Normalization of Left Ventricular Function Following Cardiac Resynchronization Therapy

— Left Bundle Branch Block as a Potential Etiology of Dilated Cardiomyopathy —

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Patients with chronic heart failure (HF) not infrequently present conduction disturbances, which are most commonly exhibited as a left bundle branch block (LBBB). LBBB is associated with intraventricular conduction delay, paradoxical septal motion, and hemodynamic deterioration, indicating an impairment of left ventricular (LV) function. However, there is controversy as to whether dilated cardiomyopathy leading to HF could develop just as a result of conduction disturbances without apparent pre-existing heart disease. We report here 2 cases of patients with non-ischemic dilated cardiomyopathy and LBBB who had complete reversal of their LV dysfunction and enlargement after cardiac resynchronization therapy, which corrects the LV activation sequence. These cases might support the idea that conduction disturbances themselves can be a principal etiology in the development of dilated cardiomyopathy. (Circ J 2008; 72: 1030–1033)

Key Words: Bundle branch block; Cardiomyopathy; Resynchronization

Cardiac resynchronization therapy (CRT) is an established therapy for patients with advanced heart failure (HF) who have depressed left ventricular ejection fractions (LVEF) ≤35%, widened QRS >120–130 ms and a New York Heart Association (NYHA) class III or IV symptoms despite recommended optimal medical therapy.1,2 CRT restores ventricular activation sequence and coordinates wall motion within left ventricles (LV), which are mechanically dyssynchronized by ventricular conduction disturbances, and also optimizes preload through the atrio-ventricular delay.3 As a result, CRT improves LV function significantly, as well as clinical findings such as symptoms, morbidity, and the risk of death.1,2 However, generally, the improvement in LV function is relatively small and the LV function is not restored to normal. The MIRACLE trial demonstrated a median absolute improvement in LVEF of 4.6% (95% confidence interval, 3.2–6.4%) at 6 months following CRT for patients with a LVEF of ≤35%.1 This is thought to be attributed to the fact that even if the LV resumes coordinated wall motions, the preexisting heart disease that resulted in myocardial damages still remains. Another group of patients (non-responders) do not respond to CRT and fail to show improvement in LV function even though they meet current CRT criteria.4 There might be an additional, rarer group of patients whose response to CRT is so dramatic that normal LV function is restored with no residual evidence of LV dysfunction. This group of “super-responders” has not been well studied. Herein, we report on such patients.

Case Reports

Case 1
A 68-year-old female patient presented with a 3-year
The ECG showed a sinus rhythm with a PR-interval of 200 ms, and a widened QRS (170 ms) with a complete left bundle branch block (LBBB) (Fig 1A). An echocardiography revealed dilated cardiomyopathy (DCM) with a low LVEF (Table 1) and a moderate mitral regurgitation (MR) (Fig 2A). Cardiac catheterization showed normal coronary arteries, diffuse severe hypokinesis of the LV with a LVEF of 25% (Fig 3A). She denied alcohol abuse. Electrolytes and thyroid function tests were normal. Except for having had well-controlled Type 2 diabetes mellitus, her past medical history was otherwise unremarkable.
Despite optimized medical therapy including angiotensin-converting enzyme-inhibitor, Î¿-blocker, digoxin and loop diuretics for at least 12 months, the patient expressed worsening HF with symptoms corresponding to NYHA class III, and her serum brain natriuretic peptide (BNP) level increased to 477 pg/ml.

The patient was referred for an implantation of a CRT pacemaker. The CRT pacemaker (InSync model 8040, Medtronic Inc, Minneapolis, MN, USA) was implanted in the left pectoral region with the use of standard right atrial (RA) and right ventricular (RV) pacing leads and a LV pacing lead (Attain model 4193, Medtronic Inc). The RA, RV and LV pacing leads were inserted transvenously and their tips were positioned in the RA septum, RV mid-septum and the lateral branch of the coronary vein, respectively. The CRT pacemaker was programmed in the biventricular DDD mode with a lower rate of 70 beats/min and the atrioventricular delay was optimized at 100 ms using Doppler echocardiography.

Immediately after the initiation of CRT, the ECG revealed a paced-QRS width of 130 ms (Fig 1B). Clinical improvement to NYHA class I was seen within 1 month with elimination of exertional and paroxysmal nocturnal dyspnea. At 5 months follow up, an echocardiography revealed the loss of LV dilatation with a normal LVEF (Table 1) and slight MR (Fig 2B). The serum BNP level decreased to 15 pg/ml. During the follow up, medications and dosages were unchanged from those pre-implant. The patient has been followed for more than 4 years thus far. She remains asymptomatic, and echocardiography continues to show normal LV size and function with mild MR.

Case 2
A 76-year-old female patient experienced 3 hospitalizations for HF due to idiopathic DCM with permanent atrial fibrillation over the last 10 years. Her heart rate had been well managed and the repeated 24-h Holter ECGs revealed the mean heart rate of 68 beats/min. Nevertheless, medical therapy for HF including angiotensin receptor blocker, spironolactone, loop diuretics and Î¿-blocker had failed to improve the HF symptoms corresponding to NYHA class III over the last 2 years. The ECG showed a widened QRS (140 ms) with complete LBBB (Fig 4A). An echocardiography revealed LV dilatation with a low LVEF (Table 1) and mild MR. Cardiac catheterization showed normal coronary arteries.

CRT was initiated using a conventional dual chamber pacemaker (Kappa DR model 701, Medtronic Inc). This was because a dedicated CRT pacemaker system was not yet introduced in Japan at that time. The pacemaker was implanted in the left pectoral region with the use of a standard RV pacing lead and an epicardial pacing lead. The RV pacing lead was inserted transvenously and the tip was positioned in the RV mid-septum. The epicardial pacing lead was connected to the atrial channel of the pacemaker and implanted surgically using a thoracoscopic technique, and the tip was positioned on the LV posterolateral. To ensure biventricular pacing, the pacemaker was programmed in the DDI mode with a lower rate of 80 beats/min and the atrioventricular delay (ie, LV to RV delay) was set to the shortest programmable interval of 30 ms.

Immediately after the initiation of CRT, the ECG revealed a paced-QRS width of 110 ms (Fig 4B). Clinical improvement to NYHA class I was seen within 1 month with elimination of exertional dyspnea. At 10 months follow up, echocardiography revealed the loss of LV dilatation with an improvement in LVEF (Table 1) and mild MR. At 18 months follow up, repeated echocardiography revealed a further improvement in LVEF, and the LVEF was considered to be normalized (Table 1). During the follow up, medications and dosages were unchanged from those at pre-implant. The patient has been followed for more than 4 years thus far. She remains asymptomatic, and echocardiography continues to show normal LV size and function with mild MR.

Discussion
The cases we report here demonstrated an extreme response to CRT for non-ischemic DCM patients with resolution of both HF symptoms and LV dysfunction, with marked reverse LV remodeling. Furthermore, it is noteworthy that the LV function has been restored to normal with the disappearance of any findings of DCM by the treatment with CRT. This is because generally residual evidence of LV dysfunction remain in varying degrees following CRT.1,2 The therapeutic target for CRT is ventricular conduction disturbances1-3 which is generally assumed to be secondary to the underlying disease process of the heart5-7 and therefore CRT will likely act to limit and/or regress the disease progression8 but does not cure the underlying disease itself.

Approximately 30% of patients with chronic HF present with conduction disturbances, which is most commonly exhibited as a LBBB pattern with a QRS width >120 ms9,10. The presence of LBBB has been shown to be an independent predictor of cardiac morbidity and mortality, particularly in patients with systolic HF11,12. There is increasing evidence that abnormal mechanical activation sequences, which are created by LBBB, are associated with intraventricular conduction delay, paradoxical septal motion, and hemodynamic deterioration, indicating a significant impair-
Conduction Disturbance as an Etiology of HF

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References