Effect of triangle ventricular pacing on haemodynamics and dyssynchrony in patients with advanced heart failure: a comparison study with conventional bi-ventricular pacing therapy

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Aims This study examined the impact of cardiac resynchronization therapy (CRT) by triangle ventricular pacing (Tri-V) on left ventricular (LV) function and dyssynchrony.

Methods and results Twenty-one patients with NYHA class III or IV heart failure were studied. For Tri-V, two right ventricular (RV) leads were connected to the CRT device via a Y-connector with one lead anchored at the RV apex and the other at the RV outflow tract. The LV lead was positioned in the posterolateral or lateral cardiac vein. CRT with standard bi-ventricular pacing (Bi-V) was performed with the RV apical and LV leads. LV function was assessed by the measurement of LV positive dP/dt (dP/dt max) and cardiac output (CO). LV dyssynchrony was assessed using the standard deviation of the time to peak myocardial velocity during the systolic phase in 12 LV segments (Ts-SD) derived from tissue Doppler images. In comparison to Bi-V, Tri-V increased dP/dt max (baseline, 746 ± 165; Bi-V, 909 ± 186; Tri-V, 959 ± 195 mmHg/s, P = 0.04) and CO (baseline, 3.1 ± 1.0; Bi-V, 3.4 ± 1.1; Tri-V, 3.8 ± 1.2 L/min, P < 0.001), decreased Ts-SD (baseline, 54.0 ± 35.0; Bi-V, 33.6 ± 15.3; Tri-V, 22.4 ± 8.1 ms, P = 0.02).

Conclusion The acute beneficial effects of Tri-V on LV function and dyssynchrony were greater than those of Bi-V.

KEYWORDS Cardiac resynchronization therapy; Heart failure; Haemodynamics; Echocardiography

Introduction Cardiac resynchronization therapy (CRT) by means of bi-ventricular pacing (Bi-V) has been established as a non-pharmacologic therapy for patients with drug-refractory heart failure and dyssynchrony. In large clinical trials, the inclusion criteria for Bi-V were (i) New York Heart Association (NYHA) class III or IV heart failure despite an optimized medical therapy, (ii) depressed left ventricular (LV) ejection fraction (<35%), and (iii) a wide QRS complex (duration >120 ms) with left bundle branch block (LBBB) morphology.† These trials showed that Bi-V significantly improved heart failure symptoms, quality of life, exercise tolerance, and LV systolic performance. However, 20–30% of patients do not respond to Bi-V. An inadequate selection criteria based on QRS duration for identifying potential responders resulted in a high rate of non-responders. Therefore, the use of echocardiography to quantify LV dyssynchrony has become a useful method for predicting a patient’s response to Bi-V. However, despite the careful selection of patients on the basis of those inclusion criteria and echocardiographic parameters, a significant number of patients do not respond to Bi-V. For such non-responders, we devised a novel CRT technology based on ‘triangle ventricular pacing’ (Tri-V), in which the conventional Bi-V of the right ventricular (RV) apex (RVA) and left ventricle is combined with pacing in the RV outflow tract (RVOT).
In previous reports, 'triple-site pacing,' i.e. standard bi-ventricular cathodal pacing of the right and left ventricles plus occasional anodal capture by the RV proximal-ring electrode, was described in high-output settings. However, this was an accidentally discovered phenomenon and was not intended to be used to obtain better resynchronization, and we hypothesized that the tip and ring electrodes of the standard bipolar RV lead were too close to each other to produce a significant resynchronization effect. In this respect, our strategy of using Tri-V differs from that in the previous reports and appears to provide better LV performance in comparison to that of conventional Bi-V. The aim of this study was to investigate the potential benefit of Tri-V on LV resynchronization and function in comparison to that of Bi-V in consecutive patients referred for CRT.

Methods
Patients
Twenty-one patients (14 men and 7 women; mean age, 64.0 ± 12.3 years) who underwent CRT were enrolled. The inclusion criteria included severe symptomatic heart failure despite optimal pharmacologic therapy. The baseline characteristics of these patients are summarized in Table 1. The patients were in NYHA class III (n = 14) or IV (n = 7) heart failure and had evidence of LV systolic dysfunction with an ejection fraction of <35% and QRS duration >120 ms in the form of a bundle branch block or intraventricular conduction delay. The aetiology of the heart failure was ischaemic in 5 patients and non-ischaemic in 16. The intrinsic rhythm at baseline was sinus rhythm in 19 patients and sinus rhythm with complete atrioventricular block in 2 patients (who were upgraded from a conventional pacemaker to a CRT device). Medications included diuretics in 95% of the patients, angiotensin converting enzyme inhibitors or angiotensin receptor blockers in 19 (90.5%), β-blockers in 16 (76.2%), and digoxin in 3 (14.3%). The study was approved by the local research ethics committee of Tsukuba University Hospital, and the patients gave their written informed consent.

Study protocol
After a placement of three ventricular leads and an atrial lead, we measured the pacing threshold of each lead and estimated the characteristics of paced-QRS morphology at each pacing site using a pacing system analyzer (Carelink 2090, Medtronic Inc., Minneapolis, MN, USA), which has one atrial pacing channel and one ventricular pacing channel. Catheter-based haemodynamic and echocardiographic variables in the following predetermined configurations of ventricular pacing were evaluated before connection of the leads to the CRT device.

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics</th>
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<tbody>
<tr>
<td>Age (years)</td>
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<tr>
<td>Sex (male/female)</td>
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<tr>
<td>IHD/non-IHD</td>
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<tr>
<td>QRS duration (ms)</td>
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<tr>
<td>NYHA III/IV</td>
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<tr>
<td>Medication, n (%)</td>
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<tr>
<td>β-blockers</td>
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<tr>
<td>ACE inhibitor/ARB</td>
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<tr>
<td>Diuretics</td>
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<tr>
<td>Digoxin</td>
</tr>
<tr>
<td>IHD, ischaemic heart disease; ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers.</td>
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</tbody>
</table>

• Baseline (intrinsic rhythm and/or AAI mode). A bipolar atrial lead was connected to the atrial pacing port of the pacing system analyzer with temporary jumper cables.
• Bi-V with RVA and LV lateral pacing. The RVA lead was connected to the anodal port of the bipolar ventricular output of the pacing system analyzer, and the LV lead was connected to the cathodal port of the bipolar ventricular output. When pacing output is above the level of anodal threshold, Bi-V begins using the RVA lead as anode and the LV lead as cathode. We could confirm initiation of Bi-V by observing the change in the paced-QRS morphology.

Pacemaker implantation
Modification of the pacemaker device to obtain triangle ventricular pacing
During the period of the study, second- and third-generation CRT devices and CRT-defibrillators were not available in Japan. First-generation CRT devices (Insync 8040, Medtronic Inc.) were implanted transvenously in all patients. The available multi-site pacemakers currently in use have only two ventricular pacing channels, one for the RV lead and one for the LV lead. We used a Y-connector (5866-38M, Medtronic Inc.) to make the modifications necessary to obtain Tri-V. First, we connected the Y-connector to the RV channel of the CRT device to bifurcate the anode and cathode of the bipolar output. Next, we connected the RVA lead to the anodal port of the Y-connector and the additional lead, which was positioned in the RVOT, to the cathodal port of the Y-connector. When the output of the pacemaker was set at a level greater than the anodal threshold, the ventricle was depolarized from all three sites, the LV lateral wall (cathode), RVOT (cathode), and RVA (anode), providing a triple-site contraction (Figure 2).

Lead type and target vein selection
Standard techniques for transvenous delivery of the CRT system have been described previously (Figure 3). Positioning of the leads was guided by both fluoroscopy and endocardial signal recordings. Selection of lead type, lead placement, and target vein were as follows.
Atrial lead placement

We selected a bipolar tined-type lead for atrial pacing in all patients (CAPSURE NOVUS 5554, Medtronic Inc., in 17 patients and IsoFlex™ S 1642T, St Jude Medical St Paul, MN, USA in 4 patients). The atrial lead was implanted in the right atrial appendage according to conventional method.

Right ventricular apex lead placement

We selected a bipolar screw-in type lead for RVA pacing in all patients (CAPSURWFIX NOVUS 5076, Medtronic Inc.), but the proximal ring-electrode was not used in our Tri-V system. The RVA lead was implanted in the apicoseptal region (a site as far as possible from the base) according to the conventional method.

Left ventricular lead insertion

We selected a large-diameter, stylet-driven unipolar lead (Attain LV 2187, Medtronic Inc.) in the first 16 consecutive patients and a smaller-diameter over-the-wire unipolar lead (Attain OTW 4193, Medtronic Inc.) in the remaining 5 patients. After performing retrograde coronary venography, we selected a lateral or posterolateral vein as the target branch of the coronary sinus to stimulate the basal or mid-lateral free wall of the LV. If attempts to access these veins were impossible due to an unusual anatomy preventing access to the coronary sinus or which resulted in poor sensing, phrenic nerve stimulation, or pacing failure, the middle cardiac vein was used as an alternative branch.

Right ventricular outflow tract lead placement

A bipolar screw-in type lead (CAPSURWFIX NOVUS 5076, Medtronic Inc.) was used in all patients. The proximal ring-electrode of the RVA lead was not needed. RVOT lead placement involved four steps: (i) advancing the lead into the pulmonary artery through the right atrium and right ventricle using a sharp angled stylet, (ii) exchanging to a gently curved stylet, (iii) pulling the lead toward the RVOT while simultaneously applying counterclockwise torque to the lead to direct it to the septal wall of the subpulmonary RVOT as close as possible to the LV. To produce the expected effect of Tri-V, it is very important to point the lead to the septal side, which is on the exact opposite side of the basal/anteroseptal wall of the LV.15

Cardiac catheterization

Left-sided cardiac catheterization was performed via the femoral artery approach using a 5F high-fidelity, micromanometer-tipped pigtail angiographic catheter (SPC-464D, Millar Instruments Inc., Houston, TX, USA). The micromanometer pressure was matched to the pressure of the fluid-filled lumen. LV pressure signals were digitized and analysed on a computer system (PC-9821-ST20, NEC, Tokyo, Japan) with software developed in-house. The LV peak systolic pressure (LVP) and LV end-diastolic pressure (LVEDP) were measured. The peak positive $dP/dt$ ($dP/dt_{max}$) was measured to evaluate global systolic function. Right heart cardiac catheterization was performed via the femoral vein approach. An 8F balloon-tipped, thermistor-equipped Swan-Ganz catheter (Baxter Healthcare, Irvine, CA, USA) was used to measure the pulmonary capillary

Figure 1 Twelve-lead electrocardiograms of a representative patient. (A) Wide QRS complexes (180 ms) with left bundle branch morphology at baseline. (B) Positive R waves in inferior leads during right ventricular outflow tract (RVOT) pacing. (C) QRS complexes during bi-ventricular pacing (Bi-V) with left ventricular and RVOT pacing. (D) Narrower QRS complexes (160 ms) during Bi-V with LV and RVA pacing. (E) Narrowest QRS complexes (110 ms) during Tri-V.
wedge pressure (PCWP) and cardiac output (CO), and its position was verified by fluoroscopy. The PCWP was measured at end-expiration, and the reported values represent the average of 5–10 cardiac cycles.

**Echocardiography**

Echocardiographic examinations were performed simultaneously with catheter-based haemodynamic evaluations. Echocardiographic examinations were performed simultaneously with catheter-based haemodynamic evaluations.

All Doppler echocardiographic examinations were performed with a Vivid 7 system (GE Vingmed Ultrasound, Horten, Norway) equipped with a multifrequency transducer. The LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LV ejection fraction (EF) were measured using a modified Simpson’s method. Colour-coded tissue Doppler images (TDI) were obtained in the apical 4-chamber, 2-chamber, and long-axis views. The image sector was set as narrow as possible, which resulted in a frame rate greater than 100 frames/s, and a cine-loop of 3 consecutive beats was stored for off-line analysis using a software package (EchoPac 6.3.6, GE Yokogawa Medical Systems, Tokyo, Japan).

**Parameters derived from myocardial tissue velocity**

Myocardial tissue velocity curves were obtained, placing the sample volume on 12 LV segments: basal and mid-ventricular segments of the anteroseptal, anterior, lateral, inferior, and inferoseptal walls. In patients with a markedly dilated LV, the sample volume position was modified to orient the LV wall as parallel as possible to the central ultrasound beam.

Figure 2 (A) Endocardial activation map of the left ventricular depicted by electroanatomical mapping system during triangle ventricular pacing (Tri-V). The activation sequence is shown in the colour order of red, yellow, green, blue, and purple. Local electrograms at the breakthrough sites from right ventricular (RV) apex pacing (a), RV outflow tract pacing (b), LV lateral pacing (c), and the latest endocardial activation site (d) are shown in this map. Site ‘a’ was the earliest activation site, which was depolarized 66 ms after the stimulation spike, and sites ‘b’ and ‘c’ were simultaneously depolarized 15 ms after the depolarization of site ‘a.’ Site ‘d’ had a fractionated delayed electrogram. (B) Propagation map during Tri-V. LVA, LV apex; LVL, lateral wall of LV; LVBA, basal/anterior wall of LV.

Figure 3 Typical lead locations in Tri-V in the right anterior oblique view (A) and left anterior oblique view (B). RVA, right ventricular apex; RVOT, right ventricular outflow tract; LV, left ventricle.
In the myocardial tissue velocity curve (Figure 4), the time to peak myocardial velocity during the systolic phase (Ts) was measured with reference to the QRS complex. Intraventricular dyssynchrony was identified with a parameter derived from TDI: the standard deviation of Ts for the 12 segments (Ts-SD).\(^9\) Interventricular dyssynchrony between the RV and LV was identified as the maximal difference in Ts between the basal lateral segment of the RV and the most delayed segment among the 12 LV segments (Ts\(_{\text{int}}\)). Eight patients were selected at random for the assessments of the intraobserver and interobserver reproducibilities of Ts measurements. To test intraobserver variability, a single observer analysed the data twice on occasions separated by an interval of 1 month. To test interobserver variability, a second observer analysed the data without the knowledge of the first observer’s measurements. Reproducibility was assessed as the mean percent error (absolute difference divided by the mean of the two observations).

### Statistical analysis

Results are expressed as the mean value ± SD. One-way analysis of variance (ANOVA) for repeated measures was used to compare the results between the variables obtained with the various pacing configurations, and ANOVA was used to compare the Ts between the RV and 6 LV segments. When significant differences between groups were present, the Scheffe test was used to compare individual groups. Correlation analysis was used to compare the relation of percent change in CO and dP/dt\(_{\text{max}}\). A P-value <0.05 was considered to indicate statistical significance. The StatView J-5.0 statistical program (Abacus Concepts, Inc., Berkeley, CA, USA) was used for the analyses.

### Results

#### Target vein selection

We performed transvenous delivery of CRT in all patients. Both the RVA and RVOT leads were placed in the optimal sites described above in all patients, and the LV lead was placed in the lateral branch in 15 patients, posterolateral branch in 4 patients, and middle cardiac vein in 2 patients. There were no major complications such as a coronary sinus dissection or cardiac tamponade.

#### Pacemaker settings

To provide anodal pacing in the RVA, we had to program high-output pacemaker settings. We confirmed anodal capture at the RVA by change of QRS morphology. We could recognize three different paced QRS morphologies in all patients as the pacing output was gradually decreased.
When the stimulation width was fixed at 0.4 ms, the voltage threshold was $3.9 \pm 1.9$ V (range: $2.0-7.5$ V). The stimulation output could be set with a margin of at least twice the threshold. We confirmed that phrenic nerve stimulation did not occur at the maximum output setting. The optimized AV interval based on the echocardiographic variables was $119 \pm 18$ ms.

**Haemodynamic responses**

The effects of CRT on QRS duration and haemodynamic parameters are summarized in Table 2. Tri-V dramatically shortened the QRS duration compared with Bi-V. Similar effects on LVP, LVEDP, and PCWP were observed between both CRT modes. Both CRT modes increased the $dP/dt_{\text{max}}$ compared with the baseline study, and Tri-V significantly increased the $dP/dt_{\text{max}}$ compared with Bi-V (baseline, $746 \pm 165$; Bi-V, $909 \pm 186$; Tri-V, $959 \pm 195$ mmHg/s; Figure 5). Both CRT modes also increased the CO compared with the baseline study, and Tri-V significantly increased the CO compared with Bi-V (baseline, $3.1 \pm 1.0$; Bi-V, $3.4 \pm 1.1$; Tri-V, $3.8 \pm 1.2$ L/min). The percent change in the $dP/dt_{\text{max}}$ and CO between the baseline study and Tri-V ($dP/dt_{\text{max}}$, $30.4 \pm 22.3\%$; CO, $21.4 \pm 13.7\%$) were significantly greater than those between the baseline study and Bi-V ($dP/dt_{\text{max}}$, $24.3 \pm 23.5\%$, $P = 0.002$; CO, $9.1 \pm 16.2\%$, $P < 0.001$).

**Resynchronization effect**

Of a total of 252 LV segments in the 21 patients, Ts was measurable in 240 segments (95.2%). With respect to reproducibilities of Ts measurements, the mean intraobserver percent error was $5.1 \pm 3.1\%$, whereas the mean interobserver percent error was $5.5 \pm 3.5\%$. The effects of CRT on conventional and tissue Doppler echocardiographic parameters are summarized in Table 3. Compared with the baseline study, the LVESV was decreased, and EF increased, by Tri-V. Both CRT modes significantly improved inter- and intraventricular dyssynchrony. When comparing the Ts in each segment between baseline, Bi-V, and Tri-V, both CRT modes significantly decreased Ts in the basal, mid-lateral, and posterior walls compared with Ts at the baseline study. In contrast, Tri-V significantly decreased Ts in basal and mid-anterior walls compared with Ts at the baseline study. Compared with Bi-V, Tri-V significantly decreased Ts-SD ($P = 0.03$) but did not decrease $T_{\text{inter}}$ ($P = 0.12$). The variability of Ts in the RV and 6 LV segments during baseline, Bi-V, and Tri-V are shown in Figure 6, in which the mean Ts of basal and mid-LV segments were used as a surrogate measure of Ts.

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**Table 3 Conventional and tissue Doppler echocardiographic parameters**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Bi-V</th>
<th>Tri-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV (mL)</td>
<td>$231 \pm 91$</td>
<td>$225 \pm 89$</td>
<td>$225 \pm 86$</td>
</tr>
<tr>
<td>LVESV (mL)</td>
<td>$174 \pm 77$</td>
<td>$165 \pm 75$</td>
<td>$157 \pm 74^*$</td>
</tr>
<tr>
<td>EF (%)</td>
<td>$25.5 \pm 5.8$</td>
<td>$27.2 \pm 6.2$</td>
<td>$29.3 \pm 7.1^*$</td>
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<tr>
<td>Ts (ms)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV</td>
<td>$195 \pm 58.4$</td>
<td>$207 \pm 48.0$</td>
<td>$214 \pm 49.1$</td>
</tr>
<tr>
<td>Basal-As (ms)</td>
<td>$209 \pm 66.9$</td>
<td>$223 \pm 67.4$</td>
<td>$221 \pm 54.0$</td>
</tr>
<tr>
<td>Mid-As (ms)</td>
<td>$209 \pm 63.4$</td>
<td>$227 \pm 64.0$</td>
<td>$225 \pm 56.5$</td>
</tr>
<tr>
<td>Basal-Ant (ms)</td>
<td>$272 \pm 92.6$</td>
<td>$250 \pm 70.7$</td>
<td>$218 \pm 61.0^*$</td>
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<tr>
<td>Mid-Ant (ms)</td>
<td>$281 \pm 78.8$</td>
<td>$253 \pm 72.0$</td>
<td>$223 \pm 64.6^*$</td>
</tr>
<tr>
<td>Basal-Lat (ms)</td>
<td>$281 \pm 77.5$</td>
<td>$241 \pm 70.7^*$</td>
<td>$236 \pm 63.2^*$</td>
</tr>
<tr>
<td>Mid-Lat (ms)</td>
<td>$284 \pm 78.7$</td>
<td>$240 \pm 73.3^*$</td>
<td>$238 \pm 62.9^*$</td>
</tr>
<tr>
<td>Basal-Post</td>
<td>$281 \pm 81.8$</td>
<td>$233 \pm 52.3^*$</td>
<td>$238 \pm 54.1^*$</td>
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<tr>
<td>Mid-Post (ms)</td>
<td>$289 \pm 76.8$</td>
<td>$239 \pm 60.7^*$</td>
<td>$241 \pm 60.4^*$</td>
</tr>
<tr>
<td>Basal-Inf (ms)</td>
<td>$245 \pm 75.8$</td>
<td>$239 \pm 60.9$</td>
<td>$226 \pm 62.6$</td>
</tr>
<tr>
<td>Mid-Inf (ms)</td>
<td>$246 \pm 75.0$</td>
<td>$236 \pm 60.0$</td>
<td>$229 \pm 68.9$</td>
</tr>
<tr>
<td>Basal-Is (ms)</td>
<td>$205 \pm 70.1$</td>
<td>$219 \pm 56.2$</td>
<td>$217 \pm 54.3$</td>
</tr>
<tr>
<td>Mid-Is (ms)</td>
<td>$206 \pm 67.8$</td>
<td>$226 \pm 57.3$</td>
<td>$220 \pm 55.4$</td>
</tr>
<tr>
<td>$T_{\text{inter}}$ (ms)</td>
<td>$159 \pm 89$</td>
<td>$87.5 \pm 39.1^*$</td>
<td>$61.0 \pm 24.0^*$</td>
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<tr>
<td>Ts-SD (ms)</td>
<td>$54.0 \pm 35.0$</td>
<td>$33.6 \pm 15.3^*$</td>
<td>$22.4 \pm 8.1^<em>$</em>**</td>
</tr>
</tbody>
</table>

Data are presented as the mean $\pm$ SD. Bi-V, bi-ventricular pacing; Tri-V, triangle ventricular pacing; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; EF, ejection fraction; Ts, time to peak myocardial velocity during the systolic phase; RV, right ventricular; As, anteroseptal; Ant, anterior; Lat, lateral; Post, posterior; Inf, inferior; Is, inferoseptal; other abbreviations are described in the text.

* $P < 0.05$ vs. baseline.
** $P < 0.01$ vs. baseline.
*** $P < 0.05$ vs. Bi-V when comparing between baseline, Bi-V, and Tri-V.
based on the similar $T_s$ between basal and mid segments (Table 3). At the baseline study, $T_s$ in the LV anterior, lateral, and posterior walls was significantly greater than that in the RV, LV anteroseptal, and inferoseptal walls. During Bi-V, $T_s$ in the LV anterior wall was significantly greater than that in the LV anteroseptal and inferoseptal walls. In addition, $T_s$ in the LV anterior and lateral walls was significantly greater than that in the RV. In contrast, during Tri-V, there was no significant difference between RV and LV segments.

The percent change in $T_s$-SD between the baseline study and Tri-V ($-46.7 \pm 25.8\%$) was significantly decreased compared with that between the baseline study and Bi-V ($-28.3 \pm 26.9\%, P < 0.001$). The percent change in $T_{s\text{inter}}$ between the baseline study and Tri-V was not more statistically significant than that between the baseline study and Bi-V ($-44.7 \pm 38.2\%$ vs. $-29.0 \pm 356.4\%, P = 0.07$).

**Correlation between percent change in parameters of dyssynchrony and haemodynamics**

The correlation between the percent change in $T_{s\text{inter}}$ and those in CO and $\frac{dP}{dt}_{\text{max}}$ are shown in Figure 7. Significant but weak correlations were observed during Tri-V but not observed during Bi-V. In contrast, similar negative correlations between percent change in $T_s$-SD and those in CO

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**Figure 6** Time to peak myocardial velocity during the systolic phase ($T_s$) in one right ventricular (RV) segment and the mean of 6 basal and 6 mid-ventricular segments of the left ventricle at baseline is indicated by a blue bar, during bi-ventricular pacing (Bi-V) by a green bar, and during triangle ventricular pacing (Tri-V) by a red bar. As, anteroseptal; Ant, anterior; Lat, lateral; Post, posterior; Inf, inferior; Is, inferoseptal. *$P < 0.01$ vs. RV, As, Is at baseline, ‡$P < 0.05$ vs. As, Is at Bi-V, §$P < 0.05$ vs. RV at Bi-V.

**Figure 7** Correlation between percent change of $T_{s\text{inter}}$ and that of the left ventricular peak positive $\frac{dP}{dt}$ ($\frac{dP}{dt}_{\text{max}}$) and cardiac output (CO) between baseline and bi-ventricular pacing (Bi-V) and triangle ventricular pacing (Tri-V). $T_{s\text{inter}}$, the maximal difference of the $T_s$ between the basal lateral segment of the RV and the most delayed segment among the 12 LV segments.
and $dP/dt_{\text{max}}$ were observed during both CRT modes (Figure 8).

**Discussion**

The present study showed that Tri-V improved LV function with better resynchronization effects, when compared with Bi-V. Confirmation of these results by the combined use of Doppler echocardiographic and catheter-based haemodynamic measurements strengthens the findings of our study.

**Electrical resynchronization by triangle ventricular pacing**

We hypothesized that conventional Bi-V in patients with severe heart failure and LBBB cannot produce a sufficient resynchronization effect in the LV anterior free wall, even if the LV lead is inserted in an optimal site and the AV and VV intervals are optimized, because the anterior free wall is so far from each pacing site in Bi-V mode that the conduction time for each Bi-V wavefront to propagate to the anterior free wall is too long.

On the basis of CARTO mapping in the normal heart, the first site of endocardial LV activation (endocardial breakthrough site from the Purkinje fibres to the working myocardium) was usually at the interventricular septum or in the anterior region.\textsuperscript{16,17} During Bi-V delivered with a short AV delay that pre-empted the intrinsic conduction through the AV node, the initial LV endocardial breakthrough site occurred not in the anterior region but in the mid- or apical LV septum,\textsuperscript{16,18,19} and thus the anterior free wall was one of the last structures in the LV to be depolarized during Bi-V.

In contrast, activation mapping of the LV performed during Tri-V and depicted by CARTO in a patient with NYHA class IV heart failure and LBBB showed that an initial LV endocardial breakthrough occurred in the LV apex (originating from RVA pacing) and almost simultaneously (15 ms later), the activation originating from RVOT pacing began in the LV basal/anterior region, and the activation originating from LV pacing began in the LV lateral region (Figure 2). In other words, the activation pattern of the LV during Tri-V was more similar to the activation pattern of the normal heart than that during Bi-V with an optimal short AV delay, especially for the activation of the anterior free wall. We believe this must be the reason why Tri-V dramatically shortened the QRS duration (Figure 1).

**Mechanical resynchronization by triangle ventricular pacing**

Tri-V significantly increased the $dP/dt_{\text{max}}$ and CO when compared with Bi-V. Previous studies have shown the percent
change in the $dP/dt_{\text{max}}$ caused by Bi-V to be between 15 and 35%. In the present study, the percent change in the $dP/dt_{\text{max}}$ obtained during Bi-V was similar to previously reported values under an optimal AV delay determined by Doppler echocardiography. Therefore, our study indicates that Tri-V improves LV contractility when compared with standard Bi-V.

An important mechanism of CRT in improving LV systolic function is the resynchronization of intra- or interventricular mechanical dyssynchrony. Recent studies have shown the importance of the evaluation of dyssynchrony by echocardiography in identifying patients who will respond to CRT. Although an index of dyssynchrony obtained by Doppler echocardiography has not been established, an index devised by Yu et al., which was determined as the standard deviation of Ts for the 12 LV segments by tissue Doppler methods has been shown to be reliable. We showed that the Yu index values during Tri-V decreased significantly compared with those during Bi-V. On the basis of LV regional tissue Doppler analysis, an important mechanism of improved resynchronization by Tri-V may be the resynchronization of the LV anterior free wall. The effect may be correlated with earlier depolarization of the LV anterior free wall benefiting from the additional RVOT pacing. In addition, we showed the relation between the acute improvement in dyssynchrony index and systolic function. These integrated data support our concept that Tri-V has greater acute beneficial effects on improvement of LV function and dyssynchrony than does Bi-V.

**Clinical implications**

We showed that the improvements in intraventricular mechanical dyssynchrony correlated with improvements in LV systolic performance based on the data obtained during Bi-V and Tri-V. These data suggest that better resynchronization contributes to a greater improvement in LV function, independent of the configuration of the CRT. In the clinical setting, our concept may not be applicable in all patients referred for CRT because our method requires relatively complex techniques. However, in patients not receiving adequate improvement in their heart failure symptoms, intraventricular dyssynchrony, and cardiac function by Bi-V, Tri-V should be considered as a viable treatment option for CRT.

**Limitations**

This study showed an improvement in CO by Tri-V in comparison to Bi-V mainly because of better resynchronization and improvement in LV contractility. In contrast, mitral regurgitation is reduced immediately after CRT. Although the improvement in CO may be associated with the acute reduction of mitral regurgitation, we did not evaluate the degree of mitral regurgitation in the present CRT study. Mitral regurgitation as a contributor to CO improvement must be confirmed in a future study.

The haemodynamic condition in patients with chronic heart failure may change during the acute haemodynamic and echocardiographic study. Although it would be ideal to test each pacing configuration in random order, they were tested in fixed order in this study. However, a 3 min interval of baseline rhythm was inserted between each pacing configuration, and the data from Tri-V was compared with the best value of AAI or Bi-V, which was tested before and after Tri-V to minimize any interference caused by the prior pacing configuration.

The study population was of relatively small size, and the majority of the patients had non-ischaemic heart disease. Considering the concept of Tri-V, the viability of the LV anterior to lateral wall in patients with ischaemic heart disease might limit the beneficial effects of Tri-V. Therefore, future studies consisting of a larger number of patients, including those with ischaemic heart disease, are required to confirm the beneficial effects of Tri-V. In addition, we evaluated resynchronization and haemodynamic effects only in the acute phase. Further long-term evaluation will be needed to confirm the chronic benefits of Tri-V.

**Conclusion**

Tri-V has greater acute beneficial effects on improvement of LV function and dyssynchrony than does Bi-V because of Tri-V's capacity to produce better resynchronization of the LV anterior free wall through the addition of RVOT pacing. Therefore, Tri-V may be an effective technology in the treatment of patients with advanced heart failure.

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**References**


