# Heart Rate-Associated Left Ventricular Morphologic Changes Observed in Two Heart Failure Patients

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## ABSTRACT

We report two heart failure cases in which the left ventricular (LV) mass increased after heart rate (HR)-lowering therapy. The initial LV mass index was 98 and 121g/m$^2$, respectively. After HR-lowering therapy, the HR was reduced from 120 and 100beats/min to 70 and 60beats/min, respectively. After HR reduction and clinical stabilization, the LV mass index was 110 and142 g/m$^2$, respectively, with LV chamber shrinking. Elevated resting HR was considered to indicate deteriorating target organ damage and worse prognosis. The present findings contrast with the previous concept that HR-lowering is good for patients' health. *Ryukyu Med. J., 37 (1~4) 91~96, 2018*

Key words: heart rate, left ventricular hypertrophy, left ventricular mass, remodeling

## Introduction:

Several lines of evidence, including basic experiments and cohort studies, indicate that elevated resting heart rate (HR) is an independent risk factor for a poor prognosis. A clear prognostic significance of HR-lowering therapy has been demonstrated in patients with heart failure[1)], and HR is considered to be a therapeutic target in this spectrum of patients. Elevated resting HR is associated with every stage of the cardiovascular continuum[2, 3)]. Left ventricular hypertrophy (LVH) is also an independent risk factor for a cardiovascular event[4, 5)]. Previous cross sectional analysis evaluating patients without heart failure, however, revealed that resting HR is negatively associated with LVH[6-8)]. We report two cases of congestive heart failure exhibiting characteristic LV morphologic changes associated with HR-lowering therapy.

## Case Presentation

**Cases 1**: A 93-year-old female patient was referred to our hospital after diagnosis and treatment of end-stage heart failure with severe aortic stenosis, atrial fibrillation, and implantation of a DDD pacemaker. The patient had a baseline physical status of New York Heart Association (NYHA) class IV, blood pressure of 100/60mmHg, and heart rate (HR) of 117beats/min. An electrocardiogram (ECG) revealed atrial fibrillation with a complete left branch block. Cardiac pacemaker program analysis indicated atrial fibrillation with all ventricular sensing. Cardiac ultrasound revealed diffuse hypokinesis with an ejection fraction of 41% and an aortic valve area of 0.52cm$^2$ (Table). After medical therapy, including diuretics and a beta blocker, her HR was reduced to 60beats/min and her general condition improved remarkably to a physical status of NYHA class II. ECG showed atrial fibrillation with all

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Table **Serial changes in echocardiographic and other clinical parameters in the two heart failure cases**

| Variables | Case 1 | | Case 2 | |
|---|---|---|---|---|
| | Baseline | 7 months | Baseline | 3 months |
| BP (mmHg) | 100/60 | 88/65 | 110/62 | 108/56 |
| HR (bpm) | 117 | 69 | 100 | 70 |
| BNP (pg/ml) | 783 | 320 | 1318 | 381 |
| LVDd (mm) | 43 | 38 | 66 | 59 |
| LVDs (mm) | 34 | 30 | 64 | 55 |
| EF (%) | 41 | 41 | 7 | 13 |
| IVS (mm) | 11 | 14 | 7 | 11 |
| LVPW (mm) | 10 | 13 | 6 | 10 |
| SV (ml) | 34 | 33 | 15 | 22 |
| RWT (%) | 0.47 | 0.68 | 0.18 | 0.34 |
| LVMI ($g/m^2$) | 95 | 128 | 112 | 180 |

BP: blood pressure; HR: heart rate; BNP: brain natriuretic peptide; LVDd: left ventricular diastolic dimension; LVDs: left ventricular systolic dimension; IVS: interventricular septum; LVPW: left ventricular posterior wall; SV: stroke volume; RWT: relative wall thickness; LVMI: left ventricular mass index

ventricular pacing beats.

**Cases 2:** An 80-year-old male patient was referred to our hospital for cardiac rehabilitation with a diagnosis of chronic heart failure due to ischemic cardiomyopathy, implantation of a DDD pacemaker, and paroxysmal atrial fibrillation. The patient had a baseline physical status of NYHA class II, blood pressure of 110/62mmHg, and HR of 100beats/min. ECG showed all ventricular pacing rhythm. Despite cardiac rehabilitation, his general condition gradually worsened to a physical status of NYHA class III. Cardiac ultrasound revealed diffuse hypokinesis and a dilated LV with an ejection fraction of 7%. ECG monitoring showed that his HR was unchanged before and after exercise. Cardiac pacemaker program analysis indicated atrial fibrillation followed by ventricular pacing beats at the upper tracking rate of 100paces/min. After adjusting the pacemaker setting in DDDR mode with rate response, his HR was reduced to a resting HR of 60 to 70beats/min, and his general condition was remarkably improved to a physical status of NYHA class II. Serial changes of the cardiac ultrasound findings in both cases are summarized in Figure 1 and the table. Figure 1 shows the serial echocardiographic changes in both cases, demonstrating increased wall thickness during the follow-up period. The LV morphologic change was revealed based on the relative wall thickness (RWT) and left ventricular mass index (LVMI). RWT is a phenotype for quantifying LVH, and is represented as the ratio of LV chamber size and LV wall thickness. This method allows for further classification of the LV mass increase as either concentric hypertrophy (RWT$>$0.42) or eccentric hypertrophy (RWT$\leqq$0.42). RWT and LV mass are calculated by the following formula: RWT=2 x IVSd / LVDd, LV mass (g)=0.8{1.04[([LVDd+IVSd+PWd)$^3$ - LVEDd$^3$)]}+0.6. LVMI ($g/m^2$) was defined as LV mass divided by body surface area ($m^2$)[9]. After the HR was lowered, the LV chamber decreased in size with an increase in the wall thickness, resulting in a higher LVMI and a higher RWT, and the plots shifted to the right (Figure 2).

## Discussion:

Evidence obtained from both basic and clinical research demonstrates that resting HR is associated with all steps of the cardiovascular continuum, including cardiometabolic risks, inflammation, endothelial dysfunction, target organ damage, and cardiovascular events[2]. Resting HR is associated with target organ damage such as chronic kidney disease[10, 11], arterial stiffness[12], and impaired cognitive function[13]. Fácila et al. evaluated 560 patients with essential hypertension and demonstrated that the odds ratio for target organ damage in patients with a resting HR of 65 beats/min and above was 2.4[14]. In other words, a lower resting HR is good for patient health. The association between

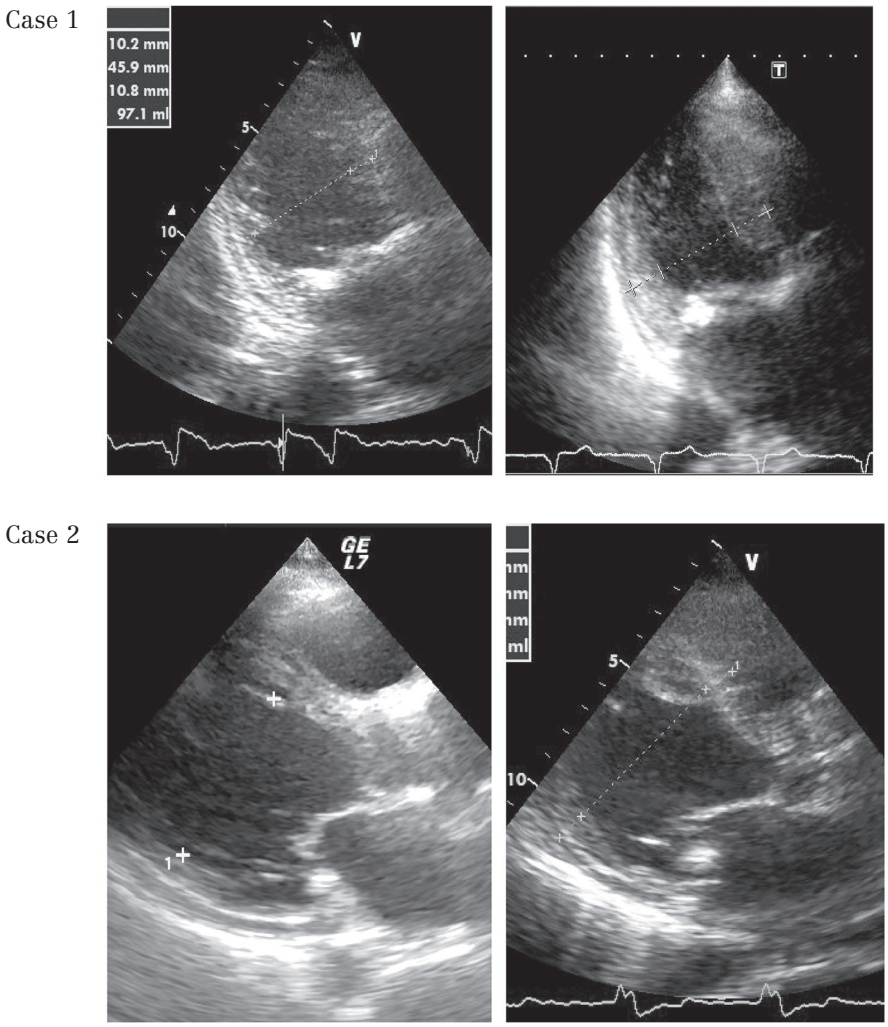


Figure 1 **Echocardiograms of both cases examined at baseline (left) and during the follow-up period (right).**

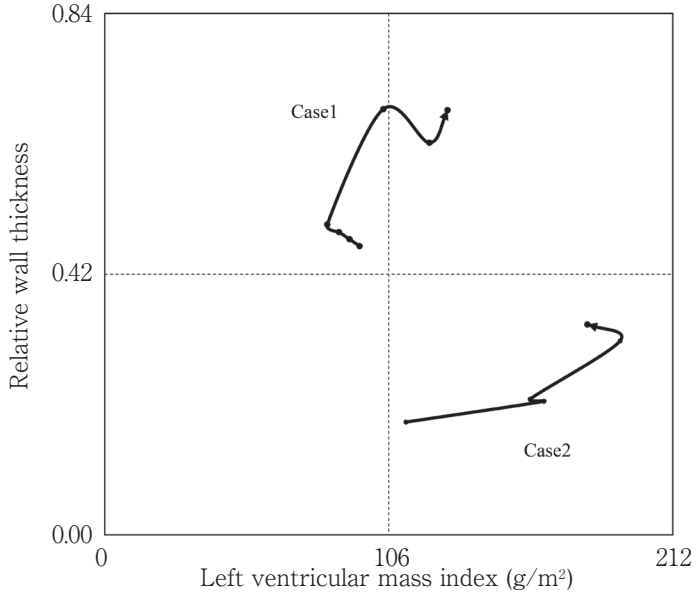


Figure 2 **Serial left ventricular morphologic changes in the two heart failure cases. In both cases, the relative wall thickness and left ventricular mass index increased over time, shifting the plot to the right.**

resting HR and LVH, however, does not support this notion. Cross sectional results evaluating normotensive and hypertensive patients without heart failure indicate that resting HR is negatively associated with left ventricular mass[6-8]. The LIFE study[15] demonstrated that angiotensin receptor blocker (losartan)-based antihypertensive therapy afforded a better prognostic outcome compared with beta blocker (atenolol)-based antihypertensive therapy. The results of the LIFE study suggest that beta blocker-derived HR-lowering might partly contribute to a worse prognosis through the development of or sustained LVH. Consistent with these findings, our previous result indicated that lower resting HR accelerates the new onset of ECG-LVH in healthy subjects without heart failure[16]. As we demonstrate in the present two cases, HR-lowering decreased the LV chamber size, but increased LVMI in patients with heart failure. These findings support the notion that lower HR or HR-lowering might be a risk factor for LVH. A possible mechanism connecting the resting HR and LVH in the present two cases includes stroke volume and stroke work. Stroke work was estimated as systolic blood pressure times stroke volume and was converted in gram-meters (g-m) by multiplying by 0.0144[17]. When cardiac output remains the same, there is a negative association between resting HR and stroke volume. Based on these assumptions, HR-lowering therapy increases stroke volume to maintain cardiac output, and subsequent stroke work increases, resulting in an increased LV mass. There might be another causal relationship between HR and LVH. Hypertensive patients with LVH have an enhanced parasympathetic tone compared with normal subjects[18]. In patients with heart failure with a reduced ejection fraction, HR-lowering therapy improves the LV chamber size[19] and prognosis[20]. In an animal model of LV dysfunction, lowering HR is essential for recovering cardiac function[21] and HR is the therapeutic target for patients with LV dysfunction. On the other hand, resting HR might increase LV mass regardless of cardiac function. The clinical benefit of HR-lowering should be reconsidered.

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