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Case Report

Changes of Sympathetic Activity in Patient with Chronic Atrial Fibrillation and Severe Congestive Heart Failure Treated with Biventricular Pacing

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The patient was a 64-year-old man with chronic atrial fibrillation with bradycardia. Left ventricular ejection fraction was 34%. He was treated with biventricular pacing. Heart failure improved from NYHA class III to II. Sympathetic nerve activity (SNA) was recorded during 6 minutes of biventricular (BV), right ventricular apical (RVA) and left ventricular (LV) pacing. SNA was significantly lower during biventricular pacing (49.5 ± 4.0/min) compared with RVA (58.8 ± 6.9/min, $p = 0.016$) and LV (63.3 ± 4.3/min, $p = 0.002$) pacing. BV pacing improves hemodynamics and decreases SNA compared with RVA or LV pacing.
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Key words: Cardiac resynchronization therapy, Pacemaker, Autonomic nervous system, Hypertrophic cardiomyopathy

Introduction

Biventricular pacing therapy is effective in patients with severe congestive heart failure. It improves the hemodynamic status acutely,[1–3] and improves heart failure symptoms, exercise capacity, quality of life, and mortality and morbidity.[4–7] There have been few studies on autonomic changes during different pacing modes.[8] We attempted to examine the effect of biventricular pacing therapy on sympathetic nerve activity using the microneurogram.[9,10]

Case Report

The patient was a 64-year-old man with apical type hypertrophic cardiomyopathy. He had had paroxysmal atrial fibrillation from age 55, and a VVI permanent pacemaker was implanted at age 59 to control chronic atrial fibrillation with bradycardia. Left ventricular ejection fraction was 34%, and he had had repeated admissions for congestive heart failure during the past two years because his hypertrophic cardiomyopathy had entered the dilated phase. He was referred to our hospital for implantation of a biventricular pacemaker. A coronary sinus lead was added via the lateral vein, and an SSIR

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pacemaker was implanted. The pacing mode was set at VVI mode 80/min and VVT mode 60/min. Pharmacological management included 0.25 mg digoxin, 2 mg temocapril, 25 mg spironolactone and 20 mg furosemide per day.

QRS width was 172 and 200 ms for intrinsic beats, 184 ms during right ventricular apical (RVA) pacing, 233 ms during left ventricular (LV) pacing and 144 ms during biventricular pacing (BV) (**Figure 1**). After implantation of the biventricular pacemaker, cardio-thoracic ratio decreased from 77.8% to 67.4% (**Figure 1**). Heart failure improved from New York Heart Association class III to II. Microneurogram study was performed 30 days after the initiation of biventricular therapy. After acceptable recordings of sympathetic nerve activity were obtained, the following protocol was performed. Non-invasive BP, respiration rate, and sympathetic neural responses to 6 minutes of pacing were recorded during BV pacing, RVA pacing, LV pacing, and re-BV pacing. Re-BV pacing was done to confirm reproducibility of sympathetic neural responses. Efferent, postganglionic muscle SNA was recorded from the right peroneal nerve. A sterile microelectrode was inserted into a fascicle of the peroneal nerve near the fibular head. The nerve signals were amplified (DPA-21E and DPA-100D; Dia Medical, Tokyo, Japan), filtered (FV-664; NF Electronic Instruments, Tokyo, Japan) at 700 to 3000 Hz, rectified, and discriminated. Raw nerve signals were integrated (time constant 0.05 s) to produce a mean voltage display for quantitative analysis (No. 1333; NEC San-ei, Tokyo, Japan). Muscle sympathetic neural bursts at baseline (during BV pacing) were readily recognized by their tight

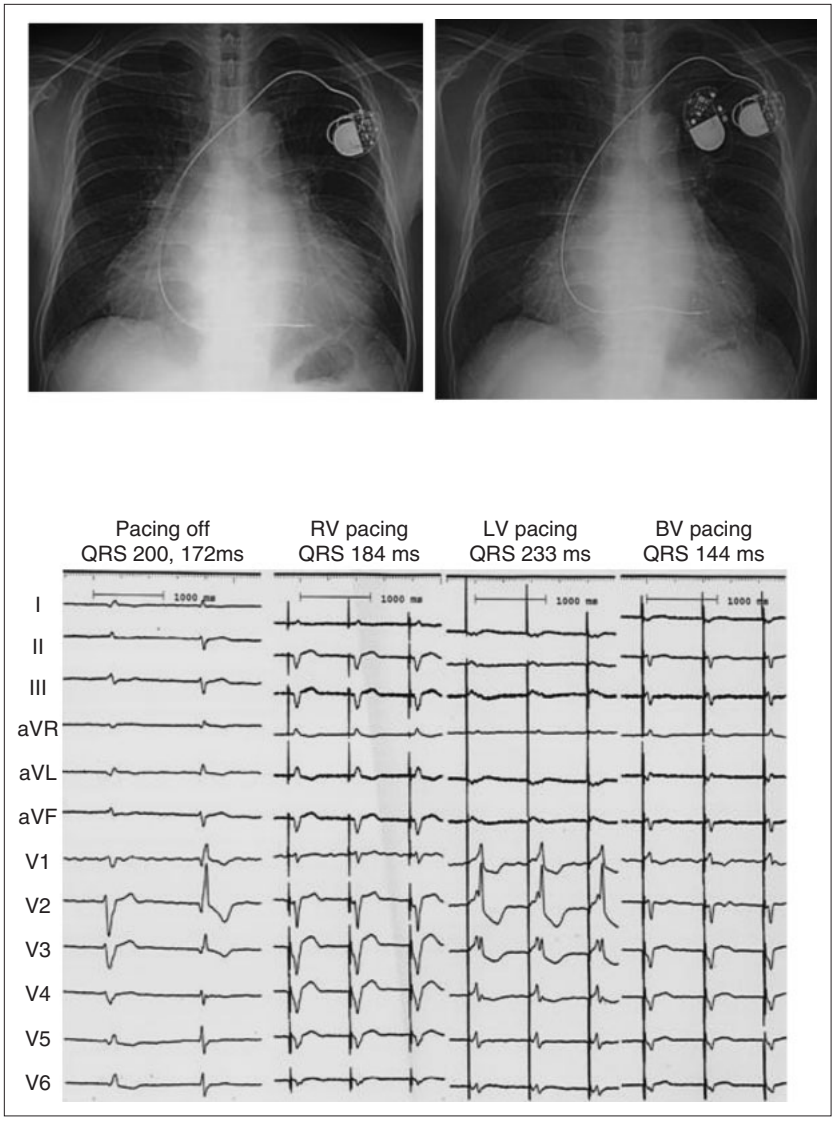

Figure 1
Upper: Chest XP before (left panel) and after (right panel) biventricular pacing. After implantation of a biventricular pacemaker, cardio-thoracic ratio decreased from 77.8% to 67.4%.
Lower: Conventional lead electrocardiogram during pacing at each site. QRS width during BV pacing was the shortest of each pacing site, and QRS width during LV pacing was the longest of each pacing site. BV, biventricular; RV, right ventricular; LV, left ventricular.

temporal relationship to the cardiac cycle, their increasing frequency during Valsalva maneuvers, and their failure to respond to arousal stimuli and stroking of the skin. SNA was quantified as the total activity derived from the mean number of the SNA bursts for a minute derived from four minutes of recording. On the same day as recording SNA, standard echocardiography including Doppler studies was performed during BV pacing, RVA pacing and LV pacing. LV dimensions and ejection fraction were measured by two-dimensional guided M-mode method. Cardiac output and stroke volume were measured by pulsed-wave Doppler echocardiography. At least 3 consecutive beats were measured, and the average value was taken. The results are shown in **Figure 2**. SNA was significantly lower during BV pacing (49.5 ± 4.0/min) compared with RVA pacing (58.8 ± 6.9/min, $p = 0.016$) and LV pacing (63.3 ± 4.3/min, $p = 0.002$). There was no significant difference between BV pacing (49.5 ± 4.0/min) and re-BV pacing (49.5 ± 2.6/min). Stroke volume was significantly greater during BV pacing ($61.0 \pm$

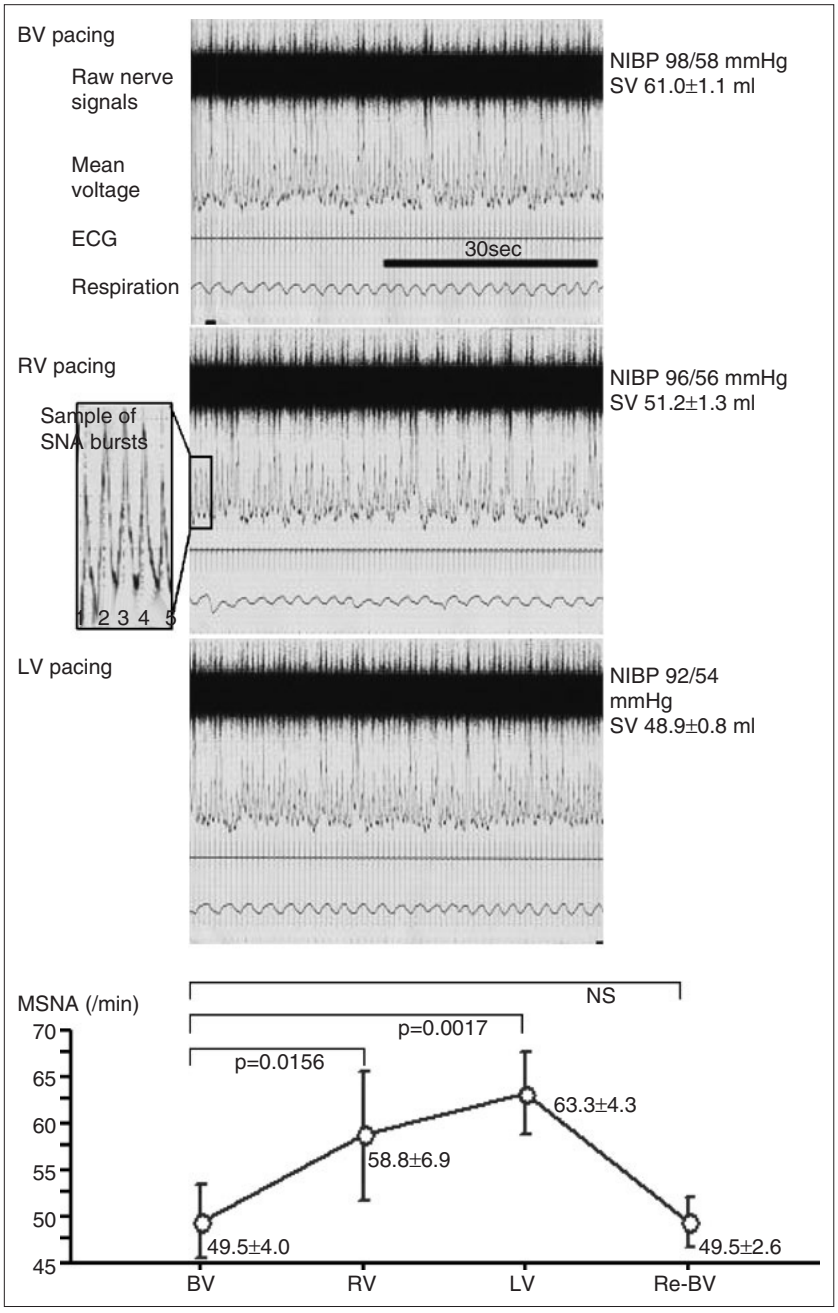

Figure 2
Upper panel: Recordings of raw nerve signals, integrated sympathetic neurogram, ECG and respiratory monitoring during pacing at each site.
Lower panel: number of muscle sympathetic nerve activity bursts. SNA was significantly lower during biventricular pacing compared with RVA pacing and with LV pacing. There was no significant difference between BV pacing (49.5 ± 4.0/min) and re-BV pacing. MSNA, muscle sympathetic neural activity; BV, biventricular; RV, right ventricular; LV, left ventricular; NIBP, non-invasive blood pressure; SV, stroke volume.

1.1 ml) compared with RVA pacing (51.2 ± 1.3 ml, $p = 0.0008$) and LV pacing (48.9 ± 0.8 ml, $p = 0.0004$).

Discussion

The main findings in this case were that (1) BV pacing improved hemodynamics and decreased sympathetic activity compared with RVA or LV pacing, (2) the change in sympathetic activity occurred within a few minutes, and (3) LV pacing alone did not improve hemodynamics or decrease sympathetic activity. Sympathetic nerve activity of humans can only be directly observed by means of the microneurogram.[9,10] Increased sympathetic activity has been shown to be a negative prognostic factor in patients with congestive heart failure.[11–13] If this finding were confirmed in many patients with chronic atrial fibrillation with severe congestive heart failure, biventricular pacing could be used to improve the prognosis of those patients. Hamdan et al. showed a decrease in SNA in patients with congestive heart failure in sinus rhythm during temporary pacing.[8] Our case was compatible with their report. However, they reported that LV pacing alone also reduced sympathetic nerve activity. LV pacing was the worst mode in our case. Our case had chronic atrial fibrillation with bradycardia and no intrinsic beats during 80 per minute pacing. Therefore, LV pacing alone could not improve dyssynchrony of the LV wall. This study was performed 30 days after the initiation of biventricular therapy. In our study, there was no significant difference between BV pacing and re-BV pacing. This fact confirms the reproducibility of sympathetic neural responses in this study, and the change in sympathetic activity and hemodynamics occurred within a few minutes in the chronic phase of biventricular pacing. The decrease in sympathetic activity may result in an improved survival rate. This case report only assessed short term change of sympathetic activity so further investigations are needed. However, our findings in this case support the use of biventricular therapy in patients with chronic atrial fibrillation and severe congestive heart failure.

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