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Left ventricular electrical activation during right ventricular pacing in heart failure patients with LBBB: Visualization by electrocardiographic imaging and implications for cardiac resynchronization therapy

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Abstract

Objective: Assess effect of right ventricular pacing (RVP) on left ventricular (LV) activation in heart failure patients with left bundle branch block (LBBB).

Background: LV activation during RVP is regarded as similar to LBBB; hence novel CRT algorithms may avoid RVP by adopting "fusion" pacing with intrinsic RBB-mediated conduction. However, other CRT techniques demand RV paced wavefronts for optimal resynchronization. Appropriate selection may require attention to interaction between RVP-generated wavefronts with preexisting conduction abnormalities posed by LBBB i.e. transseptal delay and LV activation. We hypothesized that LV activation during RVP would differ to LBBB.

Methods: Eleven patients (59 ± 19 years, 8 male, LV ejection fraction 25 ± 10%; ischemic etiology 45%) were studied 5.4 ± 5 months after CRT implant. All had intact AV conduction with LBBB (PR interval 204 ± 55; QRS 167 ± 27 ms) prior to CRT. None had mid-septal/outflow tract lead positions. Using non-invasive electrocardiographic imaging (ECGI), LV activation was contrasted in each patient between intrinsic conduction and RVP with minimized AV interval (i.e. committing ventricular excitation to the paced wavefront).

Results: RVP affected LV activation variably. Transseptal time decreased in 64% of patients. More LV conduction barriers were created than resolved, slowing LV free wall activation from 67 ± 29 ms during intrinsic conduction to 104 ± 24 ms with RVP ($p = 0.025$). The load of late-activated LV myocardium increased in 73% but decreased in 27% patients. Changes were not reflected by QRS duration.

Ultimate action of RVP in any patient depended on summary effects of transseptal breakthrough and following LV activation. If both were enhanced then LV preexcitation occurred. If one was delayed but other accelerated, then the outcome of their balance determined the ultimate effect on LV depolarization.

Conclusions: RVP may aggravate or resolve LBBB-induced conduction problems at one or more levels. Its avoidance vs integration (or timing relative to LV pacing) during CRT depends on its electrical action in any particular individual.

Keywords: Ventricle; Electrocardiographic imaging; LBBB; Heart failure; Right ventricular pacing; CRT

Introduction

The contribution of the right ventricular pacing (RVP) component of biventricular pacing to LV activation during cardiac resynchronization therapy (CRT) is little investigated. This is because ventricular activation during RVP is widely regarded as similar to left bundle branch block (LBBB). Since appropriate CRT candidates already have LBBB, RVP may be redundant. This perception has led to development of device-based algorithms which avoid RVP during biventricular stimulation, or to abandoning RV electrode placement altogether [1,2]. Under these conditions, CRT delivery depends on LV pacing combined with intact RBB conduction i.e. "fusion pacing" (CRT-LV). In direct contrast, modeled ventricular activation *necessitated* contribution from an RV paced wavefront, to meet the LV paced wavefront in the mid-LV (CRT-BiV), to ensure resynchronization [3]. These opposite viewpoints demand elucidation. This requires firstly attention to the interaction of RV paced wavefronts generated by RVP with preexisting conduction

Abbreviations: CRT, cardiac resynchronization therapy; LV, left ventricle; RV, right ventricle; RVP, right ventricular pacing; RBB, right bundle branch; LBBB, left bundle branch block; ECGI, electrocardiographic imaging; RVP, right ventricular pacing

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abnormalities posed by LBBB, before adding the effect of LV pacing (itself unpredictable [4]). Fundamentally, LBBB is conceived to be a state of delayed LV activation resulting from transseptal delay. LV depolarization depends on transseptal conduction initiated by RBB-mediated conduction. LV free wall activation itself may be influenced by variable conduction barriers since "LBBB" represents an inhomogeneous set of conditions [5,6]. The effects of LV pacing on this electrical substrate are complex [4]. Those of RVP are unknown, yet presumed to be constant. Previously, echocardiographic studies have suggested dissimilarities in LV mechanical activation between intrinsic LBBB and RVP, but electrical actions have not been elucidated [7].

Here, we hypothesized that effects of RVP on transseptal conduction and LV activation vary, and differ to RBB-mediated depolarization. We tested this in CRT patients with LBBB.

Methods

CRT patients providing written informed consent for this IRB approved study protocol were studied. All were NYHA Class III patients with underlying LBBB on optimized medical therapy on no antiarrhythmic therapy. LBBB was defined as QRS > 120 ms, rS with rapid initial forces in V1 and V2, and evidence of left ventricular activation delay. Interventricular electrical dyssynchrony (Esyn) was assessed by the difference between mean activation times of mid-left and right ventricular free walls during simultaneous biventricular mapping. A negative Esyn value, indicating relative LV activation delay was present in all patients in the presence of normal RV activation during intrinsic conduction (findings reported previously [8]) i.e. normal RBB conduction was responsible for both right and left ventricular depolarization. Intrinsic conduction was compared to RVP using non-invasive ventricular mapping with ECGI methodology e.g. Fig. 1 [8,9].

LV activation (referenced to onset of QRS/pacing stimulus) was contrasted in each patient between intrinsic conduction and RVP with shortened AV interval (i.e. committing ventricular excitation to the paced wavefront). Thus, patients could act as their own control and ventricular activation could be directly compared. LV transseptal time (interval between QRS onset and initiation of LV depolarization) and LV activation duration (onset to end of free wall depolarization) were measured. Terminally depolarized regions were identified. To compare conduction velocity in the posterolateral LV during either RVP or LBBB, the area of myocardium activated in the terminal 30 ms (approximately 3 isochrones) was estimated from the posterior ECGI projection. This single view visualizes most of the LV free wall, and the 30 ms threshold represents ~50% of normal LV activation time [9]. The burden of late-activated myocardium during RVP relative to LBBB was directly contrasted by the following method. In each individual, the time point demarcating the terminal 30 ms of LV activation during intrinsic conduction was identified. The number of LV segments [10] activated beyond this threshold was estimated in the posterior ECGI projection (a maximum of 5 complete segments may be visualized in this view). Then, during RVP, the number of segments activated beyond this same threshold time point was estimated and compared to LBBB.

LV voltage assessment was performed. Prior work has shown that areas of low voltage, which usually represent scar, in some cases may change in response to ventricular pacing [5,11]. To assess whether similar functional barriers contributed to LBBB patterns, we contrasted the distribution of low LV voltage territories between intrinsic conduction and RVP. ECGI reconstructs epicardial voltages assuming a homogeneous torso without taking into account the conductivities of tissues surrounding the heart. This facilitates practical application of ECGI in patients without compromising accurate reconstruction of voltage patterns (e.g. low voltage regions). While absolute voltage values may not be preserved, relative magnitudes (ratios of potential amplitudes in different regions) are reconstructed under the homogeneous torso approximation. This methodology permitted accurate evaluation of individual changes in epicardial voltage occurring during pacing relative to intrinsic conduction [12,13].

Statistics

Data are reported as mean ± SD. Groups were compared by using unpaired two-tailed *t* tests for independent samples

Fig. 1. Activation (top panels) and voltage (bottom) maps during intrinsic conduction contrasted side-by-side to RVP in 2 views, in 3 different patients. **A. During intrinsic conduction** (LBBB, CRT off, QRS duration 140 ms), anterior and posterolateral LV activation is rapid (posteroanterior (PA) view — arrow across widely spaced isochrones) despite extensive distribution of low voltage zones (red) in these regions (below panels). **RVP** (*) slows conduction across the posterolateral LV wall (2 sets of crowded isochrones marked by short arrows, PA view), coinciding with extension of low voltage zones. Terminal activation occurs in the basal posterolateral LV, similarly to intrinsic conduction, but delayed (180 ms), and QRS prolonged (190 ms). During LBBB, 50% of the LV was activated after 100 ms from QRS onset, but this extended to 80% during RVP (extension from 2 to 4 segments, blue isochronal areas) indicating increased burden of late-activated myocardium, extending to mid-ventricular segments. **B**. **Intrinsic conduction**. An anterior conduction barrier (thick black line, lateral view) coincides with diminished voltage (below panels). LV activation is "U shaped". Terminal activation occurs anteriorly 175 ms post-QRS onset (posterior view, dark blue isochronal area). **RVP** disintegrates the mid-segment of anterior conduction barrier (with resumption of normal voltage here (below)) but reinforces an inferolateral zone of slow conduction (thick black line, posterior view) with development of low voltage. Once posterolateral LV wall activation begins, it proceeds rapidly. Terminal activation occurs 175 ms post-QRS onset (dark blue isochronal area) but extends across an approximately threefold larger area of the posterior LV compared to LBBB (4 vs 2 segments). Approximately 25% of the posterior wall is activated after 145 ms in LBBB contrasting with almost 90% during RVP. (Despite this large increase in load of late-activated myocardium, QRS duration increased only marginally (RVP vs LBBB = 190 vs 180 ms)). **C**. **Intrinsic conduction**. Rapid even spread of activation across the LV followed by terminal activation in a small anterobasal area within 140 ms of QRS onset. **RVP** (*) elicits irregular zones of slow conduction anteriorly (isochronal crowding), delaying LV free wall activation (ending 165 ms post-QRS onset). QRS duration increases from 140 to 170 ms. Terminal activation (dark blue isochronal area) extends across a fourfold larger posterior LV area compared to intrinsic conduction (from 1 to 3 segments) involving mid-ventricular segments. Virtually normal LV epicardial voltage (blue) during intrinsic conduction contrasts with RVP when lower voltage electrograms develop anteriorly, coinciding with new conduction barriers.

and effects of pacing interventions were compared in individuals within each group by paired sample analysis (SPSS software, version 13, SPSS Inc., Chicago, IL). A value of $p < 0.05$ was considered significant.

Results

Eleven patients (59 ± 19 years, 8 male, LV ejection fraction 25 ± 10%; ischemic etiology in 45%) were studied 5.4 ± 5 months after CRT implant (Table 1). All had intact AV conduction with LBBB (PR interval 204 ± 55; QRS 167 ± 27 ms). None had mid-septal/outflow tract RV lead positions, confirmed during CT imaging.

Intrinsic conduction

Ventricular activation occurred firstly in the right ventricle (34 ± 13 ms post-QRS onset), reflecting RBB-mediated depolarization (Fig. 1) [8]. First LV activation (i.e.

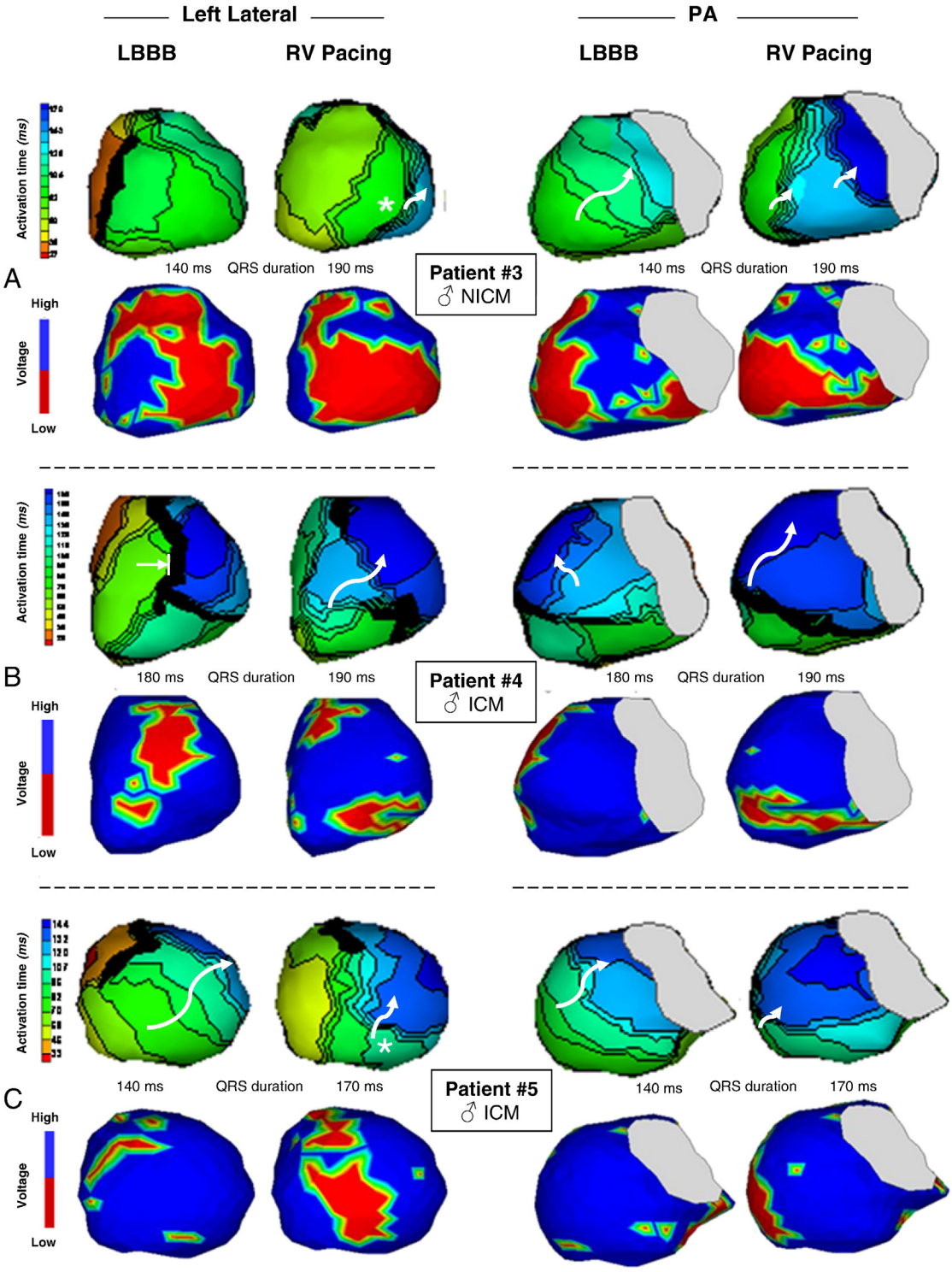

Table 1
Patient data.

Pt #	Age (years)	Sex	Path	Scar	LVEF %	QRS duration (ms)		Left ventricular								E Syn (ms)
								Transseptal conduction (ms)		LV activation duration (LVAD, ms)		%LV activated during terminal LV activation		LV segments activated during terminal LV activation		
						LBBB	*RVP*	LBBB	*RVP*	LBBB	*RVP*	LBBB	*RVP*	LBBB	*RVP*	LBBB
1	75	M	ICM	IP AS	25	160	*200*	44	*86*	108	*99*	15	*75*	1	*4*	−50
2	72	F	ICM	IP	35	180	*150*	112	*62*	61	*84*	90	*90*	4	*1*	−93
3	45	M	NICM	–	15	140	*190*	71	*82*	55	*127*	50	*20*	2	*4*	−71
4	72	M	ICM	AS	40	180	*190*	116	*76*	70	*110*	25	*80*	2	*5*	−113
5	72	M	ICM	IP	20	140	*170*	68	*70*	66	*74*	35	*75*	1	*3*	−73
6	53	M	ICM	Global	10	194	*200*	90	*90*	60	*92*	80	*70*	2	*4*	−88
7	50	M	NICM	–	20	138	*225*	81	*40*	45	*155*	80	*80*	4	*5*	−35
8	54	M	NICM	–	35	130	*140*	54	*41*	44	*103*	85	*85*	4	*5*	−45
9	19	M	NICM	–	15	180	*190*	110	*95*	32	*99*	85	*75*	4	*4*	−81
10	74	F	NICM	–	20	186	*210*	135	*17*	65	*120*	75	*90*	4	*0*	−122
11	76	F	NICM	–	25	174	*200*	26	*20*	134	*75*	80	*35*	4	*0*	−115
Mean	**60.2**				**23.6**	**163.8**	**187.5**	**82.5**	**61.7**	**67.3**	**103.5**[a]	**63.6**	**70.5**	**2.91**	**3.18**	**−80.5**
SD	**17.9**				**9.5**	**22.9**	**25.1**	**33.8**	**30.0**	**29.4**	**24.0**	**27.2**	**22.4**	**1.3**	**1.94**	**29.3**

M: male; F: female; Path: pathology; ICM: ischemic cardiomyopathy; NICM: non-ischemic cardiomyopathy; scar: distribution of scar/akinesis; IP: inferoposterior; AS: anteroseptal; LVEF: left ventricular ejection fraction; LBBB: left bundle branch block; RVP; right ventricular pacing. (Note Pt #5 had >50% RVP burden prior to CRT upgrade); LVAD: onset to end of left ventricular free wall activation; terminal LV activation refers to the last 30 ms of LV activation; Esyn: Interventricular electrical dyssynchrony.

[a] $p < 0.03$ compared to LBBB.

transseptal breakthrough) occurred later (83 ± 34 ms post-QRS onset). Subsequent LV free wall activation was relatively rapid (LV activation duration 67 ± 29 ms) but pattern heterogenous, as previously described [11]. Propagation could progress rapidly across the anterior and lateral walls (Fig. 1C; Patient #8 Fig. 2) or be shaped by areas of conduction slowing or block e.g. U-shaped around an anterior line of block (Fig. 1B), or its reverse (Patient #2, Fig. 2). Terminal LV activation was always basal (involving posterolateral LV segments in 9/11 (82%) cases and anterior in 2/11 (18%) (Fig. 1B)). The area of LV myocardium depolarized in the last 30 ms of activation in each individual was confined to just 1 segment in only 2/11 (18%) cases (e.g. Fig. 1C), but extended beyond a single LV segment to involve mid-ventricular (non-basal) segments in 9/11 (82%) cases (mean 2.9 ± 1.3 segments). Estimated area was 64 ± 27%, but ranged from 15% in patient #1, indicating slow terminal activation, to 90% in patient #2 (Fig. 2) illustrating rapid free wall propagation. Hence, the burden of LV myocardium subject to late activation varied widely. Notably, propagation could occur rapidly in the presence of low voltage regions (Fig. 1A). The overall delay in LV activation relative to RV activation [8] resulted in interventricular dyssynchrony (Esyn: −81 ± 29 ms) (Table 1).

Right ventricular pacing

RVP reshaped LV activation patterns compared to RBB-mediated conduction, with marked inter-individual heterogeneity (Fig. 3). Overall, transseptal conduction decreased from 83 ± 34 to 62 ± 30 ms ($p = 0.13$). However, LV septal breakthrough was variably affected. Thus, onset of LV free wall activation *decreased* in 7/11 (64%) cases (Table 1) (Fig. 3). LV free wall activation usually slowed: onset to end of LV depolarization increased from 67 ± 29 ms during intrinsic conduction to 104 ± 24 ms with RVP ($p = 0.025$). The interval between QRS onset and end of LV free wall activation (sum of transseptal activation time and ventricular activation duration) did not change significantly (149.7 ± 29 to 165.2 ± 34.2 ms with RVP ($p = 0.33$)). However, these summary data concealed significant inter-individual variations since slowing occurred in most but acceleration in a minority (3/11 cases; e.g. patient #2 Figs. 2, 4). Thus, the overall action of RVP in any individual was represented by the combined effects of transseptal breakthrough and the following LV activation. If both were enhanced then LV preexcitation occurred. If one was delayed and the other component accelerated, then the outcome of their balance determined the ultimate effect on LV depolarization (e.g. Patient #8 Fig. 2).

RVP altered LV activation patterns. LV conduction barriers could be dissolved or created, or both, in any single individual. For example, RVP disintegrated an anterior line of block present during RBB-mediated conduction but consolidated an inferolateral conduction barrier in patient #4 (Fig. 1B). Low electrogram voltage marked these lines of block (in comparison to Fig. 1A). Across the studied population, a total of only 4 extensive lines of block involving the LV were observed during intrinsic conduction compared to 12 during RVP i.e. pacing dramatically increased the propensity to develop ventricular conduction barriers. Terminal LV activation still occurred basally during RVP, but areas affected were different compared to LBBB (Fig. 1). Interestingly, conduction velocity in the basal LV region *per se* was slowed by RVP in

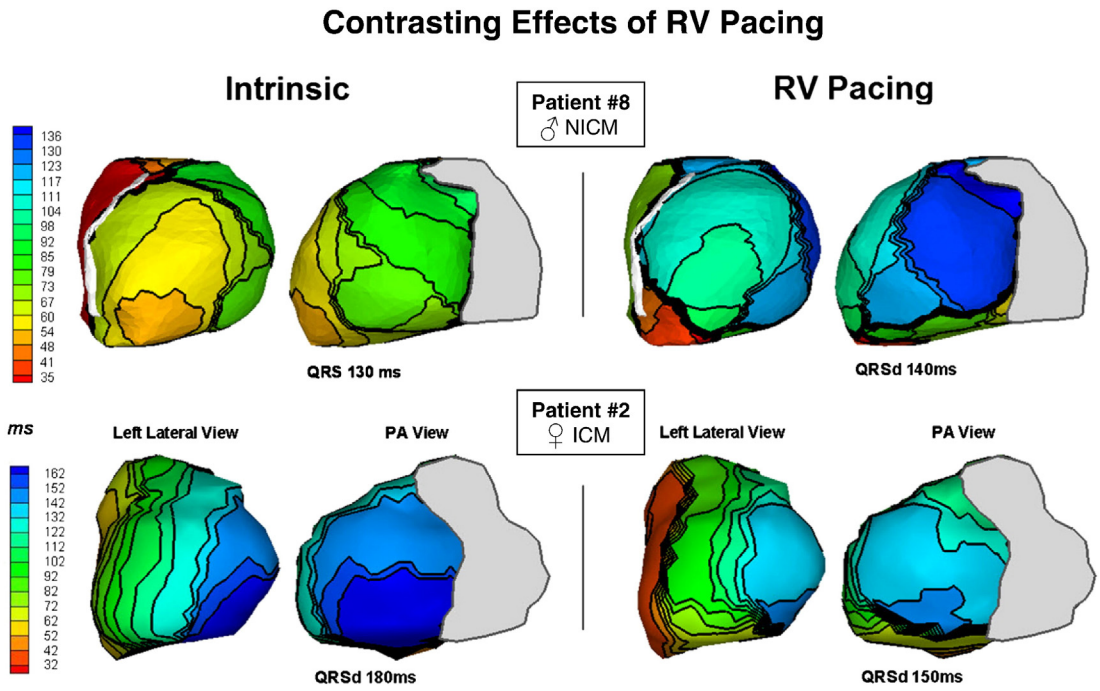

Fig. 2. Contrasting LV effects of RV pacing in 2 separate patients.**Top**. During intrinsic conduction (left panels), LV epicardial breakthrough occurs 48 ms after QRS onset and then proceeds rapidly (widely spaced isochrones) across the anterolateral wall. During RVP, although LV epicardial breakthrough is earlier (red isochrones (40 ms)), subsequent propagation is impeded by development of conduction barriers from the anterobasal LV extending laterally. LV activation duration increased. Notably, a large proportion of posterolateral LV myocardium (dark blue isochronal >123 ms) is activated late. QRS duration changes marginally (130 to 140 ms) despite significant RVP-induced LV delays.In contrast, **below**, RVP facilitates LV depolarization. During intrinsic activation (left panels), the wavefront propagates anterolaterally then inferiorly ("reverse U" shape), producing terminal LV depolarization inferolaterally at 175 ms. 60% of the LV free wall is activated within 145 ms. RVP promotes earlier transseptal breakthrough (red ischochronal area) followed by rapid free wall propagation. LV depolarization completes within 150 ms of QRS onset (i.e. QRS duration shortens from 180 to 150 ms) with rapid posterolateral free wall activation (90% area depolarization within 145 ms). The area of late-activated myocardium observed during intrinsic conduction (area enclosing dark blue isochrones >152 ms) is eliminated. Note that RVP accelerated transseptal activation in both cases but ensuing LV activation differed.

only 4/11 cases (e.g. Figs. 1A, 2 top). The burden of late-activated LV myocardium was increased overall by RVP. Areas of terminally activated myocardium extended into the mid-ventricular regions in 8/11 cases (Figs. 1, 2). These increases were not consistently reflected by QRS duration (Figs. 1B, 2 top). When directly compared, the number of segments affected in the area specified by the isochrone marking the last 30 ms of intrinsic conduction was 2.91 ± 1.3 during LBBB contrasting with 3.18 ± 1.94 segments (range 1–5) activated beyond the same time point during RVP. Again, individual differences were significant. Pacing usually increased this number (7/11) (64%). However, in 3/11 cases (27%), LV activation was preexcited and load of late activated myocardium was reduced (Fig. 2 patient #2; Fig. 4 patient #10). It was unchanged by pacing in only 1/11 case (9%).

Discussion

This is the first study to examine electrical responses to RV endocardial pacing, specifically of septal and LV conduction barriers posed by LBBB, and their interaction. The results contradict the notion that RVP is equivalent to intrinsic conduction in CRT patients with LBBB. RVP exerts electrical actions at any one or more of multiple levels of LV activation, and may resolve or create conduction barriers at both the level of transseptal and also free wall propagation, compared to intrinsic RBB-mediated conduction. Inter-individual variations are significant. These observations have implications for choice of pacing therapies.

CRT aims to resolve late LV activation during LBBB, conventionally by biventricular (i.e. CRT-BiV: RV and LV) pacing. Results are likely governed both by substrate and effect of pacing. In support, patient selection according to presence and pattern of late LV activation inferred from the surface QRS strengthens their probability of CRT response [14]. There is, however, little corresponding work on reaction of electrical substrate to pacing, logically an important ingredient to outcome. CRT may not elicit a uniform electrical response since paced ECGs among individuals differ. Moreover, these differences carry prognostic value [15–17]. More detailed descriptions of cardiac electrical activation during biventricular pacing are few but indicate that inter-individual differences influence hemodynamics and outcomes [11,18–20]. Characterization of constituent elements of CRT, i.e. RBB, RV and LV paced wavefronts, may aid understanding of diverse clinical responses to CRT and guide possible solutions. Recently, it has become appreciated that a surface ECG pattern of LBBB in heart failure patients conceals variable septal and LV activation patterns [5,11], and effects of LV pacing on this electrical substrate are unpredictable [4]. In this light, it is unlikely that those of RVP will be constant. This hypothesis was confirmed here.

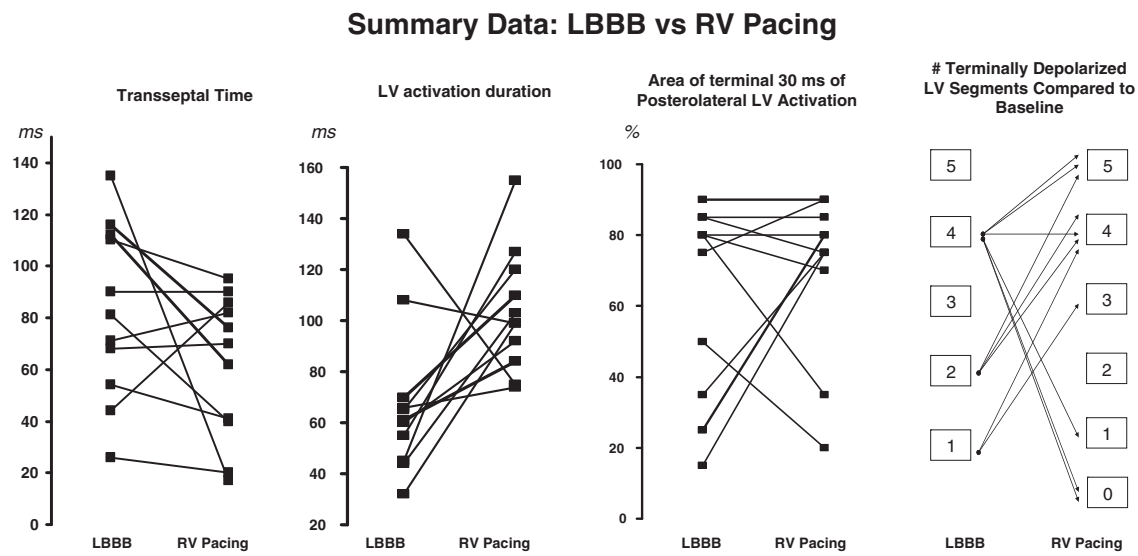

Fig. 3. Summary of group data.**Transseptal time** tended to decrease (7/11 patients); **LV activation duration** increased in most (8/11); **LV area terminally activated** (in final 30 ms) was decreased by RVP in 4/11 patients i.e. posterolateral free wall activation slowed; **LV segments activated terminally** increased during RVP (indicating increased load) but reduced in 3/11 patients, when compared directly to LBBB.

Effects of RVP in CRT recipients with LBBB were heterogenous, with potential implications for CRT prescription. Those resolving existing conduction barriers at transseptal and/or LV free wall level(s) and enabling LV preexcitation (i.e. ameliorating the electrical problems caused by LBBB) are potentially desirable, facilitating mid-cavity collision with an LV paced wavefront (CRT-BiV) [3]. However, opposite effects to aggravate transseptal delay and/or decelerate LV activation suggest RVP should be withheld during CRT, to favor intrinsic RBB-mediated conduction to fuse with LV paced wavefronts (CRT-LV). Pacing algorithms avoiding RVP (or avoiding RV lead implantation) may be beneficial in this condition [1,2]. Intermediate effects e.g. transseptal acceleration followed by LV delay (Fig. 2 top) may merit setting interventricular timing during CRT-BiV to capture only the favorable action of RVP on initial LV activation [21]. These observations have potential implications for LV lead position. For example, when RVP changes LV activation compared to intrinsic conduction via native RBB conduction, it could be that the area of latest LV activation changes to such extent that a standard or even previously tailored LV epicardial pacing lead would be in the wrong position.

Thus current results argue against simply excluding or including an RVP component during CRT in any particular patient while electrically blind. This may explain why studies comparing CRT-LV to CRT-BiV between populations have been inconclusive [1,22,23]. Selecting either one or the other for all patients tested is likely to cause mixed effects, yielding an overall neutral result. An individualized prescription may be preferable. This hypothesis is indirectly supported by results from one crossover trial demonstrating an advantage of CRT-LV in some patients vs CRT-BiV in others [22], and from a randomized study indicating superior outcomes with CRT programmed to achieve optimize electrical resynchronization [21]. Conversely, inattention to this factor may be deleterious e.g. when acute electrical results during CRT-BiV indicated major conduction barriers limiting wavefront propagation, this presaged chronic CRT failure [24]. The mechanism(s) underlying differences between RVP and RBB-mediated conduction, and implicitly impermanent ("functional") conduction barriers, are speculative. Functional properties (previously shown with LV epicardial pacing) may be determined by interaction of geometry and direction of propagation in diseased tissue [25]. This phenomenon is likely responsible for changes in distribution of low voltage areas (indicating that these do not necessarily equate with scar), also noted during endocardial mapping [5]. This property needs to be considered in addition to the known ability for scar to modulate propagation [26].

Strengths and limitations

Epicardial mapping as used here generally provides more complete ventricular activation data, avoiding the significant losses encountered during endocardial mapping and attributed to "unmappable" intramural delays [5]. However, in our study, in several patients QRS duration remained longer than the sum of the transseptal activation time and the LV activation duration. The explanation for this discrepancy is uncertain and may be due to such intramural delays or from terminal activation occurring in regions not mapped here e.g. outflow tracts. Transseptal activation time may be underestimated since LV depolarization probably starts endocardially. Areas of LV myocardium were estimated without accounting for natural curvature. Examination was performed at variable time intervals after implantation and a remodeling effect that influenced the results cannot be excluded. This was a short series (precluding most statistical comparisons) but sufficient to demonstrate that RVP can change LV activation unpredictably, at a variety of levels, and in different directions. The prevalence of these effects need to ascertained in a larger study population. RVP effects

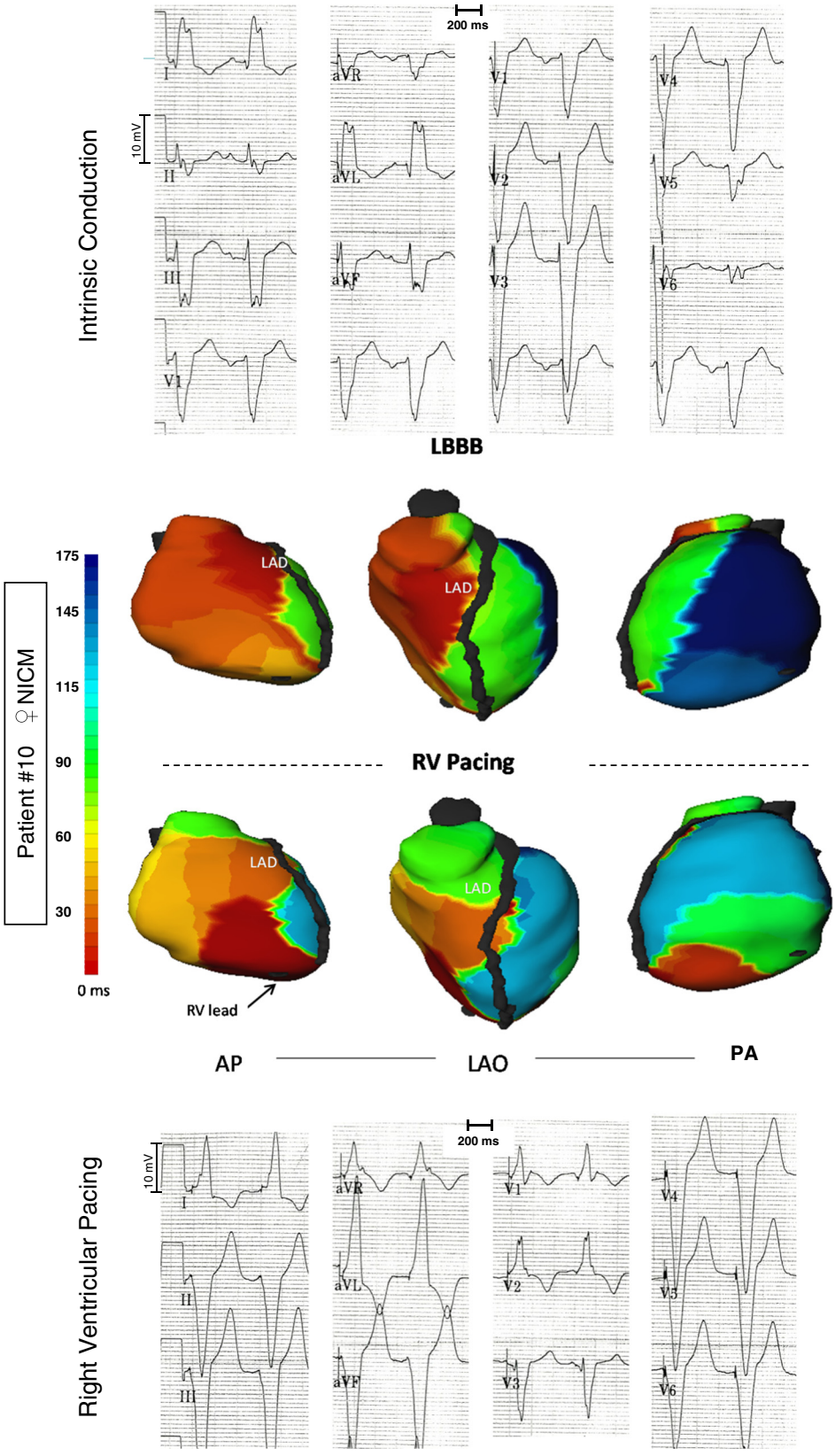

Fig. 4. Patient #10. ECGs and activation maps (LAD marked in black). **Intrinsic conduction**. ECG (25 mm/s; standard calibration) shows LBBB. Rapid rS inscriptions in V1 and V2 indicate normal RBB conduction. ECGI map (top) depicts a large posterolateral LV wall region exhibiting delayed terminal activation (dark blue isochronal region). **RVP** (bottom) promotes rapid inferoapical LV breakthrough (red isochronal area, LAO), followed by swift (wide isochronal spread) propagation across the posterolateral LV, completed in 120 ms (light blue isochronal area). The late-activated area (dark blue) observed during intrinsic conduction is completely eliminated. LV depolarization proceeds from apex to base, i.e. a normal vector. Therefore, LV depolarization, delayed by LBBB, is preexcited by RVP with development of an R wave in V1.

were studied in isolation so that these could be compared directly with RBB-mediated conduction in each individual. Therefore, interaction with LVP wavefronts during CRT was not studied here. Translated mechanical effects of differing patterns of propagation were not evaluated, but the electrical responses described likely underlie differences in LV mechanical activation between intrinsic LBBB and RVP noted on echocardiography [7]. Lines of block and areas of conduction delay in the LV free wall correlate with hemodynamic depression [19].

Our data may explain why RVP alone in patients with LBBB and LV dysfunction increases mortality, without altering surface ECG morphology, since RVP usually introduced LV conduction barriers, prolonged free wall activation, and exaggerated the load of late activated myocardium, i.e. factors associated with depressed LV function [27,28]. The current results cannot be extended to patients with normal conduction or RBBB. However, some of the observations shown here may underlie the small but real incidence of heart failure occurring in patients with normal LV function and heart block on chronic exposure to RVP. In support, a wider RV paced QRS complex (a cruder indicator of significant LV activation delay [29]) correlated with reduced contractility, and chronically, with development of LV dysfunction and heart failure hospitalizations, indicating the importance of induced electrical disturbance [30–32]. Exploration of RVP induced electrical dysfunction with ECGI may identify patients susceptible to its deleterious effects. This is important since the right ventricle remains the commonest site for permanent endocardial pacing. Effects of non-apical RV pacing sites (RV mid-septum and RVOT) were not studied here. Whether these alternative positions yield similar heterogeneity to that observed here remains to be determined. All studied patients had LBBB during intrinsic conduction. Recently, refinements to ECG diagnostic criteria for LBBB, accounting for gender, have been proposed [33]. Reconciling these indirect determinations of LV activation delay with direct biventricular mapping results (e.g. Esyn used here) requires further evaluation. The limited series in the current ECGI study precludes analysis by heart failure etiology or gender, both of which affect CRT [34].

Conclusion

RVP effect in CRT candidates is not monolithic i.e. does not produce a singular LV activation pattern among different patients. RVP may aggravate or resolve baseline conduction problems created by LBBB at one or more levels. Hence, avoidance vs integration (or timing relative to LV pacing) of RVP during CRT merits individualized prescription according to its electrical action. The hypothesis that this approach may aid resynchronization and enhance CRT response requires prospective evaluation.

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