Systolic Improvement and Mechanical Resynchronization Does Not Require Electrical Synchrony in the Dilated Failing Heart With Left Bundle-Branch Block

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**Background**—Biventricular (BiV) and left ventricular (LV) pacing similarly augment systolic function in left bundle-branch block (LBBB)–failing hearts despite different electrical activation. We tested whether electrical synchrony is required to achieve mechanical synchronization and functional benefit from pacing.

**Methods and Results**—Epicardial mapping, tagged MRI, and hemodynamics were obtained in dogs with LBBB-failing hearts during right atrial, LV, and BiV stimulation. BiV and LV both significantly improved chamber hemodynamics (eg, 25% increase in dP/dt<sub>max</sub> and aortic pulse pressure) compared with atrial pacing–LBBB, and this improvement correlated with mechanical resynchronization. Electrical dispersion, however, decreased 13% with BiV but increased 23% with LV pacing (P<0.01).

**Conclusion**—Improved mechanical synchrony and function do not require electrical synchrony. Mechanical coordination plays the dominant role in global systolic improvement with either pacing approach. *(Circulation. 2002;106:1760-1763.)*

**Key Words:** heart failure ■ pacing ■ electrical stimulation ■ bundle-branch block ■ ventricles
loxane, maintaining end diastolic shape, and electrode, pacing lead, and head locations were digitized (Microscribe 3DLX). The apex and interventricular septum were also located as anatomic landmarks.

Data Analysis
Electrical signals were averaged over ~20 consecutive beats for each pacing mode. Local depolarization at each electrode was at -dV/dtmax referenced to the earliest ventricular activation time. Short- and long-axis tagged images were processed as described,11 with the displacement field modeled by a 4-dimensional B-spline,11 and circumferential strain (εc) determined over the entire LV-midwall. LV strain was spatially referenced to electrical maps using the position digitization data. Mechanical dyssynchrony was indexed by a circumferential uniformity ratio estimate (CURE), εc at 24 circumferentially-distributed locations around each short-axis section was plotted versus spatial position for each time-frame. The more oscillatory the plot, the more dyssynchrony among segments around the short axis. Plots for ~6 midwall short-axis slices (excluding the most apical and basal regions) were subjected to Fourier analysis, and the results were averaged over space and time to yield CURE regions were subjected to Fourier analysis, and the results were averaged over space and time to yield CURE

Results
LBB-ablation widened QRS duration from 54±7.1 to 118±29 ms (P<0.01) without altering PR interval (102±14 versus 100±12 ms). After 3 weeks of pacing, left ventricular ejection fraction (LVEF) was 33±4%, mean LV end diastolic diameter was 49±5 mm, and estimated pulmonary artery pressure (Doppler) was 37±13 mm Hg.

Both LV and BiV Pacing Enhance Systolic Function
Both LV and BiV stimulation enhanced systolic function (Table). With exception of a slightly greater peak systolic pressure with BiV, responses with both pacing modes were virtually identical. These responses were little altered (+3%) of peak), despite varying of the AV delay by ±30 ms from the primary value used.

Electrical Synchrony Is Reduced With LV-Only but Enhanced by BiV Stimulation
Despite similar global mechanics, there were marked differences in electrical synchrony between pacing modes (Figure 1). With RA-LBBB, electrical activation spread from right to left with a net delay of 97.8±2.1 ms. LV-only pacing reversed this pattern, increasing net delay to 121.5±2.1 ms (P<0.0001 versus RA-pacing), whereas BiV pacing improved electrical synchrony as conduction spread from opposing sides toward the midchamber (85±2.4 ms; P<0.001 versus RA-pacing; P<0.0001 versus LV-pacing). Endocardial septal activation was concordant with epicardial activation-times overlying the same region (Figure 1B). To further rule out electrical fusion with LV-pacing, AV-delay was correlated to atrial (electrical)-LV (mechanical, time at 10% dP/dtmax) delay. This relation has unity slope with full LV capture but a flatter slope if fusion is present. The mean slope was 0.984±0.032 (r2=0.98). Electrical activation with zero AV-delay was virtually identical to that at 70 ms, which was the average value used for mechanical analysis (data not shown).

Both LV and BiV Pacing Improve LV Mechanical Synchrony
Figure 2A shows example 3D strain maps for each pacing-mode at time of mitral valve (MV) closure, mid-systole, and late-systole. Displayed numbers are time intervals between septal and lateral wall electrical activation and the mechanical events. RA-LBBB pacing induced both septal shortening (blue) and lateral-wall stretch (yellow) by MV-closure through to mid-systole. Lateral contraction occurred in late systole. With LV-pacing, contraction started at the lateral pacing site with less marked stretch of the opposite (septal) wall. Note that by mitral valve closure, septal electrical-activation had already occurred. Lateral contraction advanced slowly, with shortening observed most prominently in the septum. These 2 areas then converged more synchronously during remaining systole. BiV activation resulted in less asymmetry at MV-closure, with 2 shortening fronts evident by mid-systole that converged during late systole. Thus, mechanical maps at mid- and late systole were similar between LV and BiV modes, both largely eliminating paradoxic stretch of the opposing wall. Concordant with this example, the CURE synchrony index similarly improved with both modes (P<0.001), correlating with dP/dtmax (adjusted for mean in each animal; r=0.84; Figure 2B). In contrast, dP/dtmax did not correlate with interelectrode maximal electrical dispersion.

<table>
<thead>
<tr>
<th>LV and BiV Pacing Response in Pacing-Induced Dilated Cardiomyopathy Combined With LBBB</th>
<th>RA (LBBB)</th>
<th>BiV</th>
<th>LV</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, min⁻¹</td>
<td>123±13</td>
<td>123±13</td>
<td>123±13</td>
<td>NS</td>
</tr>
<tr>
<td>AV delay, ms</td>
<td>144±10</td>
<td>69±18*</td>
<td>69±18*</td>
<td>0.0001</td>
</tr>
<tr>
<td>LV systolic pressure, mm Hg</td>
<td>86.6±7.7</td>
<td>97.4±12.6‡</td>
<td>91.7±9.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV end-diastolic pressure, mm Hg</td>
<td>14.0±4.5</td>
<td>11±3.2†</td>
<td>10.7±3.1†</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>dP/dtmax, mm Hg/s</td>
<td>1048±242</td>
<td>1392±413*</td>
<td>1309±339*</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>dP/dtmax, mm Hg/s</td>
<td>−960±162.2</td>
<td>−1152±250◊</td>
<td>−1125±211§</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>22.8±6.8</td>
<td>28±6.5‡</td>
<td>26.5±7†</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>23±12.7</td>
<td>27.5±16.2§</td>
<td>28±16.1§</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*P<0.001; †P<0.005; §P<0.05 vs RA (LBBB). ‡P<0.05 vs LV.
Discussion

BiV pacing was first proposed to treat failing hearts with discoordinate contraction, as it seemed the most logical way to achieve resynchronization. To date, most clinical studies have used this method, using simultaneous stimuli and highlighting QRS narrowing. LV-only pacing, however, produces similar mechanical and energetic effects as BiV pacing. The present study indicates that LV-pacing actually increases electrical dispersion over that from LBBB or BiV pacing, despite improving mechanical function and coordination. Lack of electrical fusion was supported by the electrode-array data, which showed an equal rise in electro-mechanical delay for an increment in AV delay, and the similar mechanical response despite substantially varied AV delays. These results support clinical data showing no correlation between change in QRS duration and mechanical response to LV or BiV pacing. Mechanical dyssynchrony rather than electrical dispersion seems to be the more relevant measure.

LV-pacing started with focal lateral-wall contraction that advanced slowly, with more prominent shortening next appearing in the septum. The precise mechanism for the apparent slow progression of antero-lateral wall shortening despite preexcitation remains to be fully resolved. We speculate that early stimulated regions interact with more prestretched (ie, preloaded) distal regions (septum), and that the resulting temporally and spatially varied load yields a nodal zone of apparent less-contracting muscle in the midlateral wall. Reduced and slowed myocardial stiffening, which is typical of failing myocardium, may be important in this regard. Importantly, LV and BiV pacing both generated less early and late systolic stretch of opposing walls versus LBBB, supporting recent clinical data. Further studies will be needed to assess the role of septal/RV loading, systemic afterload, pacing site and extent of stimulation, and underlying cardiomyopathy to these observations. At present, we can conclude that mechanical rather than electrical synchrony...
seems most important for functional improvement with these therapies.

Acknowledgments
This work was supported by grant P50:HL52307 (Dr Kass) and RO1: HL64795, HL45683 (Dr Halperin) and the French Federation of Cardiology (Dr Leclercq).

References

Figure 2. A, Mechanical LV activation maps for 3 pacing modes. LV contraction was dyssynchronous with RA (LBBB) stimulation, with early septal shortening (blue) and LV–free wall stretch (yellow) followed by lateral shortening. For BiV and LV pacing, mechanical activation was more synchronous, with less early and late systolic dyskinesia, and mechanical maps were remarkably similar by mid-late systole. Numbers shown reflect time duration from electrical stimulation to septal and lateral sites to time when mechanical data were displayed. B, Chamber synchrony (CURE) improved similarly with LV and BiV modes. *P<0.001. C, CURE positively correlated with dP/dt max but not with electrical delay. dP/dt max is adjusted for its mean value in each respective animal.
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Circulation. 2002;106:1760-1763
doi: 10.1161/01.CIR.0000035037.11968.5C

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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