanding its mechanism and clinical outcome. However, electrical data from patients have been limited because of the requirement for invasive mapping. Electrocardiographic imaging provides the necessary tool to noninvasively obtain this information. We applied electrocardiographic imaging to 8 patients undergoing CRT during their native rhythm and various (single-ventricular and BiV) pacing modes with the following observations: (1) native rhythm activation was heterogeneous with latest activation in lateral left ventricular (LV) base (3 of 6 patients) or in anterolateral, midlateral, or inferior LV; (2) when accompanied by fusion, LV pacing was as effective as BiV; (3) right ventricular pacing was not effective for resynchronization; (4) efficacy of CRT depended strongly on patient-specific electrophysiologic substrate.

Introduction

In more than 30% of advanced heart failure cases, left ventricular (LV) activation is delayed.

¹ To restore synchrony of ventricular contraction, biventricular (BiV) pacing has been applied as a therapeutic approach termed cardiac resynchronization therapy (CRT). Cardiac resynchronization therapy improves patients' symptoms and echocardiographic measures and decreases mortality.² However, approximately 33% of patients do not respond to CRT.³ Being an electrical approach, CRT uses pacing and electrophysiologic principles to modify mechanical function. Therefore, failure to achieve resynchronization and improved cardiac performance could be due to abnormal electrical substrate in these patients. Understanding the electrophysiologic effects of CRT is essential in understanding the resynchronization mechanism and for optimizing its clinical application. Obtaining such information requires high-resolution electrical mapping of ventricular excitation. Until recently, this was not possible because of the invasive nature of cardiac mapping.

In this conference proceeding's article, I summarize the results of a recently published study of CRT in 8 patients with heart failure.⁴ In this study, a novel noninvasive imaging modality for cardiac electrophysiology (electrocardiographic imaging [ECGI]) developed in our laboratory was used to image cardiac excitation during various modes of CRT pacing. The results provided important insights into the myocardial electrical responses during CRT.

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Methods

Eight patients with heart failure (6 men and 2 women; age, 72 ± 11 years; New York Heart Association functional class III-IV) with LV conduction delay and implanted atrial BiV pacing device for CRT participated in the study. They were selected retrospectively at different times after device implantation. Responders to CRT were identified based on echocardiographic findings (improved LV ejection fraction and reduced LV internal dimensions at end-diastole and end-systole). Data were acquired during right ventricular (RV) pacing, LV pacing, native rhythm (NR), and BiV pacing. Details of the ECGI methodology were provided in previous publications.⁵⁻⁷ Briefly, body surface potentials are recorded from 220 to 250 sites around the entire torso surface. A thoracic computed tomography scan, obtained with the electrodes attached to the subject, provides epicardial-surface geometry and torso geometry (torso electrode positions) in the same frame. The body surface potentials and computed tomography images are combined and processed by a custom ECGI software package, CADIS, to reconstruct epicardial potentials, electrograms, and isochrones (activation sequences) on the heart surface during a single beat. In addition to examining the imaged activation sequences and spatial differences in activation times (indicative of the degree of synchrony), we computed a quantitative index of electrical synchrony, Esyn, as the mean activation time difference between lateral RV and LV free walls. Right ventricular preexcitation corresponds to negative Esyn and LV preexcitation to positive Esyn. Esyn equal to 0 indicates interventricular synchrony.

All protocols were approved by the Institutional Review Board at university hospitals of Cleveland, and informed consent was obtained from all patients.

Results

Native rhythm

Right ventricular activation patterns were consistent with those imaged in normal hearts, with epicardial activation spreading from RV breakthrough that occurred 29 ± 7 ms after onset of body surface QRS (somewhat delayed relative to that in normal young adults).⁸ The duration of entire RV activation after epicardial breakthrough was 25 ± 12 ms. Left ventricular activation patterns were consistent with left bundle branch block and displayed large interpatient variability. The mean delay of LV activation relative to RV activation was 90 ms (the delay is < 40 ms in normal hearts). Most patients had line(s)/region(s) of conduction block in anterior LV. This prevented the RV activation front from crossing directly to the LV. The activation front circumvented the block region via apical or inferior LV ("U-shaped" activation pattern⁹), with latest activation occurring most often at the lateral LV base.

Right ventricular pacing

Pacing electrodes were located in the low apical region, except in 2 patients who had a midseptal lead (all RV pacing sites were endocardial). Right ventricular activation during pacing was very different from NR. Duration of RV activation was much longer during pacing (51 ± 15 vs 25 ± 12 ms), probably because of limited participation of the conduction system during the paced beat. Left ventricular activation during RV pacing was similar to that of NR, with some differences in location/shape of lines of block on anterior LV. Overall, RV pacing failed to improve synchrony and was not effective for CRT.

Biventricular pacing

Activation patterns and electrical synchrony during BiV pacing were very heterogeneous among patients. Electrical activation of the lateral LV wall was advanced in all patients with lateral LV leads, improving electrical synchronization. In patients with anterior LV lead

placement, the electrical activation pattern during BiV pacing showed significant RV preexcitation, which was similar to that of NR. In these patients, electrical synchrony was not improved. The inefficacy of anterior LV pacing was due to regions of block and slow conduction in the anterolateral aspects that interfered with propagation from the anterior to the lateral wall and with lateral wall activation.

Left ventricular pacing and fusion beats

In 3 of 4 patients, LV pacing alone showed fusion between intrinsic ventricular excitation and the LV paced beat. The degree of fusion varied, depending on the relative length of the PR interval and the programmed atrial LV pacing delay. At longer atrial LV delay, intrinsic excitation coupled to the paced beat earlier, resulting in greater degree of fusion and improved synchrony. In fact, in these patients, LV pacing alone was as effective for electrical resynchronization as BiV pacing.

Discussion

Noninvasive ECGI was used to determine ventricular activation during NR and pacing in 8 patients undergoing CRT. The following observations were made: (1) activation patterns during NR were very heterogeneous among patients; (2) RV pacing alone was not effective for improving electrical synchronization in most patients; (3) LV pacing alone often improved electrical synchrony as much as BiV pacing, and this was achieved through fusion with intrinsic excitation; (4) anterior LV pacing was less effective than lateral pacing in improving synchronization because of anterior regions of block and slow conduction; (5) efficacy of LV pacing depended on lead placement relative to the electrophysiologic substrate (eg, lines and regions of inexcitability or conduction block). The ability of ECGI to image the electrophysiologic substrate noninvasively could be used to facilitate proper patient selection for CRT and to guide lead placement. The large heterogeneity of the substrate among patients may account for the highly variable clinical response to CRT. A substrate-dependent individualized lead placement, guided by ECGI, could greatly facilitate electrical resynchronization and improve clinical outcome.

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