Detailed analysis of ventricular activation sequences during right ventricular apical pacing and left bundle branch block and the potential implications for cardiac resynchronization therapy

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BACKGROUND Left bundle branch block (LBBB) leads to prolonged left ventricular (LV) total activation time (TAT) and ventricular electrical uncoupling (VEU; mean LV activation time minus mean right ventricular [RV] activation time); both have been shown to be preferential targets for cardiac resynchronization therapy (CRT). Whether right ventricular apical pacing (RVAP) produces similar ventricular activation patterns has not been well studied.

OBJECTIVE The purpose of this study was to compare electrical ventricular activation patterns during RVAP and LBBB.

METHODS We performed ECG mapping during sinus rhythm, RVAP, and CRT in 24 patients with LBBB.

RESULTS We observed differences in the electrical activation pattern with RVAP compared to LBBB. During LBBB, RV activation occurred rapidly; in contrast, RV activation was prolonged during RVAP (46 ± 21 ms vs 69 ± 17 ms, $P < .001$). There was no significant difference in LVTAT; however, differences in conduction pattern were observed. During LBBB, LV activation was circumferential, whereas with RVAP, LV activation proceeded from apex to base. Differences in the number, size, and orientation of lines of slow conduction also were observed. With LBBB, VEU was nearly twice as long as during RVAP (73 ± 12 ms vs 38 ± 21 ms, $P < .001$). CRT resulted in a greater reduction in VEU relative to LBBB activation ($P < .001$).

CONCLUSION RVAP produces significant differences in ventricular activation characteristics compared to LBBB. Significantly less VEU occurs with RVAP, and as a result CRT produces a smaller relative reduction in VEU. This may explain the finding that CRT appears to be more effective in patients with LBBB than in those who were upgraded because of high percentages of RV pacing.

KEY WORDS Cardiac resynchronization therapy; Electrocardiography; Electrical dyssynchrony; Ventricular mapping; Left bundle branch block

ABBREVIATIONS **BVP** = biventricular pacing; **CRT** = cardiac resynchronization therapy; **HF (REF)** = heart Failure (with reduced ejection fraction); **LBBB** = left bundle branch block; **LV** = left ventricle; **LVTAT** = left ventricular total activation time; **NYHA** = New York Heart Association; **RV** = right ventricle; **RVAP** = right ventricular apical pacing; **RVTAT** = right ventricular total activation time; **TAT** = total activation time; **VEU** = ventricular electrical uncoupling

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Introduction

Several randomized control trials have found cardiac resynchronization therapy (CRT) to be beneficial in heart failure patients with reduced left ventricular (LV) ejection fraction and prolonged QRS duration.[1–6] Subanalysis of data from these trials suggests that patients with left bundle branch block (LBBB) are most likely to benefit.[7,8]

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We previously found that interventricular dyssynchrony, measured by epicardial noninvasive ECG mapping, may be even better at predicting clinical CRT response than QRS duration or the presence of LBBB.[9]

Right ventricular apical pacing (RVAP), like intrinsic activation with LBBB, is expected to result in delayed LV activation. Therefore, patients who receive a high percentage of RVAP and have impaired LV function have been proposed as a group of patients who may also stand to gain from BVP. However, the results of small nonrandomized studies that have assessed this strategy have been contradictory.[10,11] In the RAFT study, a minority of the included patients were previously chronically paced in the RV, and subanalysis suggested that this group did not obtain benefit from the addition of an LV lead.[12] No physiopathologic mechanism has been proposed to explain this absence of benefit. Indeed, no detailed activation mapping has been previously performed to compare the respective electrical activation sequences during LBBB and RVAP.

The first aim of the present study was to systematically describe and compare qualitative and quantitative characteristics of ventricular electrical activation during LBBB and RVAP. In order to eliminate anatomic substrate as a variable, within-patient comparisons were made. The second aim of the study was to determine the impact of BVP on these activation characteristics.

Methods

Execution of the study conformed to the principles outlined in the Declaration of Helsinki on research in human subjects. All patients granted written approval to participate in the study, which was approved by the local institutional ethics committee.

Patient population

The study population consisted of 24 patients with LBBB who were scheduled for CRT-device implantation based on the following criteria: New York Heart Association (NYHA) functional class II or III despite optimal medical therapy, LV ejection fraction ≤35% during intrinsic rhythm, and typical LBBB activation on 12-lead ECG to the most recent AHA/ACCF/HRS criteria.[13]

Mean patient age was 70 ± 9 years, 18 (75%) were male, 6 (25%) had an ischemic cardiomyopathy (defined as a history of myocardial infarction or prior revascularization), 7 (29%) patients were in NYHA class II, and 17 (71%) were in NYHA class III. Mean LV echocardiographic ejection fraction was 26.5% ± 5%, and mean baseline QRS duration measured from the 12-lead surface ECG was 162 ± 13 ms.

The 24 patients were implanted with a CRT-defibrillator via a percutaneous transvenous approach. The RV lead was systematically positioned at the RV apex. The final LV lead position depended on coronary venous anatomy, lead stability, pacing threshold, and the need to avoid phrenic nerve stimulation. Within 72 hours of device implantation, all patients had undergone ECG mapping.

Noninvasive mapping of electrical activation

Ventricular epicardial activation maps were acquired using a noninvasive, high-resolution ECG mapping system (ECVUE, CardioInsight Technologies Inc, Cleveland, OH) during intrinsic rhythm (LBBB), RVAP, and biventricular pacing (BVP) in VDD or DDD mode. During ventricular pacing, the sensed/paced AV delay was programmed to the longest delay that resulted in complete ventricular capture. Twelve-lead ECG was used to determine the onset of ventricular fusion, which was defined as any changes in the width or morphology of the QRS.

As previously described in detail, body surface potentials were recorded from 252 sites around the entire surface of the torso.[14] A thoracic computed tomography scan was acquired with the electrodes attached to the patient. The body surface potentials and computed tomography images then were combined and processed to reconstruct 1500 epicardial unipolar electrograms. The different local ventricular activation times were calculated from the onset of the QRS or the pacing spike to the maximal negative slope of each unipolar electrogram. An epicardial breakthrough site was defined as the earliest location identified on the isochrones map. A line of slow conduction was recorded if the onset of activation of adjacent points differed by ≥50 ms (Figure 1). The following electrical dyssynchrony indexes were derived from intrinsic (LBBB) and paced (RVAP and BVP) activation maps using a point-by-point method: right ventricular total activation time (RVTAT), defined as the difference between the latest and earliest (in milliseconds) sites of RV activation; left ventricular total activation time (LVTAT), defined as the difference between the latest and earliest sites of LV activation; and ventricular electrical uncoupling (VEU), defined as the difference (in milliseconds) between mean LV and RV activation times.

Statistical analysis

Categorical variables are given as absolute numbers (percentages), and continuous variable are expressed as mean (SD) or median (minimum–maximum). McNemar test was used to compare the LV latest activated area and the number and length of lines of slow conduction between RVAP and LBBB. The dyssynchrony parameters (TAT, RVTAT, LVTAT, and VEU) were compared among the different electrical activation patterns (LBBB, RVAP, BVP) using repeated measures analysis of variance. Bonferroni correction was used for post hoc comparisons. Statistical analyses were performed using SPSS software (version 18.0, SPSS Inc, Chicago, IL). Statistical significance was assumed at $P < .05$.

Results

RV electrical activation

We observed similarities but also major differences in terms of RV electrical activation during LBBB and RVAP. In both situations, there was only 1 RV breakthrough. During LBBB, we observed a single anterior (n = 17 [71%]) or