Functional Abnormalities in Isolated Left Bundle Branch Block

The Effect of Interventricular Asynchrony

Cindy L. Grines, MD, Thomas M. Bashore, MD, Harisios Boudoulas, MD,
Shari Olson, BS, Phillip Shafer, MD, and Charles F. Wooley, MD

Eighteen patients with isolated left bundle branch block (LBBB) were compared with 10 normal control subjects. Apexcardiograms, phonocardiograms, electrocardiograms, two-dimensional and dual M-mode echocardiograms, and radionuclide ventriculograms (RNV) were performed. There were no differences in the timing of right ventricular events between LBBB and normal subjects; however, striking delays in left ventricular systolic and diastolic events were apparent in the LBBB group. The delay was associated with shortening of left ventricular diastole and resultant increase in the ratio of right to left ventricular diastolic time in LBBB (1.2±0.08) compared with normal (1.0±0.06), p < 0.0001. First heart sound (S1) amplitude, expressed as the ratio S1/S2, was decreased in LBBB compared with normal (0.67±0.2 compared with 1.34±0.25, p < 0.01), in part due to wide separation of the valvular contributors to S1. The abnormal interventricular septal motion in LBBB corresponded to periods of asynchrony in contraction, ejection, end systole, and end diastole between right and left ventricles. Radionuclide ventriculograms revealed decreased regional ejection fraction of the septum in LBBB (40±16%) compared with 67±7% in normal subjects (p < 0.001), while the apical and lateral regional ejection fractions were similar in the two groups. This loss of septal contribution resulted in a reduction in global ejection fraction in LBBB compared to normals (54±7% compared with 62±5%, p < 0.005). The magnitude of systolic septal motion (echocardiography) and septal ejection fraction (RNV) were closely correlated to the ratio of right to left ventricular diastolic time (r = -0.86 and -0.85, respectively). Thus, isolated LBBB caused global ventricular abnormalities manifested by abnormalities in diastolic filling times, heart sounds, interventricular septal motion, and left ventricular ejection fraction. (Circulation 1989;79:845–853)

Ventricular hemodynamics in patients with left bundle branch block (LBBB) have been extensively evaluated. Previous investigators have studied a small number of LBBB patients and used different techniques such as phonocardiography and pulse tracings,1–4 echocardiography,5–7 radionuclide studies,8,9 or cardiac catheterization.10–14 Each method has intrinsic advantages and limitations; thus, variability in techniques alone may in part account for conflicting results. Furthermore, LBBB patient populations have not been well defined and the reported abnormalities may relate not only to the conduction delay but also underlying myocardial disease.

We hypothesized that abnormal ventricular activation itself may lead to interventricular asynchrony and global cardiac abnormalities. To test this hypothesis, we studied a well-defined population of patients with isolated LBBB in the absence of other cardiac disease. To overcome intrinsic limitations of each noninvasive technique, we used all of the available noninvasive methods to study each patient.

Methods

Patient Population

Through screening of admission electrocardiograms, 18 patients with LBBB in the absence of other cardiac disease were identified. LBBB was defined as QRS duration >0.12 seconds; notching or slurring of the QRS with an initial R wave in I, aV1, and the left precordial leads and with the peak

From the Division of Cardiology, Department of Internal Medicine, The Ohio State University, Columbus, Ohio.
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Address for reprints: Cindy L. Grines, MD, Division of Cardiology, MN670, University of Kentucky Medical Center, 800 Rose Street, Lexington, KY 40536-0084.
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of the R wave occurring relatively late in the QRS interval; and displacement of the ST segment, and usually the T wave, in a direction opposite that of the principal QRS deflection.

There was no evidence of mechanical heart disease (previous myocardial infarction, congenital, valvular or myocardial disease) by history, physical examination, echocardiography, or radionuclide ventriculography (RNV). Each subject had a normal left ventricular end-diastolic diameter (<5.8 cm), and all had normal left ventricular wall motion (excluding septum and apex) by both visual radionuclide evaluation and two-dimensional echocardiography. Patients were excluded if there was evidence for cardiac disease other than conduction system disease or if the requisite diagnostic studies were technically inadequate. The etiology of the LBBB was considered to be primary conduction disease in all patients. Ten healthy hospital employees with a normal history, physical examination, electrocardiogram, echocardiogram, and RNV served as a control group.

**Graphics**

After informed consent was obtained, patients and control subjects underwent a history and physical examination and a 12-lead electrocardiogram. Simultaneous electrocardiogram, phonocardiogram, and two-dimensional and dual M-mode echocardiograms were obtained with a Diasonics V-3400R phased-array echocardiogram with hard copy data stored on video cassette or 4333 alpha thermal printer or both. With the two-dimensional echocardiogram, care was taken to ensure proper orientation of the M-mode beam within the left ventricular cavity for recording of the septum and posterior wall motion, as well as the opening and closure of each valve relative to the beginning of the QRS complex.

Phonocardiography was obtained in the supine position with two external microphones appropriately placed for maximal recording of each heart sound, with simultaneous carotid and apex impulse tracings. Hard copy was recorded on paper at a speed of 100 mm/sec.

**Measurements**

Right and left ventricular events were obtained from simultaneous dual M-mode echocardiograms. Intervals were measured from the QRS onset to mitral and tricuspid valve closure, pulmonic and aortic valve opening, pulmonic and aortic valve closure, and mitral and tricuspid valve opening. Additional measurements included both the duration of the first heart sound (S₁) and the amplitude of S₁ compared with the second heart sound (S₂), measured from a microphone placed at the apex. To determine the onset of left ventricular contraction, the upstroke of the apex impulse and the onset of left ventricular posterior wall contraction (M-mode echocardiogram) were measured relative to the beginning of the QRS complex. Isovolumic contraction time was measured from the upstroke of the apex impulse to echocardiographic aortic valve opening; isovolumic relaxation time was measured from aortic valve closure to mitral valve opening. Left ventricular diastolic time intervals were measured from the echocardiogram as the time from mitral valve opening to closure and from the phonocardiogram as the cardiac cycle (RR interval) minus left ventricular systolic time (Q to the aortic component of S₂) as previously described in our laboratory. Right ventricular diastolic intervals were measured from the echocardiogram as the time from tricuspid valve opening to closure and from the phonocardiogram as the RR interval minus right ventricular systolic time (Q to the pulmonic component of S₂). To allow for differences in heart rate, diastolic intervals were expressed as a ratio of right/left ventricular diastolic time. When technically possible, dual M-mode echocardiograms were used to time right and left ventricular events simultaneously. Dual M-mode echocardiograms could not be obtained in 11 LBBB patients and three normal subjects and required independent calculation of right and left ventricular intervals from cardiac cycles that did not vary by more than 30 msec. Five to ten consecutive beats were averaged to allow for respiratory variation.

Interventricular septal motion was visualized by M-mode echocardiography and recorded at a paper speed of 50 or 100 mm/sec. The onset of each anterior or posterior deflection of the septum was measured from the left septal surface and timed relative to the beginning of the QRS. The magnitude of systolic septal motion was calculated by the distance between the left septal surface and the chest wall, a fixed reference point (Figure 1). Septal position during systole was measured during left ventricular ejection at the point of maximal excursion in either an anterior (considered paradoxical) or posterior direction. The early diastolic septal position was measured during the first one third of

![Figure 1.](image-url)
left ventricular diastole. To determine the degree of paradoxical septal motion, the septal position during early diastole was subtracted from the systolic position. The resulting number was (+) if septal motion was normal and (−) if paradoxical motion was present.

Left ventricular shortening fraction was determined from M-mode echocardiograms as the end-diastolic diameter minus systolic diameter/end-diastolic diameter.16

Radionuclide Studies

Erythrocyte labeling was performed in vivo for RNV imaging. Twenty to 25 mCi 99mTc pertechnetate were given intravenously 20 minutes after 1.7 mg stannous pyrophosphate. All studies were acquired for 200,000 counts per frame with 20 frames per RR interval in the "best septal" left anterior oblique position. The data were processed on an MDS A2 40,000 system in a 64 × 64 matrix after acquisition on a Picker Dyna-Mo gamma camera with a general purpose collimator. Electrocardiographic gating was obtained with use of a Physio-Control Lifepak 6.

To reduce late count variability, the final two frames were dropped before both spatial and temporal filtration. Ejection fraction was calculated in routine fashion with a standard semiautomatic, background subtracted algorithm. Regional ejection fraction was calculated by segmenting the left anterior oblique view of the left ventricle into six equal wedges with a common centroid at the center of mass.17 The ejection fraction of each segment was then noted. The most superior segments were eliminated because these regions often contain the aortic root and left atrium. Each segment was then labeled as septal, apical, or lateral regions. The stroke counts over end-diastolic counts in each segment were used to determine the regional ejection fraction.

The global radionuclide ventriculographic data were then fitted on a pixel-by-pixel basis with a first harmonic approximation, with a phase-shift histogram and phase image created as described previously.9 The phase-shift histogram for both the right and left ventricles was then determined after each ventricle was isolated by handdrawn regions of interest. The resultant data for each phase-shift histogram were then displayed as noted in Figure 2, with the relative difference in phase angles converted to msec by assuming the 360° were equal to the RR interval minus the duration of the two dropped frames. In this manner, the onset and duration of initial phase across each ventricle could be described in msec. As shown, this allowed for accurate description of the onset of right ventricular versus the onset of left ventricular contraction (phase delay) and provided further data documenting the delay in interventricular activation.

![Figure 2](image-url)

**Figure 2.** From radionuclide images, plots showing the onset of contraction of each pixel within the right ventricle (RV) and left ventricle (LV) were graphically displayed as a phase histogram. In normal subjects, RV and LV contraction occurred simultaneously; in left bundle branch block (LBBB) patients, LV activation was delayed by 85 ± 31 msec.

Statistical Evaluation

Data are presented as mean ± SD unless otherwise stipulated. Paired and unpaired Student’s t tests were used as well as univariate linear regression analysis where appropriate. Differences were considered significant at the p < 0.05 level.

Results

Patient Characteristics

Mean age of the 18 patients with LBBB was 67 years (range, 38–88); 14 were women and four were men. All patients were in sinus rhythm with a heart rate of 71 ± 8 beats/min (range, 57–87) at time of study. Mean age of the 10 normal subjects was 31 years (range, 25–38); seven were women and three were men. The mean heart rate was 68 ± 11 beats/min (range, 54–85).

Interventricular Asynchrony

The onset of left ventricular contraction was delayed in LBBB compared with normals as measured by apexcardiography, echocardiography, and RNV phase imaging (Table 1). As determined from RNV phase histograms, there were no differences in the onset of right ventricular contraction between the normal subjects and the LBBB population. The onset of right and left ventricular contraction occurred nearly simultaneously (6 ± 8 msec delay) in normal subjects. LBBB patients had an asynchro-

<table>
<thead>
<tr>
<th>Table 1. Onset of Left Ventricular Contraction (msec)</th>
<th>LBBB</th>
<th>Normal subjects</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q to apex</td>
<td>72 ±20</td>
<td>35 ±12</td>
<td>0.0005</td>
</tr>
<tr>
<td>Q to posterior wall contraction</td>
<td>163 ±25</td>
<td>122 ±22</td>
<td>0.0001</td>
</tr>
<tr>
<td>Radionuclide phase delay (between right and left ventricles)</td>
<td>85 ± 31</td>
<td>6 ± 9</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

LBBB, left bundle branch block.
nous onset of contraction with left ventricular contraction occurring 85 msec after the onset of right ventricular contraction ($p < 0.0001$).

There were no differences in left ventricular isovolumic contraction time between normals (62 msec) and LBBB (68 msec). However, in LBBB patients, the range of isovolumic contraction time was wide (20–100 msec).

The delay of left ventricular events in LBBB patients compared with normal subjects continued throughout the cardiac cycle as evidenced by Q to aortic opening (133 ± 30 compared with 93 ± 14 msec, $p < 0.001$), Q to aortic closure (445 ± 32 compared with 394 ± 29 msec, $p < 0.001$) and Q to mitral opening (542 ± 41 compared with 430 ± 33 msec, $p < 0.0001$) (Table 2). Although the mean time of mitral valve closure was not prolonged in LBBB patients (67 ± 26 msec) versus normals (69 ± 14 msec), the range was wide in the LBBB group (0–110 msec). Patients with long PR intervals (> 200 msec) had early mitral closure (mean, 42 msec; range, 0–70), accounting for this unexpected finding.

The auscultatory intensity of $S_1$ appeared to be diminished in LBBB patients; this was confirmed on the phonocardiograms as a diminished ratio of $S_1$ amplitude to $S_2$ (0.67 ± 0.20) compared with normals (1.34 ± 0.25, $p < 0.01$). The diminished $S_1$ amplitude was in part related to wide separation of the valvular contributors of $S_1$ (Table 2). Mitral valve closure and aortic valve opening were separated by 66 msec in LBBB patients compared with only 24 msec in normal subjects. Accordingly, the duration of the first heart sound was longer in LBBB compared with normal subjects (78 ± 31 compared with 33 ± 12 msec, $p < 0.01$).

Due to delayed aortic component of the second heart sound in LBBB patients, a relative decrease in the duration of left ventricular diastole occurred. This resulted in an increased ratio of right/left ventricular diastolic time in LBBB patients compared with normal subjects (1.12 ± 0.04 compared with 0.93 ± 0.01, $p < 0.0001$). Echocardiographic mitral and tricuspid valve opening occurred simultaneously in normal subjects, while mitral valve opening was delayed in LBBB patients (Table 2). This resulted in prolongation of left ventricular isovolumic relaxation time (94 ± 31 compared with 36 ± 20 msec, $p < 0.0001$), shortened left ventricular filling time, and an increased ratio of right/left ventricular diastolic filling duration (1.22 ± 0.08 compared with 1.02 ± 0.06, $p < 0.0001$) in LBBB patients compared with normal subjects.

Left ventricular systolic and diastolic events either preceded or occurred simultaneously with the right ventricle in the normal group (Figure 3). Patients with LBBB had a reversal of the usual sequence of events with right ventricular systole and diastole markedly preceding that of the left ventricle. This reversal of the normal sequence between right and left ventricular mechanical events resulted in a dynamic interventricular asynchrony throughout the cardiac cycle.

### Interventricular Septal Motion

Fifteen of 18 LBBB patients demonstrated high amplitude oscillations of the interventricular septum (Figure 4). The timing of these septal deflections appeared to correspond to periods of interventricular asynchrony (Figure 5). Two LBBB patients had normal interventricular septal motion, and one had grossly paradoxical septal motion.

Right ventricular contraction in LBBB patients occurred much earlier than left ventricular systole and was associated with an abrupt displacement of the interventricular septum into the left ventricle (Figure 5, 1). Pulmonic ejection occurred during left
ventricular isovolumic systole and was associated with septal displacement toward the right ventricle (Figure 5, 2). During simultaneous right and left ventricular ejection, the septal motion was usually flat or paradoxical (Figure 5, 3). Left ventricular systole continued after pulmonic valve closure and was associated with displacement of the septum into the right ventricle (Figure 5, 4). Septal displacement toward the left ventricle occurred with tricuspid valve opening (Figure 5, 5) and was reversed after mitral valve opening (Figure 5, 6). Further displacement of the septum occurred with atrial systole (Figure 5, 7). Thus, interventricular septal oscillations that occur in LBBB may in fact be related to asynchrony in contraction, ejection, end systole, and end diastole between right and left ventricles.

The magnitude and direction of systolic septal motion appeared to be associated with the ratio of right/left ventricular filling duration. Patients with a prolonged right/left ventricular filling ratio (an indication of interventricular asynchrony) tended to have more striking paradoxical interventricular septal motion \((n=26, r=-0.86, y=-2.96x+3.47; p<0.0001)\) (Figure 6).

**Ventricular Function**

Despite similar left ventricular end-diastolic diameters \((4.7\pm0.5\text{ compared with }4.8\pm0.6\text{ cm})\), left ventricular systolic dimension was increased in LBBB \((3.4\pm0.5\text{ cm})\), compared with normal subjects \((3.0\pm0.5\text{ cm}), p=0.06\). This resulted in a reduced left ventricular shortening fraction in LBBB patients \((0.30\pm0.08\text{ compared with }0.37\pm0.06, p<0.01)\). Because the systolic excursion of the posterior wall was similar in LBBB patients and normal subjects \((1.2\pm0.2\text{ and }1.0\pm0.1\text{ cm}, respectively)\), the reduced left ventricular shortening fraction in LBBB patients was due to septal motion abnormalities.

To determine whether the abnormal septal motion in LBBB patients contributed to abnormalities in left ventricular performance, radionuclide ventriculograms were obtained. Apical and lateral regional ejection fractions were similar in LBBB patients and normal subjects (Figure 7). However, interventricular septal contribution to ejection fraction was strikingly diminished in LBBB compared with normal subjects \((40\pm16\%\text{ compared with }67\pm7\%, p<0.001)\). Similar to echocardiographic findings, abnormalities in septal ejection fraction were associated with a prolonged right/left ventricular filling ratio \((n=26, r=-0.85, p<0.0001)\). As a result of abnormal septal contribution, left ventricular global ejection fraction was reduced in LBBB patients \((54\pm7\%)\) compared with normal subjects \((62\pm5\%), p<0.005)\.

![Figure 4](http://circ.ahajournals.org/)

**Figure 4.** Abnormal interventricular septum oscillations were noted in 15 of 18 left bundle branch block patients.
Interventricular Septal Motion

It is well known that septal motion may be affected by alterations in right ventricular pressure or volume.\textsuperscript{22,23} Pearlman et al\textsuperscript{24} demonstrated that septal motion during systole is toward the center of ventricular mass, such that the end-diastolic position of the septum determines its subsequent systolic movement.\textsuperscript{24} Other studies have concluded that the position and shape of the septum are determined by the interventricular transseptal pressure gradient. Reversal of the transseptal pressure gradient resulted in septal displacement into the left ventricle during diastole and paradoxical systolic motion.\textsuperscript{25}

Abnormal interventricular activation and mechanical asynchrony in LBBB may result in dynamic changes throughout the cardiac cycle in both pressure and volume between the ventricles. These differences in transseptal pressure or volume may be reflected via the septum and cause septal displacement. In the present study, the onset of contraction in the right ventricle occurred before the left ventricle in LBBB patients. As a result, increased pressure during right ventricular isovolumic systole presumably exceeded left ventricular end-diastolic pressure and the septum was displaced into the left ventricle (Figure 5, 1). This observation is supported by Kingma and Little’s observations with right ventricular pacing.\textsuperscript{26,27} They reported that the upstroke of right ventricular systolic pressure occurred earlier than that of the left ventricle and that with reversal of transseptal pressure gradient,
abrupt displacement of the septum into the left ventricle occurred. Although this septal deflection occurs well after the electrocardiographic R wave, physiologically it may represent the “true” left ventricular end-diastolic septal position.

Abrupt anterior septal motion (Figure 5, 2) occurred at the time of decreasing right ventricular volume with pulmonic ejection. Moreover, by this time, left ventricular systole had begun, normalizing the transseptal pressure gradient and moving the septum toward its equilibrium position.

Tricuspid valve opening and right ventricular filling occurred much earlier than mitral valve opening and left ventricular filling. This additional right ventricular volume may be responsible for early diastolic displacement of the septum into the left ventricle (Figure 5, 5).

During biventricular ejection, septal motion was variable in both direction and amplitude. Our data agree with Pearlman’s observation that the direction of systolic septal motion may be influenced by the septal position during diastole.24 Our method of measuring the amplitude of systolic septal motion varied considerably from Pearlman’s study. Since recognizable echoes from right ventricular endocardium, epicardium, and right septal surface could not be distinguished in the majority of our patients, we chose to measure the position of the left septal surface relative to the chest wall. Septal motion was determined by subtracting diastolic from systolic septal positions, obviating the importance of location of the fixed reference system. In addition, we chose to compare systolic septal motion with early diastolic, rather than end-diastolic septal position. Due to the delay in left ventricular activation, we believed that conventional use of electrocardiographic Q or R waves to represent end diastole26 may not be valid in the setting of LBBB. In fact, our data demonstrated that the septum is displaced into the left ventricle before the onset of left ventricular systole (Figure 5, 1). This location may represent the true left ventricular end-diastolic septal position. Thus, displacement of the septum in LBBB patients may occur as a result of a relative increase in right ventricular volume (as assessed by an increased ratio of right/left ventricular diastolic time) or pressure (right ventricular contraction during left ventricular end-diastole). Diastolic displacement of the septum in LBBB patients may result in reduced or paradoxic systolic septal motion and a diminished septal contribution to ejection fraction.

Ventricular Function
That isolated LBBB may affect left ventricular function was demonstrated in a report of seven patients with intermittent LBBB, all of whom had normal wall motion and left ventricular ejection fraction during normal conduction.29 The development of LBBB was associated with an abrupt decrease in ejection fraction and abnormal motion of the interventricular septum or apex. The adverse effect of intermittent LBBB on left ventricular performance has also been described in other case reports.30–32 In the absence of any apparent mechanical heart disease, LBBB patients in our study also demonstrated abnormal left ventricular function. The hemodynamic deterioration associated with isolated LBBB appears to be due to loss of interventricular septal contribution to ejection fraction. The magnitude of interventricular septal motion abnormality and resultant hemodynamic compromise appeared to be directly related to the degree of interventricular asynchrony.

Limitations
Although it is generally agreed that “benign” LBBB can occur in the presence of other cardiac disease, our patients may in fact have a subtle cardiomyopathy, clinically silent coronary artery disease, or other undetected disease states that may contribute to the functional abnormalities. Patients did not undergo exercise testing or catheterization to exclude ischemia as the etiology of left ventricular dysfunction. Septal thallium defects have been reported in LBBB patients even in the absence of coronary disease, raising the question of functional ischemia.33 Timing of right and left ventricular diastolic intervals may be affected by respiration, heart rate, and day-to-day variability. Expressing right and left ventricular diastolic intervals as a ratio...
was used to eliminate heart rate as a variable. Averaging intervals over five to 10 consecutive cardiac cycles may reduce variability and measuring errors. Although the LBBB group was of substantially greater age than the control group, it would be highly unlikely that all of the described abnormalities in the LBBB population were due to aging alone. Previous studies have demonstrated that phonocardiograms, left ventricular end-diastolic dimension, area, volume, ejection fraction, and wall motion at rest were similar in young and elderly populations. 34, 35 Although aging may affect left ventricular compliance, 34 the ratio of right to left ventricular diastolic time should not be affected. Nevertheless, some of the abnormalities described in the LBBB group may in part be due to aging; thus, the results must be interpreted with some caution.

Conclusions

Altered electrical activation in patients with isolated LBBB caused global ventricular abnormalities manifested by abnormal diastolic filling times, abnormal heart sounds, abnormal interventricular septal motion, and abnormal left ventricular regional ejection fraction. A postulated mechanism for these global ventricular abnormalities is shown schematically (Figure 8). LBBB causes a delay in left ventricular depolarization resulting in delayed left ventricular contraction and relaxation compared with the right ventricle. Delay in left ventricular systole results in a relative shortening of left ventricular diastole, which may contribute to displacement of the interventricular septum. Furthermore, asynchronous right-left ventricular contraction and relaxation may produce dynamic alterations in transseptal pressure and volume that may be responsible for the abnormal septal deflections. Finally, this abnormal septal motion results in an altered regional ejection fraction, with a diminished interventricular septal contribution to global left ventricular performance.

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References


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