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Variegated left ventricular electrical activation in response to a novel quadripolar electrode: Visualization by non-invasive electrocardiographic imaging☆

Niraj Varma, MA, DM, FRCP*

Cardiac Electrophysiology, Cleveland Clinic, Cleveland, OH, USA

Abstract Improving response to cardiac resynchronization therapy (CRT) remains challenging. Appropriate candidates may be identified by the presence of left ventricular (LV) conduction delay. An additional determinant may be the electrical effect elicited by LV pacing, which may vary among and within individuals. However, this is little explored, reflecting the lack of means for both easily altering lead position in any individual patient and of rapidly assessing its electrical effects. However, the advent of both multipolar LV electrodes and non-invasive single-beat electroanatomic mapping potentially resolves these challenges. These were investigated here. Results confirmed wide variations in electrical responses to LV pacing. In any individual patient, different pacing configurations elicited different electrical effects. Conversely, any one stimulation vector produced different effects in different patients. Thus, the reaction of electrical substrate to LV pacing is inconsistent. This observation introduces an added level of complexity in the understanding CRT electrical action. Attention to this factor may influence response to electrical resynchronization therapy.

Keywords: Electrocardiographic imaging; Left ventricular pacing; Heart failure; CRT; Quadripolar lead

Introduction

Cardiac resynchronization therapy (CRT) with atriobiventricular pacing in heart failure patients with left bundle branch block (LBBB) imparts survival benefit [1]. However, the lack of response in a significant proportion remains a vexing problem despite a decade of investigation [2]. Interest has moved from using mechanical measures for candidate selection to electrical parameters. This is intuitive since CRT is an electrical therapy for an electrical disorder. Thus, baseline electrical disturbances (ie, QRS morphology and duration) are now recognized to be significant determinants of ultimate CRT effect [3–5]. Logically, the reaction of this electrical substrate to pacing should also be important. Therapy may be ineffective in some because the intended pacing effect, to achieve resynchronization, is not reached. Any variability may contribute to heterogeneity in clinical response. In support, differences in paced QRS configurations correlated with future outcome in some reports [6–9]. However, the 12-lead ECG has modest predictive value. Electroanatomic mapping offers further insight. A preliminary series showed that identical CRT pacing configurations elicited differing electrical effects among different individuals [10]. Understanding this phenomenon demands detailed attention to the constituent components of CRT, ie, paced responses to RV pacing (described previously [11]) and to LV pacing. Variations in LV responses to LV pacing were difficult to explain since underlying electrical activation during intrinsic conduction itself differed among studied patients. Hence it was unclear whether these heterogeneities among paced effects were caused by underlying pathology and/or whether they could be affected by different positions of the LV pacing electrode in any individual patient. A notable discovery was that wavefront propagation could be modulated not only by infarcted territory but also by non-scar-related ("functional") mechanisms. These factors are important to consider because response to CRT may potentially be enhanced, with accompanying survival advantage [12,13], if electrical effect can be optimized.

Recently, multipolar left ventricular (LV) electrodes have been developed to overcome some technical challenges encountered during implantation, e.g. phrenic nerve stimulation and high capture threshold [14]. However, these also offer the potential opportunity to change the electrical action of CRT in any individual patient, LV pathology

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* Cardiac Electrophysiology, Cleveland Clinic, Cleveland, OH 44195, USA.

E-mail address: varman@ccf.org

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Table 1
Patient characteristics.

	Case 1	Case 2	Case 3
Age (years)/Gender	55/Female	39/Male	68/Female
Pathology	Non-ischemic cardiomyopathy	Ischemic cardiomyopathy	Non-ischemic cardiomyopathy
NYHA functional class	III	II	III
QRS configuration and duration	LBBB; 154 ms	RBBB; 144 ms	LBBB; 140 ms
Pathology	Idiopathic	Myocardial infarction; coronary artery bypass grafting; recurrent ventricular tachycardia (135 bpm)	Remote radiotherapy and chemotherapy for left breast carcinoma
Antiarrhythmic drugs	–	Amiodarone	Digoxin
Heart failure drugs	Beta-blocker; ACE inhibitor, nitrates; hydralazine	ACE inhibitor, beta-blocker	Beta-blocker; angiotensin receptor blockade, spironolactone
LV function			
Ejection fraction (LVEF)	15%–20 %	20%–25%	20%–25%
End-diastolic dimension (cm)	5.2	5.8	5.3
End-systolic dimension (cm)	4.3	4.8	4.5
LV lead position	Inferolateral	Posterolateral	Posterolateral
Interval between LV lead implant and ECGI imaging	25 months	6 days	18 weeks

permitting. This was tested here with detailed electrical characterization with non-invasive single-beat electrocardiographic imaging (ECGI).

Methods

Three patients receiving multipolar LV electrodes were studied post-CRT implant during sinus rhythm and pacing with ECGI. Their demographics are presented in Table 1. All patients granted their written approval to participate in the study, which was approved by the institutional ethics committee. CRT devices had been implanted according to standard indications, ie, NYHA functional class III or IV, QRS duration ≥ 120 ms during intrinsic conduction, left ventricular (LV) ejection fraction $\leq 35\%$ persisting during optimal medical therapy. Conventional bipolar right atrial and right ventricular apical (RV) electrodes were implanted. The LV lead (St Jude Medical 1458q) was a quadripolar electrode [3 ring electrodes at 20 (M2), 30 (M3) and 47 (P4) mm from tip electrode (D1)], deployed to available basal lateral LV positions [14]. The final position was determined by coronary venous anatomy, stability and an acceptable pacing threshold(s) without phrenic nerve capture. The system offers 10 possible pacing configurations when including the RV electrode in the paced vector. To assess their isolated effects on LV electrical activation, all vectors were imaged during LV pacing at short atrio-ventricular delay in sinus rhythm, ie, to prevent confounding fusion effects from concomitant RV stimulation during biventricular pacing or intrinsic right bundle branch conduction with extended atrio-ventricular intervals [15]. Different vectors were programmed during one sitting in each patient. Following each programming change, pacing was continued for 30 seconds. A single beat was reconstructed by ECGI from the end of each pacing train.

Imaging

Electrocardiographic imaging (ECGI, CardioInsight Technologies, Cleveland, Ohio) provides noninvasive high-resolution electrical mapping of epicardial cardiac excitation [16]. Methodology has been detailed previously [17,18]. Briefly, over 200 channels of body surface electrocardiograms are acquired using a multi-electrode 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 >1500 over the heart surface), isochrones, and repolarization patterns are constructed. Ventricular activation times are calculated from the onset of the QRS to the maximal negative slope of each unipolar electrogram. An epicardial breakthrough site was defined as the earliest location identified on the isochrone map. All images are obtained during a single beat. The velocity of LV activation was measured by LV total activation time (LVTAT), defined as the duration (ms) from the earliest to latest site of LV activation.

Results

Overall data are presented in Table 2. Notably, LVTATs during intrinsic conduction were all <50 ms,

Table 2
Left ventricular total activation times (LVTAT, ms) during intrinsic conduction contrasted to differing LV pacing configurations in three separate patients.

	Case 1	Case 2	Case 3
Intrinsic conduction	48	47	47
D1–M2	73	87	64
D1–P4	63	66	62
D1–RV coil	57	98	64
M2–P4	72	84	67
M2–RV coil	84	79	82
M3–M2	72	77	75
M3–P4	64	80	74
M3–RV coil	67	61	56
P4–M2	77	96	–
P4–RV coil	59	84	–

–: no LV capture in response to stimulation.