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Optimizing Hemodynamics in Heart Failure Patients by Systematic Screening of Left Ventricular Pacing Sites

The Lateral Left Ventricular Wall and the Coronary Sinus Are Rarely the Best Sites

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Objectives We sought to evaluate the impact of the left ventricular (LV) pacing site on hemodynamic response to cardiac resynchronization therapy (CRT).

Background CRT reduces morbidity and mortality in heart failure patients. However, 20% to 40% of eligible patients may not fully benefit from CRT device implantation. We hypothesized that selecting the optimal LV pacing site could be critical in this issue.

Methods Thirty-five patients with nonischemic dilated cardiomyopathy referred for CRT device implantation were studied. Intraventricular dyssynchrony and latest activated LV wall were defined by tissue Doppler imaging analysis before the study. Eleven predetermined LV pacing sites were systematically assessed in random order: basal and mid-cavity (septal, anterior, lateral, inferior), apex, coronary sinus (CS), and the endocardial site facing the CS pacing site. For each patient, $+dP/dT_{max}$, $-dP/dT_{min}$, pulse pressure, and end-systolic pressure during baseline (AAI) and DDD LV pacing were compared. Two atrioventricular delays were tested.

Results Major interindividual and intraindividual variations of hemodynamic response depending on the LV pacing site were observed. Compared with baseline, LV DDD pacing at the best LV position significantly improved $+dP/dT_{max}$ ($+31 \pm 26\%$, $p < 0.001$) and was superior to pacing the CS ($+15 \pm 23\%$, $p < 0.001$), the lateral LV wall ($+18 \pm 22\%$, $p < 0.001$), or the latest activated LV wall ($+11 \pm 17\%$, $p < 0.001$).

Conclusions The pacing site is a primary determinant of the hemodynamic response to LV pacing in patients with nonischemic dilated cardiomyopathy. Pacing at the best LV site is associated acutely with fewer nonresponders and twice the improvement in $+dP/dT_{max}$ observed with CS pacing. (J Am Coll Cardiol 2010;55:566–75) © 2010 by the American College of Cardiology Foundation

Despite recent advances in its pharmacologic treatment, congestive heart failure remains a growing health care problem in the Western world (1). Cardiac resynchronization therapy (CRT) was used extensively during the past decade for the management of patients with drug-refractory, end-stage heart failure. Large randomized trials have demonstrated in selected

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patients that CRT improves quality of life, symptoms, and exercise capacity and reduces all-cause as well as heart failure morbidity and mortality (2–9). However, individual results vary, and 20% to 40% of implanted patients do not respond to CRT according to these studies. Different strategies have been developed to improve the responder rate to CRT such as improving pre-implantation patient selection and optimizing device programming and left ventricular (LV) lead position.

Based on previous studies, the current consensus is to position the LV lead in a lateral or posterolateral branch of the coronary sinus (CS) (10,11). The concept that this site is optimal for all patients has been challenged by hemodynamic studies suggesting that the actual pacing site is of critical importance to CRT (12,13). However, such studies have been limited by the number of LV pacing sites compared, either due to the constraints of CS anatomy or the LV sites that are accessible by thoracotomy. To date, no study has systematically investigated whether optimal LV pacing sites, selected individually from sites throughout the LV wall, might decrease the rate of nonresponders or optimize the benefit of CRT among responders.

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We hypothesized that LV hemodynamics may be optimized by pacing at sites that do not coincide with conventional CS pacing sites and that the optimal site may lie remote from the lateral LV wall or from sites of maximal mechanical LV delay. We tested this hypothesis by comparing the quantitative hemodynamic response to pacing at each of 10 transseptally accessed endocardial sites with the response at the conventional CS site in patients with nonischemic cardiomyopathy and clinical indications for CRT.

Methods

Patients. Thirty-five consecutive patients (mean age 63 ± 12 years; 28 men) with New York Heart Association functional class III or IV heart failure despite optimal medical therapy, echocardiographic LV ejection fraction <35%, and a left bundle branch block pattern on the surface electrocardiogram with a QRS duration of >140 ms, scheduled for implantation of a CRT device were included in this single-center prospective study. The protocol was approved by the CHU Bordeaux ethics committee, and all patients gave informed consent. All patients included in this study had appropriate investigations to exclude reversible causes of dilated cardiomyopathy and ischemic disease. They were on an optimal medical regimen, including angiotensin-converting enzyme inhibitors and beta-blockers. Patients with ischemic or valvular cardiomyopathy were excluded from participation.

LV pressure and volume measurements. To acquire real-time pressure-volume loops during the study, a 7-F combined pressure-conductance catheter (CD Leycom, Zoetermeer, the Netherlands) was inserted through a femoral artery and advanced to the LV apex through a 0.025-inch flexible guidewire via the retroaortic route. The catheter was connected to a cardiac function analyzer (Leycom CFL512, CD Leycom) that recorded and displayed online pressure and 7 segmental volumes delineated by the electrodes at a sample frequency of 250 Hz. For the purpose of the present study, the volume data were not used.

Abbreviations and Acronyms

AVD = atrioventricular delay
BiV = biventricular
CRT = cardiac resynchronization therapy
CS = coronary sinus
ESP = end-systolic pressure
LV = left ventricular
PP = pulse pressure
TDI = tissue Doppler imaging

The pigtail of the conductance catheter was positioned in the apex and was adjusted to the long heart axis under fluoroscopic guidance. Temporary pacing leads were placed in the right atrium (Josephson, Bard Electrophysiology, Lowell, Massachusetts) and in a lateral branch of the coronary sinus (Xtrem catheter, ELA Medical, Le Plessis-Robinson, France) via the femoral vein. A deflectable-tip catheter (Celsius 4 mm, Biosense Webster Inc., Diamond Bar, California) was placed in the left ventricle via the transseptal route and used for pacing the predetermined LV endocardial sites. Pulsatile arterial pressure was measured continuously.

Echocardiographic assessment. In addition to the invasive hemodynamic study described in detail in the following, patients underwent echocardiography with intraventricular dyssynchrony assessment. Recordings were performed using a GE Vingmed Ultrasound system (System 7, GE Vingmed Ultrasound AS, Horten, Norway) equipped with a 2.5- to 5-MHz imaging probe and offline cine loop analysis software. All images were recorded digitally and analyzed by the same operator. Mitral regurgitation was quantified and graded by the proximal isovelocity surface area method. Intra-LV dyssynchrony was determined using tissue Doppler imaging (TDI) to assess segmental wall motion, as previously described (14–16). In brief, TDI was performed by placing the sample volume in the middle of the basal and mid-segmental portion of the septal, lateral, inferior, anterior, posterior, and anteroseptal walls. Gain and filter settings were adjusted as needed to eliminate background noises and to allow a clear tissue signal. The TDI velocities were recorded and measured at a sweep speed of 100 mm/s using online calipers. The intra-LV $\text{delay}_{\text{peak}}$ was then calculated as the difference between the shortest and longest of the 12 segmental electromechanical $\text{delay}_{\text{peak}}$ values, and the latest activated LV wall was defined as the wall with the longest electromechanical $\text{delay}_{\text{peak}}$ (14–17).

Experimental protocol. All measurements during baseline and LV pacing were performed at a constant atrial pacing rate of 10 beats on the resting heart rate (Table 1). Two atrioventricular delays (AVDs) were tested; a short AVD was set as the longest AVD that allowed complete ventric-