Multidirectional left ventricular performance detected with three-dimensional speckle-tracking strain in patients with chronic right ventricular pacing and preserved ejection fraction

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Aims

Although right ventricular (RV) pacing has a detrimental effect on global left ventricular (LV) function even in some patients with preserved ejection fraction (EF), its mechanism remains unclear.

Methods and results

We studied 116 subjects; 56 patients with RV pacing and preserved EF (all ≥50%), 30 EF-matched controls, and 30 heart failure (HF) patients with RV pacing and reduced EF (all ≤35%). Radial, circumferential, and longitudinal dys-synchrony and function were quantified as standard deviations of the time-to-peak strain and global peak strain from all 16 LV segments using three-dimensional (3D) speckle-tracking strain. The degree of radial and circumferential dyssynchrony and function were similar for patients with RV pacing and preserved EF and controls. However, patients with RV pacing and preserved EF showed a greater longitudinal dyssynchrony of 46 ± 14 vs. 31 ± 9 ms (P < 0.01) and lower global longitudinal strain at 25 ± 4 vs. 34 ± 7% compared with controls (P < 0.001). Furthermore, longitudinal strain at the apical level was significantly lower than that at the mid- and basal level (20 ± 4 vs. 27 ± 5 and 26 ± 5%, P < 0.001), and longitudinal dyssynchrony at the apical level was significantly larger than at the mid- and basal level (44 ± 19 vs. 36 ± 20 and 32 ± 15 ms, P < 0.05) in patients with RV pacing and preserved EF. In contrast, HF patients with RV pacing and reduced EF showed greater radial, circumferential, and longitudinal dyssynchrony, and lower global radial, circumferential, and longitudinal strain than did controls (all P < 0.001).

Conclusion

Three-dimensional speckle-tracking strain was found to be useful for evaluating early subtle changes associated with chronic RV pacing, and may thus play a clinical role in predicting future global LV dysfunction.

Keywords

Echocardiography • Pacing • Speckle tracking • Dyssynchrony • 3D echocardiography

Introduction

Right ventricular (RV) pacing is the only effective treatment for patients with symptomatic atrioventricular block. Several trials have shown that conventional RV pacing is associated with left ventricular (LV) dysfunction and an increased risk of heart failure (HF) and death.1–4 Although the exact cause of the deleterious effects of RV pacing, specifically from the apical site, is not known, the prevailing hypothesis is that RV pacing may create mechanical dys-synchrony, which in turn may induce LV dysfunction and clinical HF.5,6 Furthermore, RV pacing has a detrimental effect on global LV function even in some patients with preserved ejection fraction (EF).7 Therefore, interest is high in the time course of LV dysfunction in these patients as a result of RV pacing because of its potential for predicting future global LV dysfunction. However, the assessment of global LV function such as EF is a relatively insensitive measure of LV dysfunction because of the...
function compared with the assessment of regional LV myocardial function, especially in the context of subclinical LV systolic dysfunction. This is due to the LV myocardial architecture, which is a complex array of longitudinally and circumferentially oriented fibres located predominantly in the epicardium/endoocardium and mid-wall, respectively.7 Multidirectional analysis of longitudinal, circumferential, and radial functions has contributed to a better understanding of regional LV myocardial functional changes in patients with subclinical heart disease. A newly developed three-dimensional (3D) speckle-tracking system using complete 3D pyramidal data sets can quantify LV dyssynchrony and function.8–10 The potential advantages of such a system are the ability to express myocardial function of the whole heart, independence of tomographic imaging planes, and the ability to analyse regional ventricular function using three different strains from the same heartbeat acquisition. Thus, the 3D speckle-tracking strain imaging system was found to be useful for the quantification of LV performance in a manner not previously possible when using 2D methods.

Accordingly, the objectives of this study were to evaluate with the aid of the novel 3D speckle-tracking strain imaging system early subtle changes caused by chronic RV pacing in patients with preserved EF, and to reach a hypothesis concerning the utility of the time course of LV dysfunction in these patients for predicting future global LV dysfunction.

Methods

Study populations

The study group consisted of 63 consecutive patients with chronic RV pacing and preserved EF (all ≥50%). Five patients (8%) were excluded from all subsequent analyses because of suboptimal quality of images to be used for echocardiographic analysis. Accordingly, the final study group consisted of 58 patients and with a mean age of 67 ± 11 years, a mean EF of 59 ± 4% (all ≥50%), and a mean QRS duration of 158 ± 26 ms (all ≥120 ms). We excluded patients with: (i) coronary artery disease, defined as a single coronary artery stenosis of a major epicardial vessel >50% or a previous history of myocardial infarction; (ii) any known cause of cardiomyopathy or a history of familial cardiomyopathy; (iii) uncontrolled hypertension despite medical therapy; and (iv) significant valvular heart disease. Thirty EF- and gender-matched normal controls and 30 HF patients with chronic RV pacing and reduced EF (all ≤35%) were also studied for baseline comparison. The normal volunteers had no history of cardiovascular disease and showed completely normal electrocardiograms and 2D and Doppler echocardiograms (EF: 60 ± 3%; QRS duration: 92 ± 11 ms). All patients with chronic RV pacing had undergone implantation of a permanent dual-chamber pacemaker at least 1 year before enrolment, and the RV lead was positioned at the RV apex through a transvenous route. Patients with chronic RV pacing ≥90% on device interrogation at the time of enrolment were considered to have a paced QRS complex. All RV pacing devices were specifically programmed to minimize RV pacing.9 There was no patient with atrial fibrillation. This study was approved by the local ethics committee of our institution, and written informed consent was obtained from all patients.

Echocardiographic examination

All echocardiographic studies were acquired with a commercially available echocardiography system (Aplio Artida; Toshiba Medical Systems, Tochigi, Japan). Digital routine greyscale 2D cine loops from three consecutive beats were obtained at end-expiratory apnoea from the standard apical views (four-chamber, two-chamber, and long-axis), parasternal long-axis view, and mid-LV short-axis views at depths of 11–20 cm (mean 16 ± 2 cm). Frame rates were 44–90 Hz (mean 59 ± 11 Hz) for greyscale imaging. Sector width was optimized to allow for complete myocardial visualization while maximizing the frame rate. The LV volumes and EF were assessed by biplane Simpson’s rule using manual tracing of digital images.11

Three-dimensional echocardiographic studies were performed with a 2.5 MHz 3D matrix array transducer. Digital LV 3D volume data were obtained from the apical views using six-beat electrocardiogram-gated acquisition. Sector width was optimized to allow for complete myocardial visualization while the volume rate was maximized. The mean volume rate was 22 ± 2 volumes/s in the apical views for greyscale imaging used for 3D speckle-tracking analysis. Digital data were transferred to the dedicated software (Ultra Extend, Toshiba Medical Systems, Tochigi, Japan) for subsequent off-line analysis.

Three-dimensional speckle-tracking data acquisition

Three-dimensional speckle-tracking analysis was performed as previously described in detail.8–10 Briefly, 3D speckle-tracking used a pyramidal volume obtained from the matrix array transducer. Acquisition of a full-volume data set required six smaller wedge-shaped subvolumes from six consecutive cardiac cycles obtained during a single breath hold, which were then combined to provide the larger pyramidal volume. The 3D data sets were displayed in five different cross-sections comprising three standard short-axis views and one apical four- and two-chamber view each that could be modified interactively (Figure 1). Regions of interest were placed on the endocardium and epicardium using apical views, and the endocardium and epicardium were retraced as necessary to attain suitable tracking.

Three-dimensional speckle-tracking multidirectional dyssynchrony analysis

Radial, circumferential, and longitudinal dyssynchrony was quantified as the standard deviation of the time-to-peak strain for each of the 3D speckle-tracking strains from all 16 LV segments (Figure 1).8,9 Furthermore, dyssynchrony at three standard short-axis levels was also quantified as the standard deviation of the time-to-peak strain from each segment (four segments for the apical level, and six each for the mid- and basal level).

Three-dimensional speckle-tracking multidirectional myocardial functional analysis

Radial, circumferential, and longitudinal myocardial function was quantified as the maximum global peak strain using 3D speckle-tracking strain imaging from all 16 LV segments (Figure 1). Similar to dyssynchrony analysis, myocardial function at three standard short-axis levels was also quantified as the maximum average peak strain from each segment (four segments for the apical level and six each for the mid- and basal level).

Statistical analysis

All group data are presented as mean ± SD and was compared with the two-tailed Student’s t-test for paired data for two groups. Proportional differences were evaluated with Fisher’s exact test or the χ² test as appropriate. Differences between the groups were assessed by one- or two-way analysis of variance followed by a Tukey multiple
comparisons test. Statistical significance was defined as $P < 0.05$. The intraclass correlation coefficient was used to determine inter- and intra-observer reproducibility from 20 randomly selected subjects. All the analyses were performed with commercially available software (MedCalc software version 10.4.0.0, MedCalc Software, Inc., Maria-kerke, Belgium). The authors had full access to the data and take full responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Figure 1 An example of colour-coded 3D LV display (left), corresponding time-to-strain curves from 16 LV sites (middle), and global strain curve (right) for longitudinal (A), radial (B), and circumferential (C) speckle-tracking strain imaging. Each dyssynchrony was quantified as the standard deviation of the time-to-peak strain by using each of the 3D speckle-tracking strains from all 16 LV segments. Furthermore, each myocardial function was quantified as a maximum global peak strain by using the 3D speckle-tracking strains from all 16 LV segments.

Results

The baseline clinical and echocardiographic characteristics of the 56 patients with RV pacing and preserved EF, 30 HF patients with reduced EF, and 30 normal controls are summarized in Table 1. Overall, 3D speckle-tracking strain analysis was possible for 94% of 1856 attempted segments from 116 subjects with technically satisfactory images. Only 6% of the segments had to be
eliminated, and the eliminated segments were mostly localized at apical segments (40%). During the mean follow-up of 1.8 ± 0.7 years, no cardiovascular death or hospitalization for HF was reported in patients with RV pacing and preserved EF, whereas 10 patients with RV pacing and reduced EF were upgraded from RV pacing to biventricular pacing due to worsening HF.

**Effect of RV pacing on LV dyssynchrony**

The degree of radial and circumferential dyssynchrony in patients with chronic RV pacing and preserved EF and controls was similar (radial dyssynchrony: 32 ± 11 vs. 31 ± 10 ms, circumferential dyssynchrony: 33 ± 11 vs. 31 ± 10 ms, Figure 2). However, patients with chronic RV pacing and preserved EF showed a greater longitudinal dyssynchrony of 46 ± 14 ms compared with 31 ± 9 ms for controls (P < 0.01, Figure 2). In contrast, HF patients with chronic RV pacing and reduced EF displayed greater radial, circumferential, and longitudinal dyssynchrony than did patients with RV pacing and preserved EF and normal controls (radial dyssynchrony: 138 ± 43 vs. 32 ± 11 and 31 ± 10 ms; circumferential dyssynchrony: 139 ± 48 vs. 33 ± 11 and 31 ± 9 ms; longitudinal dyssynchrony: 113 ± 39 vs. 46 ± 14 and 31 ± 9 ms, respectively, all P < 0.001; Figure 2).

To evaluate the effect of RV pacing on longitudinal dyssynchrony at different LV short-axis levels for patients with RV pacing and preserved EF, we analysed longitudinal dyssynchrony at three standard short-axis levels. Longitudinal dyssynchrony at the apical level was significantly larger than that at the mid- and basal level (44 ± 19 vs. 36 ± 20 and 32 ± 15 ms, P < 0.001 and 0.02, respectively, Figure 3). Furthermore, averaged time-to-peak longitudinal strain in the septum was significantly earlier than that in the posterior and lateral (septum vs. posterior: 252 ± 49 vs. 301 ± 43 ms, septum vs. lateral: 252 ± 49 vs. 285 ± 62 ms, both P < 0.001, Figure 4A). Averaged time-to-peak longitudinal strain in the anterior was also significantly earlier than that in the posterior (277 ± 48 vs. 301 ± 43 ms, P < 0.001, Figure 4A).

**Effect of RV pacing on LV myocardial function**

The degree of radial and circumferential myocardial function of patients with chronic RV pacing and preserved EF and of normal controls is shown in Table 1. The data are presented as mean ± SD. AV, atrioventricular; EF, ejection fraction; RV, right ventricular.

*P < 0.001 compared with normal controls.

### Table 1  Clinical and echocardiographic characteristics of subjects

<table>
<thead>
<tr>
<th>Baseline variable</th>
<th>Patients with RV pacing and preserved EF (n = 58)</th>
<th>Normal controls (n = 30)</th>
<th>Patients with RV pacing and reduced EF (n = 30)</th>
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<tr>
<td>Age (years)</td>
<td>67 ± 11</td>
<td>63 ± 8</td>
<td>65 ± 10</td>
</tr>
<tr>
<td>Gender (women) [n (%)]</td>
<td>24 (40)</td>
<td>11 (37)</td>
<td>10 (33)</td>
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<tr>
<td>QRS duration (ms)</td>
<td>158 ± 26*</td>
<td>92 ± 11</td>
<td>162 ± 24*</td>
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<tr>
<td>End-diastolic volume (mL)</td>
<td>70 ± 17</td>
<td>71 ± 12</td>
<td>190 ± 39*</td>
</tr>
<tr>
<td>End-systolic volume (mL)</td>
<td>29 ± 8</td>
<td>28 ± 5</td>
<td>138 ± 40*</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>59 ± 4</td>
<td>60 ± 3</td>
<td>28 ± 6*</td>
</tr>
<tr>
<td>Duration of RV pacing (years)</td>
<td>3 ± 2</td>
<td>6 ± 4</td>
<td></td>
</tr>
<tr>
<td>Indications for chronic RV pacing [n (%)]</td>
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<td></td>
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<tr>
<td>Complete AV block</td>
<td>38 (66)</td>
<td>15 (50)</td>
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<tr>
<td>Sick sinus syndrome</td>
<td>10 (17)</td>
<td>7 (23)</td>
<td></td>
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<tr>
<td>AV node ablation due to atrial fibrillation</td>
<td>4 (7)</td>
<td>4 (13)</td>
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<td>2:1 AV block</td>
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<tr>
<td>Second-degree AV block</td>
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</table>

Data are presented as mean ± SD. AV, atrioventricular; EF, ejection fraction; RV, right ventricular.

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**Figure 2** Comparison of LV dyssynchrony among groups, demonstrating that the degree of radial and circumferential dyssynchrony for patients with chronic RV pacing and with preserved EF and for controls was similar. However, patients with chronic RV pacing and preserved EF showed greater longitudinal dyssynchrony compared with that of controls. On the other hand, HF patients with chronic RV pacing and reduced EF showed greater radial, circumferential, and longitudinal dyssynchrony than did patients with RV pacing and preserved EF and normal controls.

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**Figure 4A** Averaged time-to-peak longitudinal strain in the septum was significantly earlier than that in the posterior and lateral regions.
controls was similar (global radial strain: 39 ± 5 vs. 40 ± 4%, global circumferential strain: 35 ± 7 vs. 35 ± 6%, Figure 4). Patients with chronic RV pacing and preserved EF, however, showed lower global longitudinal strain at 25 ± 4 vs. 34 ± 7% than did controls (P < 0.001; Figure 4). In contrast, HF patients with chronic RV pacing and reduced EF featured lower global radial, circumferential, and longitudinal strain compared with patients with RV pacing and preserved EF and to normal controls (global radial strain: 15 ± 4 vs. 39 ± 5 and 40 ± 4%, global circumferential strain: 16 ± 5 vs. 35 ± 7 and 35 ± 6%, global longitudinal strain: 14 ± 4 vs. 25 ± 4 and 34 ± 7%, respectively, all P < 0.001; Figure 5).

Next, we focused on longitudinal myocardial function at different LV short-axis levels in patients with RV pacing and preserved EF. The average longitudinal strain at the apical level was significantly lower than that at the mid- and basal level (20 ± 4 vs. 27 ± 5 and 26 ± 5%, P < 0.001; Figure 6). Furthermore, averaged maximum longitudinal strain in the septum and anterior was significantly lower than that in the posterior and lateral (septum vs. posterior: 23 ± 7 vs. 29 ± 8%, septum vs. lateral: 23 ± 7 vs. 26 ± 8%, both P < 0.001, anterior vs. posterior: 24 ± 6 vs. 29 ± 8%, P < 0.005, anterior vs. lateral: 24 ± 6 vs. 26 ± 8%, P = 0.04, Figure 4B).

Reproducibility

The intraclass correlation coefficients for inter-observer reproducibility of 3D speckle-tracking dyssynchrony indices were 0.969 [95% confidence interval (CI), 0.924–0.987] for radial, 0.946 (95% CI, 0.870–0.978) for circumferential, and 0.944 (95% CI, 0.865–0.977) for longitudinal dyssynchrony, while the corresponding coefficients for intra-observer reproducibility were 0.871 (95% CI, 0.703–0.947), 0.891 (95% CI, 0.561–0.973), and 0.894 (95% CI, 0.753–0.956), respectively. The intraclass correlation coefficients

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**Figure 3** The effect of RV pacing on longitudinal dyssynchrony at different LV short-axis levels in patients with RV pacing and preserved EF, demonstrating that longitudinal dyssynchrony at the apical level was significantly larger than that the mid- and basal-level.

**Figure 4** (A) The effect of RV pacing on longitudinal dyssynchrony at different LV walls in patients with RV pacing and preserved EF, demonstrating that averaged time-to-peak longitudinal strain in the septum was significantly earlier than that in the posterior and lateral. Averaged time-to-peak longitudinal strain in the anterior were also significantly earlier than that in the posterior. (B) The effect of RV pacing on longitudinal myocardial function at different LV walls in patients with RV pacing and preserved EF, demonstrating that averaged maximum longitudinal strain in the septum and anterior were significantly lower than that in the posterior and lateral.
for inter-observer reproducibility of global 3D speckle-tracking peak strain were 0.949 (95% CI, 0.876–0.976) for radial, 0.949 (95% CI, 0.876–0.979) for circumferential, and 0.948 (95% CI, 0.875–0.979) for longitudinal strain, while the corresponding coefficients for intra-observer reproducibility were 0.926 (95% CI, 0.824–0.970), 0.909 (95% CI, 0.785–0.963), and 0.918 (95% CI, 0.805–0.966), respectively.

**Discussion**

The findings of our study demonstrate that chronic RV pacing has a detrimental effect on only the longitudinal myocardial function of patients with preserved EF. Furthermore, radial, circumferential, and longitudinal dyssynchrony showed different patterns resulting from chronic RV pacing, and larger longitudinal dyssynchrony was observed in association with impaired longitudinal myocardial function. Furthermore, chronic RV pacing was seen to induce heterogeneous myocardial longitudinal dysfunction and dyssynchrony. We also found that 3D speckle-tracking strain imaging may be useful for evaluating early subtle changes caused by chronic RV pacing, and could thus play a clinical role in predicting future global LV dysfunction.

**Impact of chronic RV pacing on LV function and dyssynchrony**

Although RV pacing may be lifesaving for patients with symptomatic or high-risk atrioventricular block, it may also induce mechanical dyssynchrony, which may have detrimental long-term consequences. Previous randomized multicentre studies have demonstrated such unfavourable effects of RV pacing on LV function. The DAVID (Dual Chamber and VVI Implantable Defibrillator) trial randomized 506 patients with implantable cardioverter defibrillators and EF ≤ 40% to rate-responsive pacing at 70/min or RV backup pacing at 40/min and observed a lower HF hospitalization rate and mortality in those with back-up pacing. It is believed that RV pacing-induced dyssynchrony contributed to the less favourable outcomes for patients with depressed EF who were RV paced more often. The aim of the PACE (Pacing to Avoid Cardiac Enlargement) study was to test whether biventricular pacing was superior to RV apical pacing for preventing deterioration of LV systolic function and remodelling in patients with a normal EF and standard indications for pacing. At 12-month follow-up, the mean EF was significantly lower for the RV pacing group than in the biventricular pacing group (54.8 ± 9.1 vs. 62.2 ± 7.0%), whereas the end-systolic volume was significantly higher (35.7 ± 16.3 vs. 27.6 ± 10.4 mL). Thus, RV pacing could contribute to less favourable outcomes even for patients with RV pacing and preserved EF. Furthermore, previous investigators have demonstrated a reduction in wall thickening by chronic RV pacing, especially septal, apical, or inferior walls. Although overall radial strain in patients with RV pacing and preserved EF and normal controls was similar (39 ± 5 vs. 40 ± 4%) in this study, radial strain at the apex was significantly lower (37 ± 6 vs. 39 ± 5 and 40 ± 6%, P < 0.01).

**Impact of chronic RV pacing on longitudinal myocardial function**

The LV wall is not homogenous and is composed of three layers of fibres. The longitudinal myocardial function is governed by the subendocardial/subepicardial myocardial fibres which are aligned longitudinally so that selective impairment of longitudinal myocardial function may be related to an increase in subendocardial/subepicardial stress. Previous investigators have demonstrated that early manifestations of cardiac abnormalities caused by various
diseases were observed in the subendocardial layer in spite of preserved global systolic function. However, the impact of chronic RV pacing on longitudinal myocardial function remains unknown. Delgado et al. used 2D speckle-tracking strain to demonstrate that apical pacing-induced acute radial dyssynchrony associated with the impairment of LV longitudinal myocardial function in a group of 25 patients with structural normal hearts referred for electrophysiological study. In this study, patients with RV pacing and preserved EF had longitudinal myocardial dyssynchrony and dysfunction, especially apical level and septal. Considering LV fibre orientation, this finding suggests that chronic RV pacing leads the deleterious effects of mainly LV subepicardial myocardial fibres because of the positioning of the RV leads. Thus, this leads us to speculate that chronic RV pacing induces heterogeneous myocardial longitudinal dysfunction and dyssynchrony.

**Regional LV dysfunction resulting from RV pacing**

Previous investigators have reported on regional LV dysfunction caused by RV pacing. Prinzen et al. observed that strain in the early-activated LV areas was lower than that in the remote areas during RV pacing by using sonomicrometry in a canine model. They also reported that blood flow in the early-activated regions was <60% of that in late-activated regions during RV pacing. Furthermore, van Oosterhout et al. reported that the early-activated regions of LV myocardium adjacent to the site of chronic RV pacing have been demonstrated to undergo thinning, compared with distant sites that have increased strain and hypertrophic myocardium in a canine model. In our study, we observed that longitudinal dyssynchrony at the apical level was significantly larger than that at the mid- and basal level, while longitudinal myocardial function at the apical level was also significantly lower than that at the mid- and basal level. Possible mechanisms of these findings were unknown, but apical dyssynchronous electrical activation from the positioning of the RV leads might be associated with significant heterogeneous distributions of epicardial longitudinal fibre strain and blood flow in this region, resulting in lower myocardial longitudinal dysfunction and larger dyssynchrony at the apex.

**Time course of LV dysfunction caused by RV pacing in patients with preserved EF**

As previously mentioned, it is well known that RV pacing has a detrimental effect on global LV function even in some patients with preserved EF, but the mechanism of this phenomenon remains unclear. Accordingly, interest is high in the time course of LV dysfunction in these patients as a result of RV pacing because of its potential for predicting future global LV dysfunction. In our study, we observed larger longitudinal dyssynchrony and impaired longitudinal myocardial function in patients with chronic RV pacing and preserved EF compared with normal controls. The reduced longitudinal strain in patients with RV pacing patients with preserved EF may be a precursor of worse LV myocardial function over time. Thus, we speculated that RV pacing leads to longitudinal dyssynchrony first, resulting in longitudinal myocardial dysfunction (while LV global systolic function is preserved). Furthermore, larger radial and circumferential dyssynchrony and lower radial and circumferential myocardial function were observed as well as longitudinal dyssynchrony and myocardial dysfunction in patients with RV pacing and reduced EF. Thus, RV pacing may lead to radial and circumferential dyssynchrony following longitudinal myocardial dysfunction and eventually to impaired global LV performance (impaired EF). Because chronic RV pacing produces the changes for LV performance over time, watchful observations could be necessary for such patients.

**Clinical implications**

Although EF is the most widely used measurement of LV function, it is reduced only in symptomatic HF patients with RV pacing referred for upgraded cardiac resynchronization therapy. According to our findings, chronic RV pacing had a detrimental effect starting from the subendocardium or subepicardium and affecting mainly longitudinal myocardial function, a process which is not well represented by EF before the development of overt cardiac failure due to RV pacing. Therefore, earlier detection of longitudinal dyssynchrony as well as longitudinal function may make earlier identification possible of patients at risk of irreversible myocardial damage among patients with chronic RV pacing and preserved EF, and could thus play a clinical role in predicting future global LV dysfunction. Previous investigators have reported the pathophysiology of RV pacing-induced dyssynchrony by means of 2D speckle-tracking strain. Although 2D speckle-tracking approaches are clinically useful, they are restricted to the assessment of LV function in a single plane. Moreover, each segment must be evaluated sequentially and, thus, is subject to beat-to-beat variability. Perez de Isla et al. showed that 3D speckle-tracking system was a new and faster tool for myocardial strain assessment when compared with 2D speckle-tracking. Thus, the potential advantages of 3D speckle-tracking strain imaging were found to be expression of myocardial function of the whole heart, independence of tomographic imaging planes, and the ability to analyse regional ventricular function using three different strains obtained from the same heart beat.

**Study limitations**

This study covered a small number of patients in a single-centre study, so that future studies of larger patient populations are necessary to validate our findings. An important limitation of our study is that the investigation of long-term clinical outcomes for patients with chronic RV pacing and preserved EF data was not part of the study. Patients with chronic RV pacing comprise different pacing modes, and this may affect ventricular dyssynchrony. Another limitation was that we could not assess the LV function of the RV patients at the time of pacemaker implantation. Furthermore, the RV pacing lead was routinely implanted in the RV apex in the patients enrolled this study, but other possible sites have been reported. The RV outflow tract is the most extensively studied part of the study. Patients with chronic RV pacing comprise different pacing modes, and this may affect ventricular dyssynchrony.

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855 Detection of LV performance with 3D speckle-tracking strain
imaging used in this study proved to be satisfactory, and we used this software to successfully quantify LV dysynchrony. Three-dimensional speckle-tracking strain analysis at a faster frame rate is being developed. Another specific limitation of 3D speckle-tracking strain imaging is the need for careful image tracing to manually fine-tune the region of interest and capture the appropriate regional strain for dysynchrony analysis.

Conclusions

Longitudinal dysynchrony was observed in patients with chronic RV pacing and preserved EF and with impaired longitudinal myocardial function. The novel 3D speckle-tracking strain imaging was found useful for evaluating early subtle changes resulting from chronic RV pacing, and may thus play a role in predicting future global LV dysfunction.

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Conflict of interest: none declared.

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References

11. Lang RM, Rieg M, Devereux RB, Flachskampf FA, Foster E, Pelikka PA et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber-Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–63.

H. Tanaka et al.