Epicardial left ventricular lead placement for cardiac resynchronization therapy: Optimal pace site selection with pressure-volume loops

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Objectives: Patients in heart failure with left bundle branch block benefit from cardiac resynchronization therapy. Usually the left ventricular pacing lead is placed by coronary sinus catheterization; however, this procedure is not always successful, and patients may be referred for surgical epicardial lead placement. The objective of this study was to develop a method to guide epicardial lead placement in cardiac resynchronization therapy.

Methods: Eleven patients in heart failure who were eligible for cardiac resynchronization therapy were referred for surgery because of failed coronary sinus left ventricular lead implantation. Minithoracotomy or thoracoscopy was performed, and a temporary epicardial electrode was used for biventricular pacing at various sites on the left ventricle. Pressure-volume loops with the conductance catheter were used to select the best site for each individual patient.

Results: Relative to the baseline situation, biventricular pacing with an optimal left ventricular lead position significantly increased stroke volume (+39%, $P = .01$), maximal left ventricular pressure derivative (+20%, $P = .02$), ejection fraction (+30%, $P = .007$), and stroke work (+66%, $P = .006$) and reduced end-systolic volume (−6%, $P = .04$). In contrast, biventricular pacing at a suboptimal site did not significantly change left ventricular function and even worsened it in some cases.

Conclusions: To optimize cardiac resynchronization therapy with epicardial leads, mapping to determine the best pace site is a prerequisite. Pressure-volume loops offer real-time guidance for targeting epicardial lead placement during minimal invasive surgery.

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Cardiac resynchronization therapy (CRT) reduces symptoms¹ and mortality^{2,3} among patients with heart failure and left bundle branch block (LBBB). For CRT, a left ventricular pacing electrode is required, which is usually placed by catheterization of the coronary sinus.

Coronary sinus catheterization is associated with a long procedure time,⁴ extensive fluoroscopy,⁴ reported implantation failure in 10% to 30% of cases,^{1,5,6} left ventricular lead dislodgment in 6% to 14% of initially successfully implanted cases,^{1,5,6} and an increased pacing threshold with time, requiring an intervention in 13% to 18% of patients.^{5,6} Perhaps the most important limitation of coronary sinus

TABLE 1. Patient characteristics

Case	Sex	Age (y)	EF (%)	NYHA	QRS width	Medications	Reason for CTS	Cause of CHF
1	M	73	32	III	280	Diuretics, BB, ACE	Lead dislocation	Ischemic
2	F	50	26	III	144	Diuretics, BB, ACE	Coronary sinus anatomy	Ischemic
3	M	33	13	III	184	Diuretics, BB, ACE, spironolactone	Coronary sinus anatomy	Nonischemic
4	M	73	41	III	170	Diuretics, BB, ACE, digitalis, spironolactone	Coronary sinus anatomy	Ischemic
5	M	67	26	III	152	Diuretics, ACE, spironolactone	Implantation failure	Ischemic
6	M	69	19	III	180	Diuretics, BB	Stenosis V subclavia	Ischemic
7	M	68	22	II-III	200	Diuretics, ACE, ARB, digitalis	Stenosis V subclavia	Ischemic
8	M	78	30	III	140	Diuretics, BB, ACE	Occlusion V subclavia	Nonischemic
9	M	64	21	III	180	Diuretics, BB, ACE	Implantation failure	Ischemic
10	M	78	45	II-III	200	BB, ACE	Occlusion V subclavia	Ischemic
11	M	68	25	III	180	BB, ACE	Occlusion V subclavia	Ischemic

EF, Ejection fraction; NYHA, New York Heart Association functional class; CHF, congestive heart failure; M, male; BB, β -blocker; ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin-renin blocker; F, female.

catheterization, however, is that only a limited number of sites can be reached on the left ventricular wall because of the anatomy of the cardiac venous system.

The position of the left ventricular lead is important for the acute hemodynamic effect and the reduction in symptoms with CRT.⁷⁻¹⁰ Recent studies showed that the best position depends on the patient.^{10,11} During surgery various sites can be reached, but no method has been described for pick the right site in the individual patient. In this study we examined a mapping technique with pressure-volume loops for optimal surgical placement of the left ventricular lead for CRT.

Methods

Patients

Eleven patients were referred for surgery because of failed coronary sinus left ventricular lead implantation. Informed consent was obtained in all cases. The reason for failure of implantation and other patient details are given in Table 1. All patients had heart failure with LBBB (QRS duration >130 ms) and a low ejection fraction, meeting the criteria for CRT.

Pressure-Volume Loops

A conductance catheter (CD Leycom, Zoetermeer, The Netherlands) was placed under fluoroscopic guidance in the left ventricle by catheterization of the right femoral artery. The catheter was

connected to a CFL512 conductance console (CD Leycom). Because only relative changes (universal atrioventricular [DDD] vs biventricular pacing) were considered, no calibration was performed during surgery. Off-line, the conductance signals were calibrated to match preoperative ejection fraction and a cardiac output of 4 L/min. Stroke volume was defined as the volume at maximal left ventricular pressure derivative (dP/dt_{max}) minus the volume at minimal left ventricular pressure derivative (dP/dt_{min}). End-diastolic volume was the volume at the R-wave of the internal electrocardiogram of the conductance catheter, and minimal volume was taken as end-systolic volume.

Surgical Procedure

With general anesthesia and single-lung ventilation with video-assisted thoracoscopic port-access techniques, the pericardium was opened parallel to the left phrenic nerve. The left ventricular free wall was then mapped with a temporary pacemaker electrode in a systematic way. The anterior, anterolateral, lateral, and posterior parts were stimulated at four to six sites across the longitudinal axis. The best site according to the pressure-volume loops was then selected for permanent pericardial pacemaker lead implantation.

Biventricular Pacing

The hemodynamic measurements during baseline and biventricular stimulation were performed with pacing in DDD mode at the lower rate of 80 beats/min with the atrioventricular interval set at 120 ms and, if applicable, a right to left ventricular delay of 0 ms.

TABLE 2. Hemodynamic data during baseline, biventricular pacing at the best site, and biventricular pacing at the worst site

Variable	Baseline	Best site	<i>P</i> value	Worst site	<i>P</i> value
Heart rate (beats/min)	79 ± 7	80 ± 7	.7	79 ± 7	.2
Stroke volume (mL)	51 ± 6	71 ± 24	.01	55 ± 10	.3
End-systolic volume (mL)	154 ± 72	144 ± 77	.04	149 ± 66	.3
End-diastolic volume (mL)	205 ± 70	215 ± 90	.6	204 ± 68	.5
Maximal left ventricular pressure (mm Hg)	79 ± 15	80 ± 15	.4	78 ± 15	.7
End-diastolic left ventricular pressure (mm Hg)	12 ± 6	13 ± 6	.6	12 ± 7	.6
dP/dt _{max}	576 ± 182	689 ± 258	.02	625 ± 218	.12
dP/dt _{min}	533 ± 176	571 ± 215	.2	548 ± 200	.9
Ejection fraction (%)	27 ± 9	35 ± 10	.007	29 ± 9	.2
Stroke work (g · m)	29 ± 10	48 ± 10	.006	35 ± 12	.2
τ (ms)	113 ± 36	99 ± 26	.11	105 ± 33	.3

τ, Time constant of left ventricular pressure decline. *P* values are versus baseline.

With these programming parameters, consistent stimulation of the right atrium and both ventricles could be achieved, with the paced atrioventricular interval shorter than spontaneous atrioventricular conduction in every case.

During the hemodynamic measurements, pacing was bipolar at the right atrial appendage and the apex. Various sites of the left ventricle were tested with both unipolar and bipolar stimulation; in the bipolar configuration, the left ventricular electrode was the cathode of the stimulation dipole and the right ventricular ring was the anode. The selection of the left ventricular segment for which stimulation resulted in the most hemodynamic improvement was followed by the selection of the pacing sites within that segment providing the best pacing and sensing characteristics.

Statistical Analysis

A nonparametric Wilcoxon signed rank test was performed to compare baseline versus biventricular pacing at the best site and baseline versus biventricular pacing at the worst site.

Results

The results, as summarized in Table 2, show that biventricular pacing had a significant acute hemodynamic effect. Relative to the baseline LBBB situation, biventricular pacing significantly increased stroke volume (+39%, *P* = .01), dP/dt_{max} (+20%, *P* = .02), ejection fraction (+30%, *P* = .007), and stroke work (+66%, *P* = .006) and reduced end-systolic volume (−6%, *P* = .04). However, Table 2 also illustrates that this only held for biventricular pacing at an optimal site on the left ventricle. When the left ventricle was paced from the worst site, none of these parameters changed significantly.

For individual patients, this point is illustrated in Figure 1. With pacing at the best site, the vast majority of patients benefited from biventricular pacing. Figure 2 shows the corresponding pressure-volume loops. At the worst site, however, biventricular pacing was actually disadvantageous in some cases. Figure 3 shows examples of pressure-volume loops during biventricular pacing at the best and worst sites.

Pacing sites on the left ventricle were classified according to the grid on Figure 4. In most cases pacing at basal, midlateral, and apical segments was tested, and in some cases more anterior and posterior segments were added (Figure 4). The pacing sites on the left ventricle that had the best and worst effects on left ventricular function differed among patients (Figure 4).

Discussion

Position of Left Ventricular Lead for CRT

This study shows that position of the left ventricular lead is a primary determinant of the acute hemodynamic effect of biventricular pacing. If the best site was selected, acute and significant beneficial effects were observed with biventricular pacing. In contrast, with the worst site no significant effects were demonstrated, with actual deterioration of function in some cases (Figures 1 and 3). Although many reasons, including patient selection, may explain the high number of those without response to CRT (30%) in the largest trial to date,¹ suboptimal positioning of the left ventricular lead, as may occur during coronary sinus catheterization, may explain some of the failures.¹²

That the site of left ventricular stimulation is important has been reported before. Auricchio and colleagues⁷ showed that patients with an electrode in the midlateral region generally had the most improvement in dP/dt_{max} with biventricular pacing. In that study, however, different sites were not compared in individual patients. Butter and associates^{8,9} did compare in individual patients an anterior with a midlateral left ventricular lead position, and they also concluded that the midlateral region was the best. On the basis of these results, the general approach at present is to place the left ventricular lead in the midlateral region.¹³

In contrast, Pappone and colleagues,¹¹ in a study that compared midlateral and basal sites, concluded that the best pacing site varied among patients. More specifically, Ansa-

Figure 1. Comparison of LBBB versus biventricular (BiV) pacing at best and worst sites in 11 patients. EF, Ejection fraction; SW, stroke work.

lone and coworkers¹⁰ found that pacing at the site of last activation (according to echocardiography) reduced symptoms and ventricular dimensions most. This site of last activation could be anywhere on the left ventricular wall.¹⁰

A limitation of all these studies is that coronary sinus catheterization was used to place the left ventricular lead.

With coronary sinus catheterization, some segments of the left ventricle cannot be reached. In this study, with surgical lead placement, no such limitation existed and multiple positions could be tested and compared in the individual patients. Our results agree with the previously mentioned results of Ansalone and coworkers.¹⁰ The acute hemody-

Figure 2. Pressure-volume loops for all patients during baseline (*solid lines*) and during biventricular pacing at best site (*dotted lines*).

dynamic effect of biventricular pacing varies with position, and the best and worst positions vary among patients (Figure 4).

Pressure-Volume Loops to Guide Epicardial Lead Placement

This study shows that pressure-volume loops are useful to select the optimal position in the individual patient. Pressure-volume loops give all the variables of Table 2 beat-for-beat and on-line, which makes the conductance technique the ideal tool during surgery because on-the-spot decisions can be made where to implant the electrode. Furthermore, because only relative changes are important to compare various positions, no calibration of the conductance catheter is necessary, which simplifies and shortens the procedure considerably.

It should be noted, however, that the design of the conductance catheter assumes that the left ventricle is a stack of cylinders that change in diameter.¹⁴ In a ventricle with LBBB, some regions (especially the septum) contract earlier than others, so this condition is clearly violated. Although this raises some doubts as to the correctness of the

conductance-derived volume during LBBB, it has the beneficial effect that the catheter reacts strongly to more synchronous contraction, which is exactly the aim during CRT. This may explain the observation that stroke volume (+39%), stroke work (+66%), and to a lesser extent ejection fraction (+30%) all reacted very strongly to biventricular pacing, whereas dp/dt_{max} was less sensitive (+20%), although that parameter may be used when pressure-volume loops are unavailable.

In this study no attempt was made to derive changes in more load-independent indices of contractility, such as the slope of the end-systolic pressure-volume relation. The problem with these indices is that they require caval vein occlusion, which is difficult in a thoracoscopic setting and would therefore require additional catheterization with a balloon catheter. Furthermore, the determination of these indices requires off-line analysis, with careful selection of preload varied beats and regression of the end-systolic points. Such analysis would substantially lengthen and complicate the procedure, especially if many different positions

Figure 3. Pressure-volume loops in patients 2 and 4 during baseline (*solid lines*), during biventricular (*BiV*) pacing at best site (*dashed lines*), and during biventricular pacing at worst site (*dotted lines*).

Figure 4. Left ventricular lead positions. Percentages of patients in which indicated sites were evaluated during procedure (*left*, multiple sites per patient); in which biventricular pacing at indicated site gave *best* acute hemodynamic effect (*center*), and in which biventricular pacing at indicated site gave *worst* acute hemodynamic effect (*right*).

(and maybe in future atrioventricular and right to left ventricular delay variations) are tested.

Coronary Sinus Catheterization Versus Epicardial Lead Placement

It has already been shown that epicardial lead placement has a shorter procedure time than does coronary sinus catheterization,⁴ and it can be expected that complications such as

implantation failure and lead dislodgment will occur less frequently during surgery. Given the results of this study, one might hypothesize that placing the left ventricular lead by thoracoscopic surgery could offer advantages relative to the coronary sinus approach. A randomized clinical trial comparing outcomes of coronary sinus catheterization versus thoracoscopy should test this hypothesis.

Improvements to Surgical Placement of Permanent Electrode

As shown in Figure 4, more posterior and anterior regions were not always evaluated in all patients in this study. The main reason was that it is not possible with current devices to place an electrode on these more remote regions during thoracoscopy. Implantation devices for permanent epicardial electrodes should therefore be improved.

Study Limitations

In this study only acute hemodynamic effects of biventricular pacing were used to select the best position. It is not known whether acute hemodynamic effects correlate with a reduction of symptoms in the long term. A study with a larger patient cohort with a longer follow-up is necessary to address this issue.

It is known that the atrioventricular delay modulates the acute hemodynamic effect of biventricular pacing.^{8,9} A limitation of this study is therefore that the atrioventricular delay was not varied at the different positions. No cases have been reported in which the atrioventricular delay could compensate for a bad position of the left ventricular lead,^{8,9} however, so the effect of position seems to be more prominent than that of the correct atrioventricular delay.

Conclusion

To optimize CRT with epicardial leads, mapping to determine the best pace site is a prerequisite. Pressure-volume loops offer real time guidance for targeting epicardial lead placement during minimally invasive surgery.

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