CARDIAC PACING

COMPLEX CASE STUDY

Multipoint Pacing Therapy in Cardiac Resynchronization Therapy Non-responder Patient

KANWAR Y. SINGH, MD and IMRAN NIAZI, MD

Aurora Cardiovascular Services, Aurora Sinai/Aurora St. Luke's Medical Centers, Milwaukee, WI

ABSTRACT. A 66-year-old man with a history of severe ischemic cardiomyopathy, a left ventricular ejection fraction of 21%, and ischemic cardiomyopathy underwent cardiac resynchronization therapy as part of the MultiPoint™ Pacing (MPP) study. A St. Jude Medical Quartet™ lead was implanted in the mid-lateral left ventricular wall. After conventional biventricular programming, the patient was switched to MPP programming at 3 months. The patient was followed up for 9 months with periodic clinical assessment and serial cardiac imaging as part of the study. The patient failed to respond to conventional cardiac resynchronization therapy and had a heart failure hospitalization while undergoing biventricular pacing. There was a marked clinical and echocardiographic response to MPP cardiac resynchronization therapy.

KEYWORDS. Cardiac resynchronization therapy, multipoint pacing, non-responder, quadripolar lead.

ISSN 2156-3977 (print)
ISSN 2156-3993 (online)

© 2016 Innovations in Cardiac
Rhythm Management

Case report

A 66-year-old man presented to our tertiary care center for electrophysiologic evaluation. He had a history of ischemic cardiomyopathy with prior inferior and anterior myocardial infarction, followed by percutaneous intervention $\times 2$. He also had congestive heart failure New York Heart Association (NYHA) Class III symptoms, pleural effusion, diabetes, and hyperlipidemia, and suffered from systolic dysfunction with a severely reduced left ventricular (LV) ejection fraction (21%) and a left ventricular end-systolic volume of 140 ml despite optimal medical treatment. The electrocardiogram showed sinus rhythm with a typical left bundle branch block, QRS 178 ms (Figure 1). The two-dimensional (2D) echocardiogram demonstrated obvious intra-LV and interventricular dyssynchrony. Cardiac resynchronization therapy (CRT) device implantation was recommended.

The patient was enrolled in the MultiPoint™ Pacing (MPP) Investigational device exemption (IDE) study. A St. Jude Medical automatic implantable CRT-defibrillator system capable of pacing from multiple poles with a Quartet™ model 1458Q LV lead (St. Jude Medical, Minneapolis, MN) was implanted. A pre-implantation occlusive coronary venous angiogram followed by post-implantation fluoroscopic images in the same views confirmed the LV lead was implanted in the lateral vein position (Figure 2). According to study protocol, the device was turned on after implantation to deliver biventricular (BiV) pacing from the M2-RV coil of the Quartet lead, since electrode M2 showed the latest local activation at an acceptable threshold. Settings were as follows: DDD mode, simultaneous RV–LV pacing, sensed atrioventricular (AV) delay 100 ms, atrial paced AV delay 150 ms, pacing at twice threshold.

The subject continued to receive conventional BiV pacing for the first 3 months after implantation. At 3 months, after completing all protocol-required testing, the subject was randomized to the MPP arm. The MPP feature was turned on and programmed to the settings shown in Table 1, as these settings provided the maximum Doppler derived velocity–time interval

Imran Niazi reports receiving research grants from St. Jude Medical. Manuscript received July 21, 2016, Final version accepted August 31, 2016.

Address correspondence to: Imran Niazi, MD, Aurora St. Luke's Medical Center, 2801 W. Kinnickinnic River Parkway, Ste. 840, Milwaukee, WI 53215. E-mail: publishing24@aurora.org

Figure 1: Twelve-lead electrocardiograms performed prior to cardiac resynchronization therapy (a), during standard biventricular cardiac resynchronization therapy (b), and during multipoint pacing (c).

Figure 2: (A) A pre-implantation occlusive coronary venous angiogram followed by post-implantation fluoroscopic images in the anteroposterior view (B) and shallow left anterior oblique view (C). Arrows point to target branch in A.

Table 1: Cardiac resynchronization therapy delays and vectors programmed during multipoint pacing (3 months to 9 months)

LV1 vector	LV2 vector	LV1-LV2 delay (ms)	LV2-RV delay (ms)
M3-RV coil	M2-RV coil	5	15

LV: left ventricle; RV: right ventricle.

across the mitral valve. This measurement has been shown to correlate best with directly measured LV dP/dt.¹

The subject was followed with MPP therapy for a further 6 months and then reassessed per MPP protocol. LV pacing >95% of the time was confirmed for the duration of follow-up.

Six weeks after implantation, while undergoing standard CRT, the subject presented to the emergency department with a 1-week history of worsening dyspnea and severe orthopnea. He reported being compliant with his medical regimen and denied dietary indiscretion or recent decrease in urinary output. He was admitted to the hospital for exacerbation of congestive heart failure,

Table 2: NYHA class and Patient Global Assessment during biventricular pacing and multipoint pacing

	Enrollment	3 months	6 months	9 months
NYHA classification*	II	III	II	II
PGA assessment [†]	–	Better [‡]	Markedly better [‡]	Markedly better [‡]

*NYHA and PGA were assessed by the blinded assessor.
[†]Relative to the enrollment visit before having the cardiac resynchronization therapy system implanted.
[‡]Relative to the 3-month randomization visit.
NYHA: New York Heart Association; PGA: Patient Global Assessment.

Figure 3: Changes in end-systolic volume and ejection fraction with biventricular pacing and multipoint pacing. BiV: biventricular; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; MPP: multipoint pacing.

placed on nasal cannula oxygen, and treated with intravenous furosemide. A chest X-ray showed findings consistent with pulmonary venous congestion. A 2D echocardiogram, performed after symptoms resolved, showed an LV ejection fraction of 25%. He was discharged home in stable condition after 4 days in the hospital.

After randomization to the MPP arm at 3 months, the patient did not experience any further heart failure events.

According to the MPP IDE study requirement, NYHA class assessment and Patient Global Assessment (PGA) were conducted by an independent assessor who was blinded to patient therapy and uninvolved in patient care. At the 3-month randomization visit, NYHA and PGA assessments showed a decline in the patient's overall status relative to assessment at the time of enrollment (Table 2).

NYHA class and PGA were assessed, and echocardiographic measurements were obtained at the 6- and 9-month visits, while the patient was receiving MPP. At 9 months, both NYHA class and PGA showed improvements relative to the 3-month randomization time point (Table 2). In addition, the patient had remarkable LV reverse remodeling and improvement in systolic function relative to enrollment (46% reduction in LV

end-systolic volume and 11 percentage points in absolute increase in LV ejection fraction) while receiving MPP therapy (Figure 3).

Discussion

The decline in NYHA class and PGA and hospitalization for heart failure during the first 3 months after CRT device implantation while the patient received conventional BiV pacing therapy indicated that this patient failed to respond to conventional CRT. Clinical failure to respond is reported in about 30% of patients in randomized CRT trials.^{2,3} However, he did respond to MPP CRT with improvement in heart failure status and significant reverse remodeling. This suggests that MPP CRT may be superior to standard CRT in individual patients and may convert some non-responders to responders.

There are several possible reasons for the superiority of MPP in select patients. Studies using two separate LV leads generally have shown improved reverse remodeling and acute hemodynamic improvement compared with standard CRT.^{4,5} A single lead with multiple poles may well have the same effect, without the complexity and time requirements necessary when using multiple leads. Delivering pacing pulses at multiple LV sites is more likely to capture a larger volume of cardiac muscle and, therefore, the site of latest electrical activation within the left ventricle may be more likely to be depolarized early, resulting in superior resynchronization. Multiple-site LV stimulation also may more closely mimic normal LV depolarization in patients with conduction system abnormalities as a larger portion of the LV is simultaneously depolarized compared with single-site LV stimulation.

Prospective randomized studies are indicated to assess the role of MPP.

References

1. Jansen AH, Bracke FA, van Dantzig JM, et al. Correlation of echo-Doppler optimization of atrioventricular delay in cardiac resynchronization therapy with invasive hemodynamics in patients with heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. *Am J Cardiol.* 2006;97(4):552–557.
2. Martin DO, Lemke B, Birnie D, et al. Investigation of a novel algorithm for synchronized left-ventricular pacing and ambulatory optimization of cardiac resynchronization therapy: Results of the adaptive CRT trial. *Heart Rhythm.* 2012;9(11):1807–1814.

3. Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med.* 2005;352(15):1539–1549.
4. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med.* 2001;344(12):873–880.
5. Niazi I, Kiemen J, Yong P, et al. Hemodynamic superiority of dual-site left ventricular stimulation over conventional biventricular stimulation in heart failure patients. *J Innov Cardiac Rhythm Manage.* 2011;2(8):412–418.