Acute effects of biventricular pacing on right ventricular function assessed by tissue Doppler imaging

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**Aims** The benefits of cardiac resynchronization therapy (CRT) on functional status, left ventricular (LV) remodelling and survival in patients with drug-refractory congestive heart failure (CHF), LV systolic dysfunction, and wide QRS have been demonstrated in randomized trials. However, the impact of CRT on right ventricular (RV) function, an independent prognostic factor in CHF remains questionable. This study examined the acute effects of various pacing modes on RV function in recipients of CRT systems.

**Methods and results** Echocardiographic examinations were performed in 15 patients (median age: 67 years, range 49–78), to compare RV function during atrial (AAI), RV and LV pacing, and biventricular (BiV) pacing, in random order. At baseline, the median LV ejection fraction was 20% (range 10–35) and the median LV end-diastolic diameter was 78 mm (range 62–85). Right ventricular function was impaired, with a median 36% fractional shortening of RV surfaces (7–59). Tissue Doppler systolic peak of velocity (Sa) recorded at the tricuspid annulus increased significantly from 9.9 cm/s (range 4.7–16.5) during AAI pacing, 10 cm/s (range 5.4–20.3) during RV pacing, and 11.7 cm/s (range 4.6–16.7) during LV pacing to 12.6 cm/s (range 6.6–19.1) during BiV pacing ($P < 0.01$). Trends toward improvements in other indices of RV function, particularly myocardial performance index and systolic excursion of the tricuspid annulus, were also observed.

**Conclusions** This short-term study showed a significant improvement in RV systolic function during BiV pacing compared with AAI, RV, or LV pacing in CRT recipients.

**KEYWORDS** Heart failure; Cardiac resynchronization therapy; Right ventricular function; Echocardiography; Doppler myocardial imaging

**Introduction**

Congestive heart failure (CHF) is a major disorder associated with poor quality of life and high mortality. Among new therapeutic strategies, cardiac resynchronization therapy (CRT) is now well established for patients with drug-refractory symptoms, advanced left ventricular (LV) systolic dysfunction, and wide QRS. However, since it was primarily developed to improve timing and function of the LV, the effects of CRT on right ventricular (RV) function, an independent prognostic factor in CHF have not been thoroughly examined. Therefore, we designed an acute study to compare the effects of AAI, LV, RV, and biventricular (BiV) pacing on RV function assessed by transthoracic echocardiography in recipients of CRT systems.

**Methods**

**Study population**

The study included 15 consecutive patients who were candidates for CRT. The indication for CRT were New York Heart Association (NYHA) CHF functional class ≥ III despite optimal drug therapy, a LV ejection fraction ≤ 35%, and presence of left bundle branch block, with a QRS duration > 120 ms on surface electrocardiogram (ECG). Patients with unstable heart disease, atrial fibrillation, or absence of spontaneous atrioventricular (AV) conduction were not included in this study. The study complied with the Declaration of Helsinki, the study protocol was approved by the local ethics committee, and informed written consent was obtained from all patients.

**Implanted devices**

All patients had undergone implantation of CRT systems. The lead system included (i) active fixation atrial leads placed in the inter-atrial septum or in the right atrial (RA) appendage, (ii) RV leads placed in the mid inter-ventricular septum in 13, or at the apex in 2 patients, and (iii) LV leads placed in a lateral cardiac
vein in 12, or in the mid-cardiac vein in 3 patients, using the technique described by Daubert et al.\textsuperscript{15}

**Study protocol**

All patients were clinically stable at the time of study. Transthoracic echo-Doppler measurements were made with the pulse generator programmed, in random order, for

(i) AAI pacing from the RA with spontaneous AV conduction,
(ii) DDD pacing from the RV,
(iii) DDD pacing from the LV, or
(iv) DDD-BIV pacing at identical heart rates.

The AV delay was individually optimized for each pacing modalities by an iterative method. It was based on measurements of the mitral inflow velocity time integral and LV filling duration. This was performed in accordance with the daily practice of pacemaker optimization in our echo-laboratory.

**Echocardiographic examination**

Each transthoracic examination was performed by the same two physicians and an agreement between them was required throughout the experiment. Each measurement was performed online using a Sonos 7500 Doppler system (Philips, Andover, MA, USA).

Standard parasternal long- and short-axis and apical views were acquired with the patient in the left lateral supine position. Pulsed-waved tissue Doppler imaging (TDI) was performed from apical four-chamber views with the sample volume at the tricuspid annulus directed toward the RV free wall (Figure 1). Peak systolic (Sa), and peak early (Ea) and peak late (Aa) diastolic annular velocities were measured with lead aVF of the surface ECG at a speed of 100 mm/s. Tissue Doppler imaging measurement were performed according to the previously published methodology\textsuperscript{16}. The scale speed and the sweep speed was systematically optimized. The electro-mechanical delay was defined as the time between the onset of the Q-wave on the surface ECG and peak ‘Sa’.

Myocardial performance index (MPI) was calculated as the sum of isovolumic contraction and isovolumic relaxation time divided by the ejection time (Figure 1).\textsuperscript{9}

M-mode echocardiography was used in apical four-chamber windows to measure the maximal tricuspid annulus plane systolic excursion (TAPSE, mm), as previously described (Figure 1).\textsuperscript{10}

Two-dimensional recordings of the four-chamber view were used for measurements of the RV end-diastolic area and end-systolic area, and the calculation of the RV fractional shortening (end-diastolic-endo-systolic/end-diastolic).

Acquiring images and measuring them later proved impractical, thus two physicians, routinely practising assessment of mechanical dysynchrony, analysed the images online and an agreement between them was required before validating the measurement for further statistical analysis.

**Statistical analyses**

Data are presented as medians and range in the text and as mean $\pm$ SD in the figures. Stepwise repeated measures of analysis of variance were used to compare the various pacing modes. If differences were detected, analysis of variance was completed by a Bonferroni test to adjust for multiple comparisons. All statistical analyses were performed using the SPSS version 10.0 statistical software (SPSS Inc., Chicago, IL, USA). A $P$ value $<0.05$ was considered statistically significant.

**Results**

**Characteristics of the study population**

The study included 12 men and 3 women. Their median age was 67 years (range 49–78). The underlying heart disease was ischaemic in 9 patients, and non-ischaemic in 6. All patients had received long-term therapy with furosemide and angiotensin-converting enzyme inhibitors.

**Figure 1**

(A) Representative example of tissue pulse Doppler tracing of the tricuspid annulus with the peak velocity ‘Sa’ (cm/s). The normal value is $>11$ cm/s.\textsuperscript{30} (B) Representative example of tricuspid annulus systolic excursion recorded in M-Mode. The normal value is $>14$ mm.\textsuperscript{31} (C) Representative example of MPI measured using the pulmonary outflow and the tricuspid inflow. The normal value is $>0.83$.\textsuperscript{27}
Furthermore, only 4 patients did not receive beta-blockers because of intolerance, and 11 received spironolactone, 25 mg daily.

The mean intrinsic QRS duration before implantation of the CRT system was 158 ± 25 (120–240) ms, and 145 ± 30 (10–180) ms with BiV pacing.

The baseline mean RV area fractional shortening in the whole study population was 36% (7–59), 9 patients had a RV area fractional shortening <40%.

The baseline median RV radial diameter measured in the two-dimensional apical four-chamber view was 41 mm (range 10–74), and the median maximal longitudinal length of the RV was 88 mm (range 68–110). No significant tricuspid regurgitation was found, preventing the estimation of increased pulmonary arterial pressure. Non-significant regurgitation was noted allowing measurement of the timing of events.

Comparison of the different pacing modalities on RV function

Median TDI 'Sa' was 12.6 cm/s (range 6.6–19.1) during BiV pacing (Figure 2), which is significantly higher than during LV pacing [11.7 cm/s (range 4.6–16.7)], RV pacing [10 cm/s (range 5.4–20.3)], or AAI pacing [9.9 cm/s (range 4.75–16.5)]. A trend was observed with respect to the measurements of TAPSE, and MPI, though these differences did not reach statistical significance (Table 1).

Figure 2 Diagram of mean value of systolic velocity of the tricuspid annulus recorded in tissue Doppler (Sa, cm/s) in the four pacing conditions tested.

<table>
<thead>
<tr>
<th>Pacing mode</th>
<th>AAI</th>
<th>RV pacing</th>
<th>LV pacing</th>
<th>BiV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sa (cm/s)</td>
<td>9.9 (4.7–16.5)</td>
<td>10.0 (5.4–20.3)</td>
<td>11.7 (4.6–16.7)</td>
<td>12.6 (6.6–19)</td>
</tr>
<tr>
<td>TAPSE (mm)</td>
<td>17.2 (9–31)</td>
<td>17.6 (12–30)</td>
<td>18.0 (9–26.1)</td>
<td>18.6 (12.7–33.1)</td>
</tr>
<tr>
<td>MPI (ms)</td>
<td>0.49 (0.16–1.12)</td>
<td>0.44 (0.08–1.6)</td>
<td>0.56 (0.19–1.06)</td>
<td>0.38 (0.2–1.06)</td>
</tr>
<tr>
<td>Ea (cm/s)</td>
<td>7.9 (4–20.3)</td>
<td>7.6 (2.6–18)</td>
<td>8.0 (4.1–20)</td>
<td>8.9 (4.7–20)</td>
</tr>
<tr>
<td>E/Ea</td>
<td>4.3 (1.5–7.3)</td>
<td>4.3 (1.7–12.9)</td>
<td>4.2 (1.5–10.3)</td>
<td>4.0 (1.5–8.4)</td>
</tr>
</tbody>
</table>

Values are medians (ranges). NS, non significant; Sa, peak systolic velocity recorded at the level of the tricuspid annulus; TAPSE (measured in M-mode); MPI measured as shown in Figure 1; Ea recorded at the level of the tricuspid annulus; E/Ea, ratio between E-wave of the tricuspid inflow and Ea-wave (early diastolic) recorded by pulsed tissue Doppler, at the level of the tricuspid annulus. This ratio correlates with filling pressure.31

Likewise, RV diastolic function examined by pulsed tissue Doppler showed no significant differences among BiV and other pacing modes. Ea recorded at the tricuspid annulus was the highest during BiV pacing (8.9 cm/s; Table 1).

Patients with ischaemic heart disease showed no specific differences compared with those without ischaemia.

Discussion

The main finding of the present study was that Sa, an index of RV function and of prognosis in chronic CHF,10,11 was significantly improved by BiV pacing during an acute comparison vs. atrial, RV- and LV-pacing. Many studies have highlighted the beneficial effects of BiV pacing on LV function and dimensions.4,5,7,17–20 Despite the predictive role of RV dysfunction on mortality and non-fatal cardiac events, the impact of CRT on RV function has not been widely studied.13 Most studies have used RVEF measured by radionuclide ventriculography or thermo-dilution techniques as an index of RV function.9–13 Echocardiography has been used less frequently probably on account of the relative complexity of the RV geometry.21,22 The RV is composed of two main chambers, and its systolic function is determined by two components. The first, related to circular fibres shortening, is particularly challenging to assess with Doppler-echocardiographic techniques.23 Therefore, echocardiography has mostly focused on the longitudinal component of RV systolic function,16–18 and a fairly close correlation between the magnitude of TAPSE and radionuclide ventriculography has been reported.21 More recently, an equivalent correlation was reported for Sa measured using pulsed-wave TDI.12,24 Furthermore, Sa was closely correlated with prognosis in patients with CHF. As demonstrated by Meluzin et al. with a cut-off value of 10.8 cm/s, the RV peak systolic velocity (Sa, cm/s) has also been shown to be sensitive in the early detection of RV dysfunction in Chagas’ disease, in contrast to conventional parameters.17,25

Our study confirms the sensitivity of Sa in a pacing CHF-population. Myocardial performance index has also been proposed as a non-geometric measurement of RV function, and its clinical value and correlation with patient survival has been demonstrated.26,27 However, MPI appears less sensitive than Sa. The trends of these two variables were parallel, but only Sa variations were significant (Sa, cm/s).

A significant increase in RV peak systolic velocity (Sa, cm/s) during BiV pacing might be of clinical importance since, to the best of our knowledge, this study is the first to...
demonstrate a significant increase in this parameter. We may hypothesize, from these acute results, that only BiV-pacing provides a significant beneficial effect on RV function. However, further studies in large groups of patients are necessary. As a matter of fact, the RV is highly sensitive to pre-load and pulmonary arterial pressures. The beneficial effects of BiV pacing on the LV, as previously demonstrated acutely, might have influenced these results. Nevertheless, in our study, increase in RV peak systolic velocity (Sa, cm/s) was not observed during LV pacing despite its positive impact on LV haemodynamics.

Thus, at least acutely, BiV appears preferable to LV pacing by the beneficial effect it exerts on RV function, which is known to be critically important in the functional status and survival of patients with CHF.

Study limitations

This was an acute study, performed in a small population. The quantitative echocardiographic evaluation was performed online by two physicians. No testing of the reproducibility of echocardiographic parameters was performed.

The global echocardiographic assessment of RV-function in the different modes of pacing implied a too prolonged examination to consider in routine practice.

Despite these limitations, we believe that our findings might be of clinical interest. However, further large studies are needed to confirm these results.

Conclusions

This acute study showed that RV systolic function was significantly improved by BiV pacing compared with AAI, RV and LV pacing in CRT recipients, with a significant increase in the peak systolic velocity (Sa, cm/s).

References


