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ORIGINAL ARTICLE

The Left Ventricular Lead Electrical Delay Predicts Response to Cardiac Resynchronisation Therapy

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Up to one-third of patients who undergo cardiac resynchronisation therapy (CRT) are not responders. To identify potential responders to CRT may be sometimes difficult and time-consuming. Forty-five patients who had undergone CRT implantation for standard indications were evaluated. Electrical left ventricular (LV) lead location was assessed by left ventricular activation time (LVAT), LV lead electrical delay (LVLED), and RV-LV interlead electrical delay (RVsense-LVsense). Anatomic LV pacing location was assessed as basal or mid-ventricular between 3:00 to 5:00 (traditionally optimal site), and all the other positions (traditionally non-optimal site). CRT response was defined as a decrease in LV end-systolic volume (LVESV) exceeding 15% at six months. LVLED was larger in the responder group than that in the non-responder group (67.3±8.5% vs. 55.3±8.1%, $P< 0.001$). In the multivariate analysis, LVLED and cLBBB morphology were the two independent predictors of positive echocardiographic response to CRT (OR=1.180, P=0.003; OR=7.497, P=0.04, respectively). A cutoff value of LVLED> 54.82% predicted responders with 96.3% sensitivity and 75.2% specificity and the area under the receiver operating characteristic (ROC) curve was 0.844 for LVLED (P=0.002). No relationship was found between the anatomic LV pacing sites and response to CRT (P=0.188). The larger left ventricular lead electrical delay may predict response to cardiac resynchronisation therapy.

Keywords Cardiac resynchronisation therapy • Response • Electrical dyssynchrony • Left ventricular pacing site • Heart failure

Introduction

Cardiac resynchronisation therapy (CRT) represents one of the main advances in recent years to treat heart failure, which can improve symptoms and cardiac dysfunction, as well as reduce mortality in patients with progressive congestive heart failure [1–3].

The main approach of identifying CRT candidates is based on QRS prolongation as measured on surface electrocardiogram (ECG) indicating electrical dyssynchrony [4,5]. However, despite standard selection criteria for CRT, accumulated data indicate that 20%-30% of these patients do not benefit from CRT [6]. The reasons for these non-responders include inappropriate candidate selection, device programming, and LV lead placement[7,8]. Few studies have systematically evaluated the value of intra-procedural data to validate the appropriate LV pacing position to achieve better clinical outcomes.

The aim of this study was to evaluate whether left ventricular electrical delay or anatomic pacing location can be used to predict CRT response.

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Methods

Patients and Study Protocol

The study prospectively enrolled 45 consecutive patients for CRT from January 2009 to October 2012. All patients showed LVEF≤35% and NYHA class III-IV symptoms on optimal medical therapy with a QRS duration of ≥120 ms. Patients with atrial fibrillation, or with chronic right ventricular pacing (RVP) upgraded to CRT were excluded from this study.

12-lead ECG and echocardiograph were obtained before and after CRT implantation. Parameters of intracardiac electrogram (IEGM) and the LV pacing site were calculated during the operation. At six months post-implantation, an echocardiograph was performed again. Analyses were performed blindly to outcome results.

Cardiac Resynchronisation Therapy Implantation and Optimisation

After cannulation of the coronary sinus (CS), a venogram was obtained. Target location for the LV lead tip was the posterolateral/lateral basal segment. If veins to this segment were unable to be successfully accessed, other cardiac veins could be used to achieve satisfactory pacing thresholds without phrenic nerve capture. The atrial lead was placed in the right atrial appendage. The right ventricular (RV) lead was recommended to be placed in the RV apex or permitted to be placed in the RV outflow to keep the longest distance between right and left leads. Echo optimisation of atrioventricular and ventricular-ventricular timing was performed at one week after implantation by using serial measurements of the aortic flow velocity envelopes [9,10].

Electrocardiogram and Intracardiac Electrogram Analysis

Standard supine 12-lead surface ECGs (25 mm/s, 10 mm/mV) prior to and following CRT implantation were analysed. Patients were divided into two groups according to their ECG morphology. One group included patients with complete left bundle branch block (cLBBB), and the other one included patients with intraventricular conduction delay (IVCD). Complete LBBB definition was derived from current AHA/ACCF/HRS criteria: QRSmax≥120 ms with broad notched/slurred R wave in I, aVL, V6 (RS is allowed in V6); absent q wave in I, V5, V6; R wave peak time >60 ms in V6 and <60 ms in V1-V3. If the baseline ECG did not conform to one of these criteria, the ventricular conduction delay was denoted as IVCD [11].

A QRS notch, which occurred after 40 ms of QRS onset, was regarded as the transition from RV to LV depolarisation and the time difference between this notch and the end of QRS was indicated as the LV activation time (LVATmax) (Fig. 1). In five patients, a notch could not be clearly delineated and therefore LVATmax was estimated with the use of linear regression (LVAT [ms]= -35.839+0.763×QRSd [ms]+0.000619×QRSd [ms]^2) [12]. After obtaining the final pacing position, Q-LVsense was measured intra-procedurally as an interval between QRS onset on the surface ECG to the peak of sensed

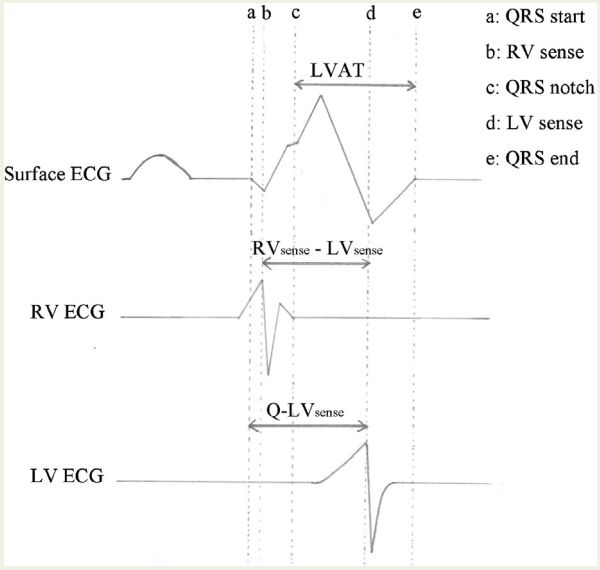

Figure 1 Example of surface ECG and EGM time interval measurements. ECG=Electrocardiograph; EGM=intracardiac electrogram.

electrogram on LV lead, and the percentage of the baseline QRS duration was recorded as left ventricular lead electrical delay (LVLED) [13]. RVsense-LVsense represents the timing difference between local RV and local LV activation on the ventricular EGMs (Fig. 1) [14]. The parameters of LVAT, QRS Duration,ΔQRS pre-implant to paced, RVsense-LVsense were performed with LEAD-2000 polyphysiograph (100m/s, Jinjiang Electronic Technology Co., Ltd. Sichuan, China).

Location of Pacing Site

The LV pacing site was defined by fluoroscopy in two planes at implantation, the left anterior oblique (LAO) view and the right anterior oblique (RAO) view. In the LAO view, the coronary sinus encircles the mitral valve with its tributaries radiating out like the hands of a watch. Using this clockwise definition, between 12:00 and 3:00 corresponded to the anterior/anteriorlateral aspect of the heart, and between 3:00 and 5:00 corresponded to the lateral/posterolateral, and between 5:00 to 6:00 corresponded to the posterior. In the RAO view, the LV was divided into three segments, and the LV pacing site was located as basal, mid-ventricular, and apical (Fig. 2) [15]. According the method, the LV pacing sites were defined as two groups: one group with basal or mid-ventricular between 3:00 to 5:00 (traditionally optimal site), and the other one with all the other positions (traditionally non-optimal site).

Echocardiographic Evaluation and Definition of Responders

Echocardiographic data were obtained by using an apparatus (VIVID, General Electric, USA). The left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) were obtained from the apical two- and four-chamber views, and LVEF was calculated by using