Electrical resynchronization induced by direct His-bundle pacing

Daniel L. Lustgarten, MD, PhD,* Susan Calame, RN,* Eric M. Crespo, MD James Calame, RN, Robert Lobel, MD, Peter S. Spector, MD*

*From the Department of Medicine at the University of Vermont School of Medicine and Fletcher Allen Health Care, Burlington, Vermont, and the *Cardiovascular Research Institute, Burlington, Vermont.*

BACKGROUND Biventricular pacing (BiV) to effect cardiac resynchronization therapy can be technically difficult and fails to elicit a clinical response in 30% to 40% of patients. Direct His-bundle pacing (DHBP) theoretically could obviate some of these problems. Although DHBP is capable of narrowing the QRS in some patients, the consistency with which this can be achieved has not been characterized.

OBJECTIVE The purpose of this study was to restore His-Purkinje functionality in consecutive patients undergoing *de novo* clinically mandated cardiac resynchronization therapy.

METHODS DHBP was temporarily implemented at the time of implantation of a permanent BiV system in patients referred for cardiac resynchronization therapy. Native conduction, DHBP, and BiV QRS duration were compared. All patients presenting for BiV cardiac resynchronization therapy were eligible for the study. Ten patients were studied.

RESULTS DHBP was successfully implemented in all 10 patients. In 7 of 10 patients, DHBP narrowed the QRS significantly compared with native conduction and BiV (mean QRS duration: native 171 ± 13 ms, DHBP 148 ± 11 ms, BiV 158 ± 21, $P < .0001$). QRS narrowing with DHBP was specifically attributable to capture of latent His-Purkinje tissue. DHBP lead implantation time (16 minutes) was shorter than standard left ventricular lead implantation time (42 minutes).

CONCLUSION DHBP was readily implemented in patients with standard indications for BiV cardiac resynchronization therapy. In most patients studied, DHBP resulted in a significantly narrower QRS compared with native conduction. DHBP may offer a physiologic alternative to BiV for cardiac resynchronization therapy.

KEYWORDS Biventricular pacing; Cardiac resynchronization therapy; Conduction disease; Congestive heart failure; Device therapy; Direct His-bundle pacing; Electrical resynchronization; Physiologic pacing

ABBREVIATIONS **BiV** = biventricular pacing; **DHBP** = direct His-bundle pacing; **LV** = left ventricular; **NS-DHBP** = nonselective direct His-bundle pacing; **S-DHBP** = selective direct His-bundle pacing

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Introduction

Longitudinal dissociation of the His bundle was recognized more than 30 years ago[1,2] and confirmed by the demonstration that direct His-bundle pacing (DHBP) normalizes the QRS axis and duration in patients and animals with proximal His-bundle lesions that cause bundle branch block.[3,4] Until recently, this intriguing electrophysiologic observation languished without broad clinical applicability. It was shown recently that some patients with congestive heart failure and His-Purkinje disease benefit clinically from cardiac resynchronization therapy.[5–7] Currently, cardiac resynchronization therapy is effected by pacing the left and the right ventricle with two separate leads. The benefit of biventricular pacing (BiV) for cardiac resynchronization therapy is not seen in 30% to 40% of patients, as measured by symptom improvement, left ventricular (LV) remodeling, and/or reduced mortality.[5,8,9] This limitation and the existence of functional dissociation in diseased His-Purkinje tissue led us to study whether DHBP could provide an effective physiologic alternative to conventional cardiac resynchronization therapy. We use the term "physiologic" to mean ventricular activation by previously latent His-Purkinje tissue during DHBP as evidenced by narrowing of the QRS in response to DHBP. This contrasts with nonphysiologic BiV in which ventricular activation occurs in response to RV endocardial and LV epicardial pacing.

With the advent of increasingly sophisticated implantation techniques and leads, induction of stable and persistent DHBP has been demonstrated to be feasible in patients requiring ventricular pacing.[10–13] However, little information is available regarding its feasibility in patients with His-Purkinje disease. Barba-Pichardo et al[14] reported success in inducing persistent DHBP in seven patients with high-grade heart block and baseline conduction defects. These patients were selected based on QRS narrowing in response to DHBP during an initial electrophysiologic study.

In our study, the feasibility of DHBP was evaluated in a group of patients who presented with standard indications for BiV car-

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diac resynchronization therapy. We sought to determine whether DHBP could be achieved and to discern whether recruitment of latent His-Purkinje tissue with resultant QRS narrowing could be elicited. We demonstrate that DHBP in patients presenting for cardiac resynchronization therapy is feasible and may provide a physiologic alternative to BiV as a means to establish cardiac resynchronization therapy.

Methods

Patient selection

All patients who presented at Fletcher Allen Health Care for *de novo* BiV–implantable cardioverter-defibrillator therapy from March 2008 to March 2009 were considered candidates for study. Ten consecutive patients willing to participate who provided written informed consent were studied with a protocol approved by the University of Vermont Investigational Review Board.

Protocol

An octapolar mapping catheter (2.5-mm interelectrode spacing, Biosense Webster, Inc., Diamond Bar, CA, USA) was advanced to the His region via the femoral venous approach. Standard implantation techniques were used for lead and device placement. A right ventricular defibrillation lead was placed in the right ventricular apex or apical septum. With the use of a SelectSite sheath lead delivery system (model C304, Medtronic, Inc., Minneapolis, MN, USA), a SelectSecure lead (model 383, Medtronic) was actively fixed at a site demonstrating a discrete His potential, localized by the mapping catheter.

The sheath was withdrawn to the level of the superior vena cava, and pacing was performed from the actively fixed DHBP lead in four pacing configurations: standard bipolar, reverse bipolar, cathodal, and anodal tip unipolar. Recordings were stored for analysis offline on a Bard electrogram acquisition system (C.R. Bard, Inc., Lowell, MA, USA). Pacing thresholds were recorded using a pace sense analyzer (model 2290, Medtronic).

The actively fixed DHBP lead was unscrewed from the His-bundle region. The lead was actively fixed in the right atrium and tested. The sheath was removed by slitting. The LV lead was placed via the coronary sinus using standard techniques. QRS duration was recorded during BiV pacing.

Statistical analysis

Data are reported as mean ± SD. All intervals reported were obtained from an average of 10 consecutive measurements. $P < .05$ was considered significant. Each patient gave rise to a set of replicated repeated observations. Student's t-test was used for paired comparisons. Baseline conducted, DHBP, and BIV QRS conditions were examined using a repeated measures analysis of variance with nonselective-DHBP and selective DHBP (see below for definitions) serving as a between-subject factor. If an overall statistical difference among the three conditions was observed, follow-up pair-wise comparisons among the three conditions were conducted with all reported P values adjusted for multiple comparisons using the Bonferroni adjustment. Computations were conducted using Systat (version 11.0, Systat Software, Inc., Chicago, IL, USA).

Results

Ten patients were studied. Six of the 10 patients had ischemic cardiomyopathy, and four had nonischemic dilated cardiomyopathy. Average ejection fraction was 18% ± 7%. Nine of the patients had left bundle branch block, and one had atypical right bundle branch block. Average QRS duration was 171 ± 13 ms. All patients studied were in New York Heart association functional class III and were on maximally tolerated drug regimens.

Comparisons of DHBP with LV lead implantation

In 9 of the 10 patients, mean time to implant the DHBP lead was 16 ± 12 minutes. In one of the first patients studied, the lead tip was not actively fixed, although DHBP was obtained in this patient by leaving the sheath deflected in the anteroseptal position. In this patient, the lead could not be fixed because of difficulties in securing the exposed helical screw; only 10 minutes was spent attempting to position the lead.

Mean time to implant the LV lead was 42 ± 13 minutes. Reasons for protracted lead placement time (>30 minutes) were diaphragmatic stimulation in two, difficult coronary sinus cannulation in three, and unstable lead position in two.

Response to DHBP

DHBP was demonstrated in all 10 patients. The observed patterns of response are summarized in Figure 1. Two basic patterns of DHBP were seen: (1) *selective DHBP* (S-DHBP), defined by ventricular activation occurring solely over the His-Purkinje system, and (2) *nonselective DHBP* (NS-DHBP), in which there was direct capture of the basal ventricular septum in addition to His-bundle capture. Specific characteristics of each pattern are described below.

Four patients exhibited S-DHBP only; three patients exhibited both S-DHBP and NS-DHBP depending on pacing conditions as described below; and three patients exhibited NS-DHBP only (Figure 1). QRS narrowing, defined as any statistically significant reduction in QRS duration, occurred in seven patients, whereas QRS narrowing did not occur in three patients during DHBP. In all instances when QRS narrowing occurred, evidence of recruitment of latent His-Purkinje tissue was seen (described below).

The QRS narrowed in 2 of the 4 patients who exhibited only S-DHBP. Among the three patients with both S-DHBP and NS-

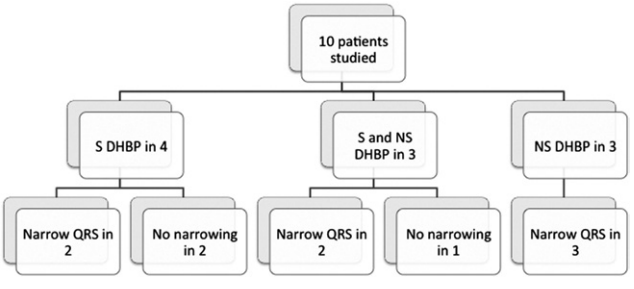

Figure 1 Summary of the types of direct His-bundle pacing (DHBP). In the two patients in whom selective direct His-bundle pacing (S-DHBP) did not narrow the QRS, the His-to-QRS and stimulus-to-QRS intervals were identical. The septal ventricular activation time was not advanced in either patient with DHBP. These findings indicate that the pacing site in these two patients was proximal to the His-Purkinje defect. NS-DHBP = nonselective direct His-bundle pacing.