The Hemodynamic Effect of Intrinsic Conduction During Left Ventricular Pacing as Compared to Biventricular Pacing

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OBJECTIVES

We sought to investigate the effect of intrinsic conduction over the right bundle on the maximum rate of left ventricular pressure rise (LVdP/dt_max) during left ventricular (LV) pacing compared to biventricular (BiV) pacing.

BACKGROUND

Simultaneous BiV pacing and LV pacing both improve LV function in patients with heart failure and LV asynchrony. We studied the hemodynamic effect of intrinsic conduction leading to ventricular fusion during LV pacing.

METHODS

In 34 patients with New York Heart Association functional class III or IV, sinus rhythm with normal atrioventricular (AV) conduction, left bundle branch block, QRS >130 ms, and optimal medical therapy, LVdP/dt_max was measured invasively during LV and simultaneous BiV pacing. The AV interval was varied in four steps starting (AV1) with an AV interval 40 ms shorter than the intrinsic PQ time and decreased with 25% for each step.

RESULTS

At AV1, LVdP/dt_max was 996 ± 194 mm Hg/s for LV pacing and 960 ± 200 mm Hg/s for BiV pacing (p = 0.0009), with all patients showing ventricular fusion during LV pacing. At AV2, 21 patients had ventricular fusion with a LVdP/dt_max of 983 ± 213 mm Hg/s and 957 ± 202 mm Hg/s for LV and BiV pacing, respectively. In the remaining 13 patients without fusion these values were 919 ± 164 mm Hg/s and 957 ± 174 mm Hg/s, respectively. The difference between LV and BiV at AV2 is significantly higher when fusion is present (p = 0.01).

CONCLUSIONS

The LVdP/dt_max is higher in LV than in BiV pacing provided that LV pacing is associated with ventricular fusion caused by intrinsic activation. (J Am Coll Cardiol 2005;46:2305–10) © 2005 by the American College of Cardiology Foundation

Several studies comparing the acute and chronic results of left ventricular (LV) and biventricular (BiV) pacing in patients with heart failure have been performed (1–7). However, in none of these studies the influence of intrinsic conduction over the right bundle on the hemodynamic effect of LV pacing was described. The present study investigates the hemodynamic effect of intrinsic right bundle activation during LV pacing measured by invasive maximum rate of left ventricular pressure rise (LVdP/dt_max).

METHODS

Thirty-four patients, 9 females and 25 males, New York Heart Association (NYHA) functional class III and IV, sinus rhythm with normal atrioventricular (AV) conduction, left bundle branch block (LBBB), QRS >130 ms, and optimal medical therapy, were selected for cardiac resynchronization therapy (CRT). Clinical characteristics of the patients are presented in Table 1. All patients had a biventricular pacing system (Medtronic 8042, Medtronic Inc., Minneapolis, Minnesota) implanted, with an LV lead positioned in one of the posterior or posterolateral branches of the coronary venous system. The pacemaker was programmed to a nonfunctional pacing mode (VVI 40 ppm) until the moment of hemodynamic evaluation, which was performed within 24 hours after implant.

Hemodynamic evaluation was performed with a 0.014-inch pressure sensor-tipped percutaneous transluminal coronary angioplasty guide wire (Radi Medical Systems, Uppsala, Sweden) with a 500-Hz frequency response introduced through a 4-F multipurpose catheter into the left ventricle (8). Subsequently the multipurpose catheter was withdrawn into the aorta, leaving the soft tip of the pressure wire in a stable position in the LV cavity. At steady-state condition, LVdP/dt_max was calculated electronically from every heartbeat for a period of at least one respiratory cycle. These results were averaged for the complete measurement period. A waiting time of at least 20 s was respected after each change of pacing mode and/or AV interval, in order to achieve hemodynamic stabilization (2). It has been shown previously that LVdP/dt_max is measured reliably in this way (9). This study was approved by the institutional review committee of the Catharina Hospital, and written informed consent was given by all patients prior to the study.

The LVdP/dt_max was first measured during intrinsic rhythm and atrial pacing 5 to 10 beats above the intrinsic
rate to eliminate the effect of heart rate variation during the study. The pacing rate was kept constant in the subsequent pacing modes with AV sequential pacing from the right ventricular (RV), LV, and simultaneous BiV pacing. Four AV pacing intervals were used for all three AV sequential pacing modalities. The first AV interval was programmed 40 ms shorter than the intrinsic PQ time in order to avoid fusion during right ventricular pacing (longest AV interval, AV1). Subsequently the AV interval was programmed to 75% (AV2), 50% (AV3), and 25% (AV4) of the AV1 value.

At the end of the procedure LVdP/dt max was measured again under baseline conditions (AAI pacing) and compared with the value at the start of the procedure, in order to check hemodynamic stability. Figure 1 shows the display of the RadiAnalyzer Physio monitor (Radi Medical Systems, Uppsala, Sweden) used for measurement of LVdP/dt.

Fusion during LV pacing was evaluated by comparing the 12-lead electrocardiogram with complete LV pre-excitation (AV 30 ms) to the actual 12-lead electrocardiogram at AV1, AV2, AV3, and AV4. Fusion was confirmed by a reduction in QRS width, a change in morphology of the surface electrocardiogram, and the RV intracardiac electrogram recorded by pacemaker telemetry (Figs. 2 and 3).

For each of the different settings of the pacing system, the mean values of LVdP/dt max for LV and BiV pacing were compared with a paired Student t test. To account for multiplicity, each of the four tests is considered significant if p < 0.0125 (Bonferroni correction). The mean difference in LVdP/dt max between LV and BiV when pacing at AV2 is compared with an unpaired t test between patients with and without fusion. The overall effect of fusion while pacing in

### Table 1. Clinical Characteristics of Study Population

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<td>181 ± 23</td>
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LV mode is analyzed by means of a repeated-measures mixed model, controlling for the effects of BiV versus LV pacing and AV delay. For this model, a value of $p < 0.05$ is considered significant. All data are presented as mean ± standard deviation.

RESULTS

The LVdP/dt$_{\text{max}}$ measurements were obtained successfully in all patients and are summarized in Table 2. The LVdP/dt$_{\text{max}}$ was 805 ± 182 mm Hg/s during intrinsic rhythm and 813 ± 197 mm Hg/s during atrial pacing ($p = 0.34$). The latter is used as baseline value. At the end of the procedure, repeated baseline LVdP/dt$_{\text{max}}$ was 809 ± 196 mm Hg/s, which was not statistically different from the value at the start of the procedure ($p = 0.49$). Increase in LVdP/dt$_{\text{max}}$ during LV and BiV pacing was observed in all patients.

At AV1, LVdP/dt$_{\text{max}}$ for LV pacing was significantly higher than for BiV pacing and was associated with ventricular fusion in all patients. The difference in LVdP/dt$_{\text{max}}$ between LV pacing at AV1 and AV2 was statistically significant in favor of the longer AV interval ($p = 0.012$). At AV2, patients were divided into two groups according to the presence (21 patients) or absence (13 patients) of fusion. Patients in whom fusion was present showed a higher LVdP/dt$_{\text{max}}$ during LV pacing ($26.5 ± 71.9$ mm Hg/s). However, when no fusion was present, BiV pacing was superior to LV pacing ($38.0 ± 58.4$ mm Hg/s). The difference between LV and BiV at AV2 is significant when fusion is present ($p = 0.01$) (Table 2). At AV3 and AV4 there was no significant difference between LV and BiV pacing; however, no fusion was present at all during LV pacing at these short AV intervals.

A multivariate repeated-measures mixed model was used to simultaneously assess the effects of LV vs BiV pacing, AV delay, and the presence of fusion. Results are summarized in Table 3. There is a significant decrease of LVdP/dt$_{\text{max}}$ with a decreasing AV delay ($p < 0.0001$). The effect of LV pacing versus BiV is not significant ($p = 0.43$). In contrast,
fusion during LV pacing had a clear and highly significant contribution to LVdP/dtmax (41.4 mm Hg/s; \( p = 0.0005 \)).

The QRS duration during LV pacing at an AV delay of 30 ms (full pre-excitation), AV1 (fusion in all patients), and AV2 with presence of ventricular fusion was 219 ± 25 ms, 163 ± 25 ms, and 189 ± 28 ms, respectively. There was no significant difference in intrinsic PR time between patients with (180 ± 25 ms) and without (185 ± 22 ms) fusion at AV2. The optimal paced AV interval for LV and BiV pacing was not significantly different: 153 ± 27 ms versus 147 ± 32 ms, respectively.

**DISCUSSION**

This study shows that intrinsic conduction over the right bundle significantly contributes to the acute hemodynamic effect of LV pacing expressed as increase in LVdP/dtmax in CRT, rendering it superior to BiV pacing at the longest AV intervals (\( p = 0.0005 \)). At a shorter AV interval (AV2), the difference between LV and BiV pacing is also significant in favor of LV pacing when fusion with intrinsic right bundle conduction is present (\( p = 0.01 \)).

Fusion at AV2 was not related to the intrinsic PR interval, which was 180 ± 25 ms for patients with and 185 ± 22 ms for patients without fusion. Ventricular fusion, however, is dependent not only on the AV interval with LV pacing and the intrinsic AV conduction (PR interval), but also on the total ventricular (right and left ventricle) activation time by LV pacing. The latter depends on the position of the LV lead, the LV mass and the ventricular conduction velocity, which varies in the individual patient.

When the mechanism of simultaneous BiV pacing is compared to LV pacing with fusion there is a difference in intra- and interventricular timing and the nature of right ventricular activation. The longest AV interval (AV1) was chosen to have complete ventricular pre-excitation during RV pacing, which implies that during BiV pacing with the same or shorter AV interval both RV and LV activation result from pacing. However, if only the LV is stimulated at the same AV interval, the interventricular conduction time from left to right allows for normal conduction to occur over the right bundle at the longest AV intervals. This results in fusion of LV pacing and intrinsic conduction, effectively producing biventricular activation with unilateral pacing. The intrinsic RV activation over the right bundle resulted in a hemodynamically superior performance to RV activation by artificial stimulation in this study.
During LV pacing with fusion, LV activation precedes RV activation, whereas during BiV pacing activation of RV and LV is simultaneous. We recently showed that sequential activation with LV preceding RV pacing is superior to simultaneous BiV activation in the majority of patients (9). We therefore postulate that the superiority of LV pacing with fusion over BiV pacing is firstly determined by the presence of intrinsic activation of the RV and secondly by a timing difference in ventricular activation, where the LV stimulation precedes RV intrinsic activation during LV pacing.

At the shortest AV intervals (AV3 and AV4) with no fusion during LV pacing, differences between LV and BiV were not significant (Table 2). The significantly lower LV$dP/dt_{\text{max}}$ at these AV intervals compared to the longer AV intervals is a result of the suboptimal AV interval and is less determined by the pacing site. Thus, conclusions with respect to the effect of fusion can not be drawn from those measurements.

Table 2. Values of $dP/dt_{\text{max}}$ for Baseline, LV, and BiV Pacing at Four AV Intervals and Subdivided for AV2 With and Without Fusion

<table>
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<th>AV Interval</th>
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<th>BiV Pacing</th>
<th>p Value</th>
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<td>996 ± 194*</td>
<td>960 ± 200§</td>
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<td>959 ± 195†</td>
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<td>813 ± 197</td>
<td>880 ± 175</td>
<td>871 ± 174</td>
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| AV2 fusion  | 21 | 800 ± 228 | 983 ± 213 | 957 ± 202 | +26.5 ± 71.9 |
| AV2 no fusion | 13 | 835 ± 139 | 919 ± 164 | 957 ± 174 | −38.0 ± 58.4 |

The $p$ values refer to the differences between LV and BiV pacing; $p < 0.0125$ is significant. The $p$ values for comparison of different AV intervals with the same pacing modality: *$p = 0.012$ (LV AV1 vs. LV AV2), †$p = 0.0002$ (LV AV2 vs. LV AV3), ‡$p < 0.0001$ (LV AV3 vs. LV AV4; BiV AV2 vs. BiV AV3; BiV AV3 vs. BiV AV4); §$p = 0.67$ (BiV AV1 vs. BiV AV2).

Results of $dP/dt_{\text{max}}$ at AV2 are divided into patients with and without ventricular fusion. The difference between LV and BiV pacing is significantly higher when fusion is present ($p = 0.01$).

AV = atrioventricular; BiV = biventricular; LV = left ventricular.
The explanation of why LV activation should precede RV activation to provide optimal hemodynamic results is speculative. In an animal model, Verbeek et al. (10) showed that endocardial activation should be restored to baseline to obtain optimal effect of pacing therapy after induction of LBBB. In case of fusion with intrinsic conduction, the slower conduction of activation resulting from LV pacing compared to intrinsic conduction could necessitate earlier left-sided activation to restore balanced electrical activation of the left ventricle.

Further, a previous study from our department showed that the optimal V-V interval was significantly longer, necessitating more pre-excitation of the LV in patients with ischemic cardiomyopathy compared to those with dilated cardiomyopathy (9). This might be explained by the presence of scar tissue resulting in a slower conduction velocity in the ischemic group (11). The slow conduction is compensated by an earlier start of activation from the LV electrode. From a mechanical point of view, reloading of the unloaded septum in patients with LBBB might also play a role in this mechanism.

Blanc et al. (1) reported no significant difference in systolic blood pressure, decrease in capillary wedge pressure, and decrease in V-wave amplitude between LV and BiV pacing. Concordant with the results of this study, Auricchio et al. (2) and Nelson et al. (3) observed a slightly higher LVdP/dt_max for LV pacing compared to BiV pacing. None of these studies, however, evaluated the effect of intrinsic right bundle activation on the hemodynamics of LV pacing. Verbeek et al. (10) found similar results comparing LV and BiV pacing in animal experiments, with the optimum effect for LV pacing at AV intervals equal to baseline PQ time with the exception of LV apex pacing. The effect of endogenous activation was not studied in detail nor discussed, but the shorter QRS duration during LV lateral wall pacing compared to BiV pacing suggested ventricular fusion during LV pacing in that study.

**STUDY LIMITATIONS**

A limitation of this study is that the pacing protocols were applied in a fixed order. It was chosen not to randomize in order to avoid programming errors. To provide for stable conditions, heart rate and surrounding conditions were kept constant during the measurements. This was confirmed by measuring baseline LVdP/dt_max at the start and end of the protocol, which were not significantly different.

A second limitation was the exclusive use of LVdP/dt_max as a single parameter for the hemodynamic effect of LV and BiV pacing. However, a previous study by Nelson et al. (3) showed that LVdP/dt_max is a more sensitive parameter than LV and aortic pulse pressure in the evaluation of CRT effects.

This study was also limited to the acute hemodynamic effects of LV pacing as compared to BiV pacing. Further studies will be necessary to investigate the relation between these acute results and chronic functional improvement.

**CONCLUSIONS**

This acute study shows that left ventricular pacing is hemodynamically superior to biventricular pacing in CRT when fusion with intrinsic conduction over the right bundle is present. In absence of the latter, biventricular pacing will be necessary to obtain maximal benefit.

**Acknowledgments**

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**REFERENCES**


