Initial Ventricular Activation in Left-sided Intraventricular Conduction Defects

DAVID S. CANNOM, M.D., MILFORD G. WYMAN, M.D., AND BRUCE N. GOLDFREYER, M.D.

SUMMARY Nine patients with ECG evidence of rate-related left bundle branch block (LBBB) were studied using His bundle electrograms, electrogams from the right ventricular (RV) apex and vectorcardiograms recorded as heart rate was increased to produce LBBB. In five patients, when LBBB occurred, initially normal septal activation reversed and the HV intervals increased 10–30 msec, while the H-RVA interval did not change (group 1). Four patients had initially normal QRS duration (90–100 msec) but reversed septal activation (group 2). When LBBB developed there was no shift in either the HV interval or H-RVA interval. Only the QRS complex itself widened to distinguish these patients from group 1. These studies defined ventricular septal activation in normal conduction and in complete LBBB (group 1) and incomplete LBBB (group 2). The conduction patterns of group 1 and 2 patients are similar but are both markedly different from normal.

USING INTRACARDIAC MAPPING techniques, a prospective study of patients with rate-dependent left bundle branch block (LBBB) clarified our understanding of ventricular septal activation patterns in LBBB. Such patients make a unique group, with each patient providing both normal control conduction and reproducible left-sided conduction defects. Precise definition of controls and altered septal activation was possible for each patient by merely altering ventricular rate.

We found that combining invasive and noninvasive techniques allowed ready comparison of three discrete subsets: (1) normal intracardiac conduction, (2) complete LBBB, and (3) an intermediate form, reproducibly identified as an incomplete form of LBBB. This study identifies markers for each type of left-sided conduction abnormality and is confined to describing their differing modes of initial septal activation.

Materials and Methods

Nine consecutive patients with apparent rate-dependent LBBB were studied over a 4-year period to assess the altered electrophysiology of the left-sided intraventricular conduction defects. In each case the investigational nature of the study was explained and informed consent obtained. No patient was taking cardiovascular medication at the time of study. Their clinical status is summarized in table 1.

A similar protocol was followed during the study of each patient. Surface electrocardiographic leads X, Y, and Z were recorded. A quadripolar catheter positioned high in the right atrium via an arm vein was used for recording an atrial electrogram and for pacing. Two catheters were inserted via separate introducers into the right femoral vein. One bipolar catheter was positioned on the atrial side of the anulus fibrosis to record the His bundle electrogram. A second bipolar or quadripolar catheter was advanced to the right ventricular (RV) apex to record the precise onset of right ventricular activation (RVA). Signals were displayed on an Electronics for Medicine DR 12 Physiologic Recorder and the case was stored on magnetic tape using a Hewlett-Packard tape recorder. At the conclusion of the case, selected portions were photographed on paper at 100 and 200 mm/sec paper speed for data analysis or transferred to a storage oscilloscope set to display at rapid sweep rates and photographed so that intervals could be measured with an accuracy of ±1 msec.

During the study a vectorcardiogram (VCG) was obtained in each patient during normal and bundle branch block conduction using an ICR Vectorcardiographic Recorder.*

Each patient was paced from a baseline narrow QRS conduction and ventricular activation sequence by gradual increments in right atrial rate until abrupt widening of the QRS complex with a typical LBBB configuration was noted. Bundle branch block occurred over a narrow paced range of 100–115 beats/min. By protocol, the pacing sequence began at rates slightly higher than the sinus rate and was increased very slowly until LBBB was noted. Only this mode of inducing LBBB was accepted for inclusion. Single atrial premature depolarizations producing LBBB were not used, thus nullifying any effect of prior cycle length on the refractoriness of the distal ventricular specialized conduction system (VSCS). One patient was in atrial fibrillation at the time of study, with frequent episodes of spontaneously increasing rate and conduction, varying stepwise from normal to LBBB in a manner comparable to pacing. These data were therefore included in the study.

Further interventions were used if clinically indicated. Measurement of sinus node function was done in most patients using pacing and single atrial

*ICR Instant VCG, Instruments for Cardiac Research, Syracuse, New York (VCG-1B).

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premature depolarizations and atioventricular refractory curves were performed in most patients, particularly when consideration was being given to permanent pacing. No drug interventions were done as part of this protocol. No complications were encountered. In one patient, an RVA time was not obtained for technical reasons.

For data tabulation, the measurement of the QRS duration in milliseconds was made from the surface ECG. Measurement of ventricular activation was done by the method of Kastor and colleagues.2

### Results

Analysis of the data focused on the initial changes in septal activation that occurred when the surface ECG widened from a QRS complex of normal duration to LBBB configuration. Two groups emerged (tables 1 and 2).

#### Group 1 Patients: Normal Conduction to LBBB

Group 1 consisted of five patients with similar electrophysiologic properties as their QRS complex widened to LBBB configuration (fig. 1). Three basic changes occurred simultaneously as LBBB developed (table 1):

1. There was a lengthening of the HV* from high normal to a markedly prolonged value, with the smallest change 10 msec and the largest value 30 msec (mean 21 msec). Changes in one patient typical for the group during study are shown in figure 2.

2. Coincident with the increased HV interval, the V-RVA time was shortened.† For the group, the ventricular activation time shortened 10-30 msec (mean 23 msec) (fig. 2). In any patient (table 1) the lengthening of the HV time in msec was comparable to the shortening of the RVA time in msec by a similar, if not exact, value.

### Table 1. Clinical and Electrocardiographic Data

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Cardiovascular diagnosis</th>
<th>HV (msec)</th>
<th>V to RVA (msec)</th>
<th>H to RVA (msec)</th>
<th>QRS (msec)</th>
<th>Septal activation (VCG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DC</td>
<td>42</td>
<td>None</td>
<td>50-60</td>
<td>35-25</td>
<td>85-85</td>
<td>80-130</td>
<td>Shift</td>
</tr>
<tr>
<td>JF</td>
<td>61</td>
<td>CAD S/P SVBG</td>
<td>55-78</td>
<td>40-15</td>
<td>95-93</td>
<td>90-140</td>
<td>Shift</td>
</tr>
<tr>
<td>ER</td>
<td>66</td>
<td>Syncpe Pacemaker No clinical CAD</td>
<td>55-75</td>
<td>25-0</td>
<td>75-75</td>
<td>90-130</td>
<td>Shift</td>
</tr>
<tr>
<td>CL</td>
<td>76</td>
<td>CAD</td>
<td>60-90</td>
<td>30-0</td>
<td>90-90</td>
<td>90-160</td>
<td>Shift</td>
</tr>
<tr>
<td>JC</td>
<td>76</td>
<td>Cor pulmonale CAD</td>
<td>65-85</td>
<td>Not obtained</td>
<td>90-140</td>
<td>Shift</td>
<td></td>
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</table>

Group 2 (incomplete LBBB to LBBB)

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Cardiovascular diagnosis</th>
<th>HV (msec)</th>
<th>V to RVA (msec)</th>
<th>H to RVA (msec)</th>
<th>QRS (msec)</th>
<th>Septal activation (VCG)</th>
</tr>
</thead>
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<tr>
<td>NM</td>
<td>48</td>
<td>Recurrent SVT None</td>
<td>55-55</td>
<td>27-27</td>
<td>82-82</td>
<td>90-120</td>
<td>No change</td>
</tr>
<tr>
<td>SF</td>
<td>68</td>
<td>None</td>
<td>50-50</td>
<td>0-0</td>
<td>50-50</td>
<td>100-120</td>
<td>No change</td>
</tr>
<tr>
<td>EB</td>
<td>70</td>
<td>Hypertension CAD S/P SVBG</td>
<td>50-50</td>
<td>0-0</td>
<td>50-50</td>
<td>100-120</td>
<td>No change</td>
</tr>
<tr>
<td>EI</td>
<td>85</td>
<td>Atrial fibrillation Sinus node dysfunction Pacemaker</td>
<td>50-50</td>
<td>20-20</td>
<td>70-70</td>
<td>90-120</td>
<td>No change</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; S/P SVBG = status post-saphenous vein bypass surgery; SVT = supraventricular tachycardia; VCG = vectorcardiogram; LBBB = left bundle branch block.

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*HV interval was measured from the initial rapid deflection of the His spike to the earliest onset of ventricular activation as measured in surface leads X, Y or Z and/or the intracardiac ventricular electrogram.

†V-RVA interval was measured from the initial rapid deflection recorded from the RV apical catheter to the earliest onset of ventricular activation as determined in surface leads X, Y or Z and/or the intracardiac ventricular electrogram. The value is expressed as a positive number in msec.
In patients 3 and 5, who presented with syncope, it was possible to demonstrate distal VSCS block during the atrioventricular refractory curve. Both of these patients received pacemakers. Two other patients in this group demonstrated infranodal block during programmed premature stimulation, but neither was paced. No group 2 patient showed infranodal block.

**Group 2 Patients: Incomplete to Complete LBBB**

The data for group 2 patients differ from those for group 1. The results in this group were somewhat unexpected but uniform (table 2), (fig. 4). Again, three primary changes occurred as the QRS widened (table 1):

1. The HV time was at the upper limit of normal in the control phase of the study and did not change when complete LBBB occurred. Thus, each patient had the same HV time with his pattern of apparently normal conduction as he did with LBBB. The mean for group 2 HV intervals was 50 msec. Figure 5 demonstrates these changes with pacing in one patient.

2. When the patient developed LBBB, the RV activation time was measured. In each case the onset of RV apical activation was identical with respect to its timing within the total QRS when the baseline measurements were contrasted to those obtained during LBBB. This was in striking contrast to group 1 patients.

3. VCG analysis of initial ventricular activation when control and LBBB conduction were compared showed no change in the sequence or direction of septal activation. However, careful VCG analysis disclosed that in each case, despite the normal QRS duration, the septum was activated abnormally even at the initiation of the pacing sequence. Thus, the sequence of ventricular activation in this patient group was abnormal initially and remained abnormal and did not change when complete LBBB developed (fig. 6).

These observations, made retrospectively, defined a group of patients with normal QRS duration but abnormal septal activation in the baseline state, who developed typical complete LBBB at a critical paced rate. The feature distinguishing group 1 from group 2 patients was the absence of HV or V-RVA change in the latter when QRS widening occurred and the abnormal septal activation initially present in group 2 patients.

One patient is of particular interest because she displayed changes that qualify for inclusion in both groups, although her data were summarized in group 1. Three types of intraventricular conduction were noted during study in this patient (fig. 7).

**Discussion**

The sequence of ventricular activation initiated by the ventricular specialized conduction system has been actively investigated by basic electrophysiologists and clinical investigators.5-17 Initial work using canine and
FIGURE 2. The two QRS complexes show normal and left bundle branch block (LBBB) conduction. Displayed are surface leads X, Y and Z. Right ventricular activation (RVA) was recorded from the catheter at the right ventricular apex. The atrial electrogram is labeled A and His bundle electrogram is labeled H. A line of identity is drawn in each beat through the onset of ventricular activation. The time lines represent 100 msec. Patient has a control HV interval of 55 msec, which increases to 78 msec with LBBB. Initially, the V-RVA was 40 msec, with a narrow QRS complex, while with complete LBBB, V-RVA was 15 msec. As the HV interval increases by 23 msec with the onset of LBBB, the V-RVA time decreased by 25 msec. QRS duration increased from 90 to 140 msec as LBBB developed. The relatively long V-RVA time of 40 msec may be indirect evidence of some proximal RBBB delay during normal conduction.

<table>
<thead>
<tr>
<th>Table 2. Electrophysiologic Properties of Normal Conduction, Complete and Incomplete Left Bundle Branch Block</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS duration (msec)</td>
</tr>
<tr>
<td>Normal QRS &lt; 100</td>
</tr>
<tr>
<td>Complete LBBB 130-160</td>
</tr>
<tr>
<td>Incomplete LBBB 100-120</td>
</tr>
</tbody>
</table>

Abbreviations: VCG = vectorcardiogram; LBBB = left bundle branch block.
FIGURE 3. Vectorcardiograms (VCGs) for a group 1 patient are shown during normal conduction (labeled NI and in black) and left bundle branch block (LBBB), shown in red. The transverse plane is shown in the upper panel and the frontal plane in the lower. Each panel shows, to the far left, LBBB initial forces, magnified for clarity and shown in red. The VCG during normal QRS conduction is presented in the middle (black) and LBBB conduction to the right of both panels (red). In the transverse plane the normal loop is directed rightward and anteriorly (arrow) then leftward and posteriorly. The loop is open and shows no evidence of intraventricular conduction delay. During LBBB the initial forces are directed leftward and anteriorly, in contrast to normal conduction, which is rightward and anterior. The remaining part of the QRS loop in LBBB is directed posteriorly, with conduction delay occurring in the middle and terminal portions. In the frontal plane during normal activation, the loop is inscribed in a clockwise rotation, forming a figure of eight. No delay in conduction is noted. The initial forces are directed inferiorly and leftward during LBBB. The QRS loop now is oriented superiorly, with intraventricular conduction delay present again in the middle and terminal portions. Each pip represents 2 msec.
human hearts culminated in elegant studies conducted in 1970 by Durrer and his group in the isolated human heart. By simultaneously mapping a large number of intracardiac and epicardial electrograms, the sequence of ventricular activation was precisely determined in the normal human heart. The findings from canine studies were validated in humans, namely that ventricular excitation occurred first in the anterior, mid- and posterior or left paraseptal surfaces and spread in a left-to-right wave front in the middle third of the septum, proceeding somewhat anteriorly and apically. Epicardial excitation patterns reflected the intramural excitation wave fronts. RV endocardial activation began near the insertion of the anterior papillary muscles about 10 msec after the onset of the left ventricular cavity potentials. This period of research, then, set the definition for normal conduction.

Studies using standard 12-lead ECGs as well as His bundle electrocardiography in rate-dependent LBBB have been clinical and have not defined the altered initial septal electrophysiology of LBBB. Denes and colleagues in 1975 studied 10 patients with rate-dependent LBBB and showed that global conduction intervals (HV time) changed little as the QRS pattern changed, and suggested that this was the common finding in patients with rate-dependent LBBB. Their conclusions and those of most investigators have focused primarily on conduction intervals (HV times) and distal VSCS refractoriness, not initial septal events. Unless initial septal activity is considered, however, the significance of an isolated HV interval is unclear. If the patient has incomplete LBBB at the outset (our group 2 patients), one would not expect HV intervals to change with the development of complete LBBB.

In a provocative letter to the editor in 1973, Castellanos used the RV apical activation interval (which he called H-RVA) in analyzing septal conduction. When LBBB occurred in his patient via the introduction of an atrial premature beat, he showed an HV interval increase but H-RVA remained the same. He suggested that the increment in the HV interval was due to longer conduction time through the right bundle when septal activation was reversed and left-sided delay was encountered. The HV lengthened with LBBB, while the H-RVA time remained the same. Although he did not specifically comment on it, his figure 1 suggests that the V-RVA time actually shortened, as expected. A companion article illustrated the same concept.

In 1975 this single observation was pursued in studies by Kastor and colleagues, who applied intraventricular mapping techniques to patients with normal QRS and right bundle branch block (RBBB). By using surface ECG leads as well as catheters at the RV apex, left ventricular apex and RV outflow tract, they were able to map the sequence of ventricular activation in altered conduction. The range of normal values for RV apical activation time with normal QRS activation was $18 \pm 9$ msec in 38 patients. A significant prolongation of the RV apical activation time was found in patients with RBBB. This study, done in a systematic fashion with a large number of patients, confirmed the usefulness of using intracardiac mapping techniques and analyzing intracardiac conduction in RBBB.

Prior electrophysiologic studies in fixed LBBB have considered almost exclusively conduction intervals and refractory periods in their analysis of LBBB, just as in rate-dependent LBBB. This work however, has not closely analyzed abnormalities in initial septal activation in all forms of LBBB which, by necessity,
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Left-sided conduction defects/Cannom et al. 627

Figure 5. Ventricular activation is shown for a typical group 2 patient. The display is similar to that for figure 2. Four beats are shown, with a line of identity drawn through the onset of activation of beats 2 and 3. The QRS complex widens from 100 to 120 msec and left bundle branch block (LBBB) develops. The V-right ventricular activation (RVA) interval is zero in the narrow QRS complexes and during complete LBBB. The HV interval does not change. The time lines are 100 msec and the arrows in the atrial electrogram denote the pacing spike.

predicate what follows in terms of QRS duration, conduction intervals and VSCS refractory periods.

In the current study, we used electrode mapping techniques in a systematic fashion in a model that seemed ideal for contrasting normal and altered conduction — rate-dependent LBBB. We began by studying all patients who had apparent rate-dependent LBBB and realized with further experience that careful analysis of the septal activation data allowed separation of normal from complete LBBB and a more precise definition of incomplete LBBB than was possible by standard ECG.

Using these techniques, we found consistent changes in true, rate-dependent LBBB. Measurements made in the control, narrow QRS phase of the study were compared with values obtained when the ECG pattern abruptly shifted to LBBB. Such a shift was obtained by right atrial pacing in a stepwise fashion, increasing the rate so the preceding cycle length did not in any way influence the refractoriness of the distal VSCS. We found that three events occurred simultaneously as conduction changed from normal to LBBB: a directional change in septal activation from left to right (normal) to right to left (LBBB) as determined by VCG; an increase in the HV interval of 10–30 msec; and a simultaneous and almost identical decrease in the V-RVA as LBBB occurred.

The explanation for these parallel changes in the five patients who showed the phenomena (group 1) is the altered septal activation typical of complete LBBB. With the normal QRS complex (shorter than 100 msec) the septum is being activated left to right, with the RV apex activated relatively late in sequence via the right bundle branch. When the heart is paced to more rapid rates, changes occur in the relative refractoriness of the left-sided conduction pathways. At a rate reproducible for each patient, conduction abruptly changes and LBBB appears as the left side of the VSCS becomes refractory. Conduction proceeds down the right bundle branch, and because the right bundle branch is longer, more time is required before ventricular activation occurs (as long as 30 msec) and the HV time increases.42–44 When the reversal of septal activation occurs as LBBB develops, conduction time through the His bundle and RBBB is unchanged.

The right ventricle is activated at the same time as before LBBB was present in group 1 patients if the His bundle potential is considered as representing zero
time. Thus, the H-RVA interval does not change as LBBB occurs. The observation that the H-RVA does not change when LBBB occurs in group I also argues against any preexisting conduction delay in the RBB. If such proximal RBB delay were present, H-RVA would have increased when LBBB occurred. We propose, then, that during LBBB ventricular activation, or "V," represents the electrical activity of the right septal surface and that this is activated before the left septal surface. Therefore, during normal conduction "V" represents the electrical activity of the left surface, which is activated before the right septal surface.

Recent clinical work has emphasized the existence of incomplete LBBB as an ECG entity. Group 2 patients had abnormal septal activation by VCG at the initiation of the study despite their relatively narrow QRS duration. No changes occurred in either HV interval or in H-RVA time as the QRS widened and LBBB developed. The absolute intervals are not important; the absence of change in HV or RVA with the development of LBBB separates them from group I. In these patients, the RV apex is activated early, as whichever portion of the left-sided VSCS normally responsible for septal activation proceeding left to right is already refractory at the onset of pacing. This
would represent the electrophysiologic substrate for what has been called electrocardiographically incomplete LBBB. This study considered septal activation in complete LBBB only in the rate-dependent LBBB group. Findings within this group were consistent and reproducible for our patients, but further studies are necessary to finalize the group distinctions presented in table 2.

Only very preliminary data in the literature report the intracardiac methods used in this study. Wyndham did epicardial mapping in four patients with complete LBBB undergoing coronary bypass and found that the earliest area of epicardial breakthrough was in the right ventricle rather than in the left ventricle as in normals. He found that the left ventricle was activated transseptally. This limited experience with epicardial mapping confirms the observations in our patients with rate-dependent LBBB. A summary of the differences in septal activation for all three groups is shown in figure 8.

The current studies do not allow us to say whether the left-sided delay involves all or part of the left bundle or whether a discrete fascicle, called, for conceptual purposes, septal activating tissue, becomes refractory. The extraordinary morphologic complexity of the left bundle should have electrophysiologic correlates. Perhaps when rate-dependent LBBB occurs we are actually recording second-degree block of dis-
Intracardiac studies in left-sided conduction disturbances in these patients simplify our understanding of the altered initial septal events. Right-to-left septal activation on surface ECG with any QRS duration longer than 95 msec may define the initial abnormality present in all forms of LBBB, whether complete or incomplete on the ECG. The critical marker in distinguishing left-sided conduction defects from normal is not confined strictly to QRS duration, but rather demonstrating early RV apical activation and resultant right-to-left septal conduction.

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References


crete left-sided septal activating tissue. However, this is hypothetical. Patterns in the patient who showed normal, incomplete, and complete LBBB (fig. 7) suggest that gradations in LBBB are possible. Perhaps this depends on the refractoriness of the septal activating tissue (partial vs complete).

Figure 8. The three panels are a schematic of differing normal conduction, left bundle branch block (LBBB) and the incomplete form of LBBB conduction. A QRS complex, a His bundle electrogram (H) and a right ventricular (RV) apical electrogram (RVA) are shown. During normal conduction the HV time is normal and RV activation occurs 20 msec after the onset of the QRS complex. As complete LBBB develops, the QRS complex widens from 80 msec to 140 msec. There is delay in the onset of activation of the QRS complex by 20 msec. The right ventricular activation time and the onset of the QRS complex are synchronous, but the RV activation time has not changed in relation to normal conduction because it occurs via a normally conducting right bundle branch. However, because there is delay in the onset of ventricular activation, the HV interval lengthens to 60 msec. In the bottom panel in the incomplete form of LBBB, the onset of ventricular activation is again delayed by the 20 msec. Again, the HV time is prolonged because the onset of ventricular activation is delayed and the HV time is 60 msec. Ventricular activation time is unchanged and is zero and again synchronous with the onset of QRS activation. The only difference between complete LBBB as shown in the middle panel and the incomplete form of LBBB shown in the bottom panel is the duration of the QRS complex (140 msec vs 100 msec).


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