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NEW RESEARCH PAPERS

Safety and Efficacy of Multipoint Pacing in Cardiac Resynchronization Therapy

The MultiPoint Pacing Trial

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ABSTRACT

OBJECTIVES The MultiPoint Pacing (MPP) trial assessed the safety and efficacy of pacing 2 left ventricular sites with a quadripolar lead in patients with heart failure indicated for a CRT-D device.

BACKGROUND Cardiac resynchronization therapy nonresponse is a complex problem where stimulation of multiple left ventricular sites may be a solution.

METHODS Enrolled patients were indicated for a CRT-D system. Bi-ventricular (Bi-V) pacing was activated at implant. Three months later, clinical response was assessed and the patient was randomized (1:1) to receive Bi-V pacing or MPP. Patients were followed for 6 months post-randomization and clinical response was again assessed.

RESULTS The CRT-D system was successfully implanted in 455 of 469 attempted implants (97%). A total of 381 patients were randomized to Bi-V or MPP at 3 months. The primary safety endpoint was met with freedom from system-related complications of 93.2%. The primary efficacy endpoint of the noninferiority comparison of nonresponder rates between the 2 arms was met. Patients randomized to MPP arm and programmed to pace from anatomically distant poles (MPP-AS) responded to therapy at significantly higher rates than MultiPoint pacing–other programmed settings (MPP-Other). Within this group, 87% were responders at 9 months, 100% designated as nonresponders at 3 months converted to responders at 9 months, and 54% experienced an incremental response compared to MPP-Other. Also within MPP-AS, 92% of patients with de novo CRT-D implant were classified as responders compared with patients with MPP-Other.

CONCLUSIONS MPP is safe and effective for treating heart failure. The study met the pre-specified hypothesis that response to MPP is noninferior to Bi-V pacing with a quadripolar left ventricular lead. (MultiPoint Pacing IDE Study [MPP IDE]; NCT01786993) (J Am Coll Cardiol EP 2017;3:1510–8) © 2017 by the American College of Cardiology Foundation.

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Cardiac resynchronization therapy (CRT) is a well-established therapy for heart failure (HF) and has been shown to produce significant clinical benefits, including reduced mortality, reduced HF hospitalizations, and improved symptoms and quality of life (1,2). However, despite technological advances, a significant proportion of patients fail to respond (3). The mean responder rate from the 15 largest contemporary CRT studies has been approximately 59% to 80%, with a 44% to 78% rate based on echocardiographic parameters (4). In the MIRACLE study, 34% of patients did not demonstrate improvement based on the clinical composite score (CCS), a composite measure defined by all-cause mortality, HF-related hospitalization, New York Heart Association (NYHA) functional class, and Patient Global Assessment (PGA) score (5).

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Although the cause of nonresponse to CRT is multifactorial, complex, and not completely understood, stimulation of multiple left ventricular (LV) sites may be an effective solution. This has been attempted by the use of 2 separate LV leads (6,7) but at the cost of increased technical difficulty and increased chance of major procedure-related adverse events. An alternative approach is to pace multiple LV sites using a single quadripolar lead, achieved by using a CRT-D system enabled with MultiPoint Pacing (MPP) programming (Quartet LV Quadripolar Lead with a Quadra CRT-D, Abbott, Sylmar, California). In this system, dual-site LV pacing using 2 different vectors can be selected. Additionally, a programmable delay (5 to 80 ms) can be introduced between the 2 LV pacing pulses (intraventricular delay) and the 2 LV pulses can be delivered either before or immediately after the right ventricular pacing pulse (V-V delay).

Small prospective studies have shown CRT with MPP can result in acute improvements in contractility, hemodynamics, and dyssynchrony compared with standard bi-ventricular (Bi-V) pacing (8–11). In a study by Pappone et al. (12), MPP therapy was shown to result in both mid-term (3 months) and long-term (12 months) improvements in LV reverse remodeling and clinical response compared with standard Bi-V pacing. Recent studies by Forleo et al. (13) and Zanon et al. (14) have shown MPP is associated with improved clinical status and an additional increase in ejection fraction, with reverse remodeling, beyond the effect caused by traditional Bi-V CRT. The present trial was designed to assess the safety and effectiveness of MPP stimulation in patients indicated for a CRT-D device.

METHODS

STUDY DESIGN AND OVERSIGHT. The MPP trial was a prospective, randomized, double-blind, multicenter clinical trial sponsored by the manufacturer of the quadripolar CRT-D system (Abbott) and approved by the Food and Drug Administration and institutional review board at each of the participating centers. All investigators agreed to abide by the conflict-of-interest guidelines described by Healy et al. (15). This trial was designed in collaboration with the Food and Drug Administration to prove the safety and efficacy of the MPP feature. Furthermore, a steering committee, with the participation of the sponsor, was responsible for the design and conduct of the trial and reporting of the findings. Clinical events were adjudicated by an independent, blinded events committee. Monitoring and collection of the data and data analyses were performed by the sponsor in partnership with the steering committee. The authors confirm the accuracy and completeness of the reported findings.

STUDY PARTICIPANTS. After obtaining written informed consent, eligible patients with a standard clinical indication for implantation of a CRT-D system (16) were enrolled. **Table 1** lists the study inclusion and exclusion criteria.

Enrolled patients had cardiac performance (2-dimensional echocardiography) and other clinical and demographic variables assessed within 30 days before implant. Patients who had the CRT-D system successfully implanted had Bi-V pacing with a quadripolar LV lead activated at that time. The LV pacing vector, atrioventricular delay, and V-V delay settings

ABBREVIATIONS AND ACRONYMS

Bi-V = bi-ventricular
CCS = clinical composite score
CRT = cardiac resynchronization therapy
EA VTI = velocity-time integral of the transmitral flow
HF = heart failure
ITT = intention-to-treat
LCB = lower confidence bound
LV = left ventricular
MPP = MultiPoint pacing
MPP-AS = MultiPoint pacing–anatomic separation/minimal intraventricular timing delay
MPP-Other = MultiPoint pacing–other programmed settings
NYHA = New York Heart Association
PGA = Patient Global Assessment

Medtronic and Abbott. Dr. Varma is on the advisory board and is a consultant for Abbott. Dr. Lee is an employee at Abbott. Dr. Tomassoni is an advisor, speaker, and on the Medical Device Board for Abbott, Biosense Webster, Medtronic, Boston Scientific, Biotronik, Siemens, STXS, Topera, Atricure, CPI, Johnson & Johnson, and Pfizer.

All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

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