High-Density Epicardial Activation Mapping to Optimize the Site for Video-Thoracoscopic Left Ventricular Lead Implant

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Optimization of Left Ventricular Lead Position. ***Background:*** **The left ventricular (LV) lead local electrogram (EGM) delay from the beginning of the QRS complex (QLV) is considered a strong predictor of response to cardiac resynchronization therapy. We have developed a method for fast epicardial QLV mapping during video-thoracoscopic surgery to guide LV lead placement.**

Methods: **A three-port, video-thoracoscopic approach was used for LV free wall epicardial mapping and lead implantation. A decapolar electrophysiological catheter was introduced through one port and systematically attached to multiple accessible LV sites. The pacing lead was targeted to the site with maximum QLV. The LV free wall activation pattern was analyzed in 16 pre-specified anatomical segments.**

Results: **We implanted LV leads in 13 patients with LBBB or IVCD. The procedural and mapping times were 142 ± 39 minutes and 20 ± 9 minutes, respectively. A total of 15.0 ± 2.2 LV segments were mappable with variable spatial distribution of QLV-optimum. The QLV ratio (QLV / QRSd) at the optimum segment was significantly higher (by 0.17 ± 0.08, $p < 0.00001$) as compared to an empirical midventricular lateral segment. The LV lead was implanted at the optimum segment in 11 patients (at an adjacent segment in 2 patients) achieving a QLV ratio of 0.82 ± 0.09 (range 0.63–0.93) and 99.5 ± 0.6% match with intraprocedural mapping.**

Conclusion: **Video-thoracoscopic LV lead implantation can be effectively and safely guided by epicardial QLV mapping. This strategy was highly successful in targeting the selected LV segment and resulted in significantly higher QLV ratios compared to an empirical midventricular lateral segment.** *(J Cardiovasc Electrophysiol, Vol. 25, pp. 882-888, August 2014)*

cardiac resynchronization therapy, left ventricular lead, epicardial mapping, video, thoracoscopic implantation, heart failure, implantable cardioverter defibrillator

Introduction

Cardiac resynchronization (CRT) is the established therapy of chronic systolic heart failure in patients with intraventricular conduction delay—wide QRS complex.[1,2] Approximately 30% of patients, however, do not respond to this therapy clinically; and in 50% of patients, CRT is not associated with left ventricular (LV) reverse remodeling.[3]

Left ventricular pacing lead position is closely associated with the response to CRT. Several methods have been advocated for optimization of its position. However, only two of them have been studied more extensively. One comprises echocardiographic local mechanical delay,[4-8] while the other consists of time interval between the onset of QRS complex and local LV lead electrogram (EGM) during spontaneous ventricular activation (QLV).[9-14] The evidence from observational studies is mounting that more optimal LV lead position (at the site of more delayed contraction and longer QLV) predicts better clinical response and reverses LV remodeling. Inappropriate LV lead position with QLV shorter than one-half of the QRS duration was associated with higher mortality in a small retrospective study.[12] Reduced mortality and reduced heart failure hospitalization rate (combined endpoint) were observed in patients randomized to echocardiographically optimized LV lead position in the TARGET trial.[4]

Unlike transvenous LV lead implantation, which is limited by the anatomy of the coronary sinus and its tributaries, minimally invasive surgical video-thoracoscopic approach has fewer constraints. In such situations, empirical selection of the LV pacing site, which is usually a central lateral segment of the LV according to previous hemodynamic studies,[15,16] and endocardial activation mapping in patients with left bundle branch block (LBBB),[17] may not be optimal. Therefore, we proposed a new method for fast epicardial mapping of QLV during video-thoracoscopic surgery to optimize the LV lead position. This study was primarily aimed at assessing the feasibility and safety of this approach. In addition, we hypothesized that the benefit of this technique could be indirectly demonstrated.

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Methods

Patient Population

All patients who were indicated for video-thoracoscopic LV lead implantation were eligible for the mapping study if they had preserved atrio-ventricular (AV) conduction with LBBB or intraventricular conduction delay (IVCD). They were recruited from among those in whom transvenous CRT device implantation was unsuccessful or in whom an LV lead was implanted but malfunctioning because of technical issues. In addition, nonresponders to CRT after a 12-month post-implant with QLV ratio <0.7 at the time of CRT implantation were screened for study eligibility. Nonresponders were defined by both New York Heart Association (NYHA) class improvement <1 and absence of LV reverse remodeling (<15% reduction in LV end-systolic volume or <10% reduction in LV end-systolic diameter). Generally, severe LV dilatation/dysfunction, atrial fibrillation and a history of open-heart surgery were not considered exclusion criteria. Eligibility for the video-thoracoscopic procedure was assessed by managing physician and implanting surgeon. Some fragile patients having excessive surgical risk were not considered like those with advanced age, multiple comorbidities or progressive end-stage heart failure.

This study was approved by the local ethics committee and was performed in accordance with the guidelines proposed in the Declaration of Helsinki. All patients gave written informed consent.

Mapping and Implantation Technique

A standard, 3-port thoracoscopic approach was used for LV free wall mapping, and subsequent LV lead implantation. After deflation of the left lung, CO_2 insufflation at a pressure of 8–10 mmHg was combined with single lung ventilation. Port positions were chosen according to size and anatomy of the heart. In most cases, the third and fifth intercostal space in the anterior axillary line were used for tools (5- and 10-mm ports), and the fourth intercostal space, between the middle and posterior axillary line, was employed for the scope (10-mm port). The pericardium was opened posterior and anterior to the phrenic nerve, and the vessels on the heart surface were identified. These pericardial incisions were wider (6–8 cm) compared to those used in an empiric implant procedure without mapping. A decapolar electrophysiological catheter was introduced through one port and systematically attached to multiple accessible LV sites in a step-by-step fashion to access all 16 predefined segments of the LV free wall (Fig. 1). The recordings started at the LV base with the catheter tip directed anteriorly. Then the catheter was shifted to a middle and apical position, with the tip still directed anteriorly. From the apical position, the catheter was rotated counter-clockwise across the apex posteriorly and further shifted back to middle and basal position, with the catheter tip now directed posteriorly. Bipolar LV EGMs during spontaneous ventricular activation were recorded and analyzed at a sweep speed of 200 mm/sec with band-pass filtering of 30–500 Hz (Cardiolab System, Prucka Engineering, GE Healthcare, Little Chalfont, UK) (Fig. 2). At each position of the catheter, a 30-second recording was performed and 5 bipolar signals were analyzed simultaneously during the same spontaneous ventricular depolarization. QRS morphology was inspected to exclude variation of the activation pattern. Attention was paid to select a heart cycle within a period of stable sinus rhythm and with good quality of all 5 local bipolar electrograms. Corresponding QLV intervals were assigned to appropriate LV segments. A bipolar, sutureless epicardial pacing lead (Myopore©, Greatbatch Medical, NY, USA) was implanted at the site with maximum QLV. The procedure was considered successful when the LV free wall epicardial map was nearly completed (at least 12/16 segments) or when the maximal mappable QLV ratio was ≥0.90, and when the LV lead was implanted to the optimum or an adjacent LV segment. At the end of the procedure, QLV was measured at the implantation site directly from the newly implanted LV lead. Procedural descriptive data were collected and patients were followed for complications until discharge from the hospital.

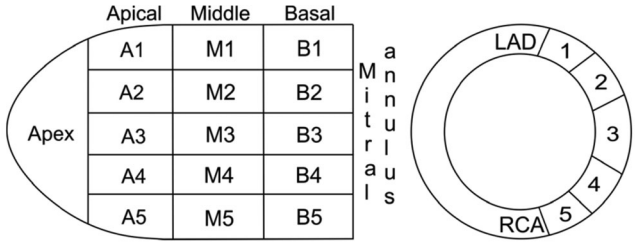

Figure 1. *A 16-segment model of the LV free wall. A lateral view of the LV divided into 4 sectors and a short-axis cross-section of the LV with clockwise segmenation into 5 sectors on the free wall.*

Data Processing and Statistical Analysis

Epicardial EGMs were assessed both in real time for the guidance of LV lead implantation, and off-line for the purpose

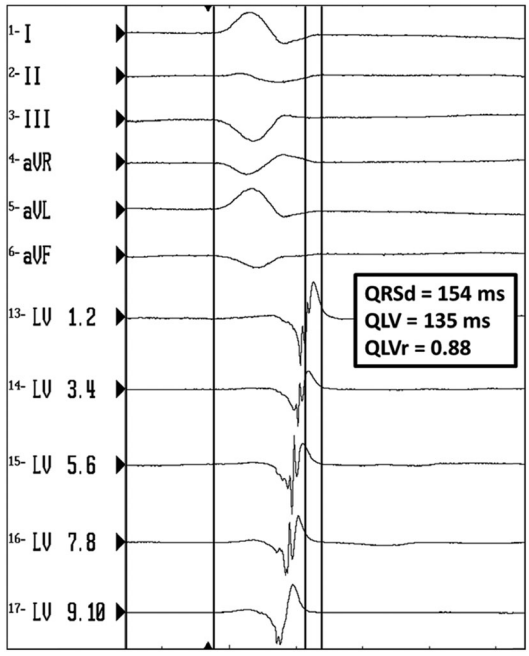

Figure 2. *Epicardial LV activation mapping assessed by decapolar catheter. Both surface ECG and epicardial EGMs recording at a sweep speed of 200 mm/second are depicted. I, II, III, aVR, aVL, aVF = ECG leads; LV 1.2 – LV 9.10—5 bipolar local EGMs registered from a decapolar catheter. Note the maximum QLV at the distal bipole (LV 1.2). QLV and QRSd are measured by an electronic caliper. QLVr = QLV/QRSd.*

TABLE 1
Baseline Characteristics (n = 13)

Age (years)	66 ± 7 (50–73)
Female	2 (15%)
Ischemic cardiomyopathy	7 (54%)
NYHA functional class	2.9 ± 0.7 (2–4)
LVEF (%)	26 ± 5 (20–35)
LVESD (mm)	58 ± 7 (50–71)
LVEDD (mm)	68 ± 6 (60–78)
LVESV (mL)	148 ± 45 (106–207)
Mitral regurgitation (grade)	1.1 ± 1.0 (0–3)
Pro-BNP (pg/mL)	2,123 ± 3,222 (122–11,002)
Paroxysmal atrial fibrillation	2 (15%)
QRSd (milliseconds)	162 ± 16 (133–183)
LBBB	11 (85%)
IVCD	2 (15%)
Previous open-heart surgery	1 (7%)

The values are mean ± standard deviation (range) or number (proportion). IVCD = intraventricular conduction delay; LBBB = left bundle branch block; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; LVESV = left ventricular end-systolic volume; NYHA = New York Heart Association; Pro-BNP = prohormone of brain natriuretic peptide; QRSd = QRS complex duration.

of detailed analysis of LV free wall activation wavefront. The analysis was done per prespecified segments in which QLV readings were averaged and standardized to QRS complex duration (QLV ratio = QLV/QRSd). QLV ratios in individual segments (and groups of segments) were compared using a 2-tailed *t*-test for dependent samples, as well as by ANOVA for repeated measures, with a Newman–Keuls test for post hoc comparisons. In particular, we assessed the difference in QLV ratio between a hypothetical empirical implantation site (central lateral segment of LV, M3), and the individual optimum LV segment (with the longest QLV). The accuracy of optimum site targeting was quantified by QLV match value (QLV of implanted LV lead divided by QLV in the segment with longest average QLV). A P-value <0.05 was considered significant.

Results

Thirteen patients were included in the study over a 14-month period. The rationale for surgical intervention was unsuccessful transvenous LV lead implantation in 5 patients, and LV lead malfunction (phrenic nerve capture or high pacing threshold) in 3 patients. All patients who were offered the surgical mapping procedure agreed to participate in the study. In addition, 10 CRT nonresponders with suboptimal LV lead position, who would benefit from the surgical LV electrode re-implantation according to general clinical judgment, were asked to enter the study. Five of them consented and thus were included in the study.

The baseline characteristics of the study population are shown in the Table 1. Epicardial mapping and LV lead implantation were successfully completed in all patients. Conversion to minithoracotomy or sternotomy was not necessary in any patient. In 2 cases, an additional thoracoscopic port had to be introduced to implant the LV lead in the selected region. The procedural and mapping times were 142 ± 39 minutes and 20 ± 9 minutes, respectively, with an average hospital stay of 6.6 ± 3.0 days.

Epicardial Mapping

A total of 15.0 ± 2.2 (range: 8–16; median: 16; interquartile range [IQR]: 15–16) LV segments were mappable through video-thoracoscopic access. In 1 patient, multiple segments (n = 8) were not accessible because of pericardial adhesions due to previous coronary artery bypass graft surgery (CABG). The average number of mapping points per patient reached 53 ± 16 (range: 14–73; median: 54; IQR: 49–58). The average number of mapping points per mappable segment was 3.5 ± 1.9 (range: 1–10; median: 3; IQR: 2–4).

We have found large interindividual variability of the LV free wall spontaneous activation pattern (Fig. 3) with widely distributed QLV-optimum segments. Only in 1 patient the best site was determined to be in the 2 anterior-most rows of segments (#1 and #2). In another subject, the best site was determined to be at the LV apex region. The QLV ratio was significantly higher at the optimum segment in comparison with an empirical M3 segment by 0.17 ± 0.08 (P = 0.000002). Despite the variability of LV activation pattern, an averaged QLV ratio map derived from pooled data revealed a clear gradient of improvement (i.e., increase of QLV ratio) in the direction from anterior to posterior segments (Fig. 4, Table 2). On the contrary, when the true apex region with incomplete data and usually low QLV ratio was excluded, no apparent gradient in QLV ratio was documented along the LV long-axis. Significance of this observation is supported by ANOVA statistics (Table 3). On average, the highest QLV ratio was found at the M5 segment (posterolateral or posterior). The QLV ratio in this segment was significantly higher than that in an empirical M3 segment by 0.10 ± 0.01 (P = 0.003). The best segment in individual subjects was still better than the best average segment M5 by 0.08 ± 0.07 (P = 0.003).

LV Lead Placement

An LV lead was successfully implanted at the segment with maximum QLV in 11 patients; it was implanted in an adjacent segment in 2 patients. In one case, the LV apex, which had the maximum QLV, was avoided because of significant scarring in this region and an adjacent apical segment was chosen instead. In the other case, the optimum segment was found to be at the very posterior part of a dilated LV, which was not accessible by thoracoscopic approach. The average QLV match was 99.5 ± 0.6% (P = 0.77 from 100%). The LV lead QLV ratio was 0.82 ± 0.09 (range 0.63–0.93) and was significantly higher (by 0.17 ± 0.08) than the average QLV ratio at an empirical M3 segment (P = 0.000005). In 5 CRT nonresponders with a previously implanted transvenous LV lead and QLV ratio of 0.55 ± 0.04, epicardial re-implantation improved the QLV ratio to 0.77 ± 0.11 (P = 0.02).

Safety

Two major procedural complications were observed in a single patient: A pneumothorax that did not require suction and an episode of ventricular fibrillation successfully terminated by DC shock, with hospital stay prolongation by 10 days. The performance of LV leads at a 6-month follow-up visit was correct in all patients.

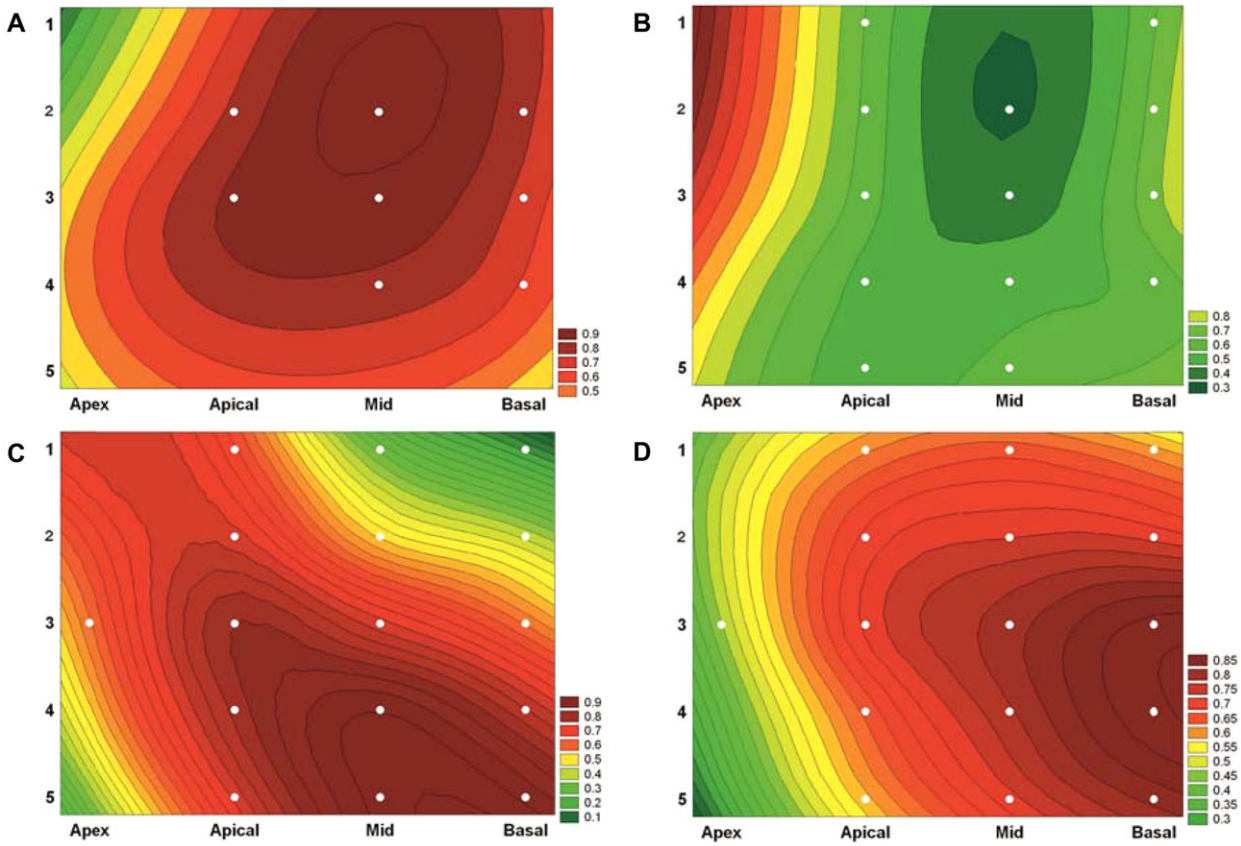

Figure 3. *Four examples of variable left ventricular activation pattern. Color-coded depictions of activation sequences are shown (green for early and red for late activation). The color scale for the QLV ratio is individualized for each case. Note the activation map in a patient with IVCD (panel B) with the most delayed activation outside of the mappable region, and the absence of bracketing of the most delayed activation in another patient (panel C).*

Discussion

This study showed that epicardial LV lead implantation can be optimized by simple epicardial QLV mapping during the standard video-thoracoscopic procedure. This approach is safe and allows successful targeting the optimum LV segment in the majority of cases with acceptable mapping time and total procedural time.

In this study, the use of a decapolar catheter, and electrophysiological recording system enabled us to perform high density mapping of the LV free wall and obtain higher amount of activation sites compared to previously published mapping techniques. The former studies utilized temporary LV lead placement in several locations (total number was not specified) during surgical implantation in order to maximize the right ventricle (RV) pace–LV delay[18] or atrial sense–LV delay.[19] Both of them, as well as atrial pace–LV delay, can be measured by device programmers independently of surface ECG acquisition. The atrial pace/sense–LV delay, which is closely related to QLV, is less precise because of tiny variations in AV nodal conduction (or change in AV delay). It cannot also be used in patients with atrial fibrillation. The RV pace–LV interval seems theoretically more relevant than QLV for LV pacing site optimization, especially when intrinsic infrahisian conduction is not about to be utilized for CRT. However, we preferred QLV because larger amount of data is available for predictive value of QLV compared to RV pace–LV interval.

Both parameters QLV[11,14] and QLV ratio[10,12] were used in previous studies and both were significantly associated with clinical outcome. QLV interval reflecting simultaneously the position of LV lead and QRS duration, which is independent predictor of CRT response per se, may be the valid choice in observational studies. Mapping results in individual patients are clearly invariant to the use of QLV or QLV ratio. QLV ratio only (as a standardized measure of LV lead position) is an optimum choice when mapping results are averaged across patients with dissimilar QRS duration like in our study.

Mapping time was not excessively long and achieved total procedural time was even shorter (142 minutes) than reported for video-thoracoscopic procedures in a larger cohort published by Navia *et al.* (232 minutes).[19] The manipulation with mapping catheter was not difficult for operator skilled in thoracoscopic procedure. This is in line with 20-minute mapping time for registering of, on average, 11 catheter positions with signal recording time of at least 30 seconds. Only in 1 patient after open-heart surgery, pericardial adhesion prevented to create a complete epicardial map. Fortunately, a segment with very high QLV ratio >0.90 was accessible even in this patient.

The average hospital stay of 6.6 days appears to be longer than expected. By excluding the patient with procedural pneumothorax, it would be 5.8 ± 0.9 days. In addition, the hospital stay was also exploited for other cardiac examination and adjustment of medical therapy in these patients with advanced heart failure. Majority of patients were discharged

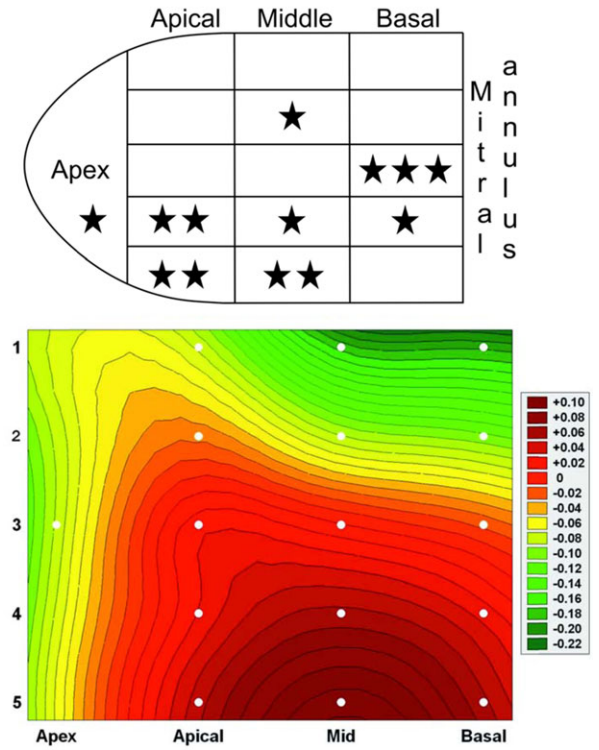

Figure 4. *Summary of results for epicardial mapping. Top panel—distribution of QLV optimum segments (asterisks for individual patients). Bottom panel—averaged QLV ratio map from all 13 cases. The color scale corresponds to the QLV ratio differences between individual segments and central lateral M3 segment. Absolute numerical results are provided in Table 2.*

TABLE 2
QLV Ratio in Individual LV Free Wall Segments

Row	Apex	Apical	Middle	Basal
#1	0.60 ± 0.18	0.55 ± 0.09	0.46 ± 0.16	0.44 ± 0.18
#2		0.63 ± 0.08	0.55 ± 0.20	0.54 ± 0.14
#3		0.69 ± 0.11	0.65 ± 0.14	0.64 ± 0.13
#4		0.64 ± 0.15	0.70 ± 0.13	0.68 ± 0.13
#5		0.68 ± 0.15	0.73 ± 0.14	0.71 ± 0.17

The numbers are QLV ratios (mean ± SD) for all patients. #1 = anterior-most row of segments in clockwise short-axis segmentation; #5 = posterior-most row of segments in clockwise short-axis segmentation. Apex-Apical-Middle-Basal denotes segmentation in the long axis.

TABLE 3
QLV Differences Between Segments Grouped Along LV Long Axis

	"1"	"2"	"3"	"4"	"5"
"1"		0.002	0.00002	0.000008	0.00002
"2"			0.00007	0.00002	0.000008
"3"				0.19	0.04
"4"					0.26
"5"					

The numbers are P-values for mutual differences in QLV ratio between individual groups of segments (ANOVA, Newman-Keuls post hoc test). The true apex was excluded from the analysis. "1" = group of the anterior-most segments; "5" = group of the posterior-most segments.

on third or fourth postoperative day, which is standard of care after video-thoracoscopic procedure in our institution.

We believe that before this method can be safely applied in clinical practice, further research should prove its validity. The ability to develop the necessary skill set is, however, a reasonable expectation of a tertiary cardiovascular center.

The TARGET trial[4] was the first randomized interventional trial that in 200 patients demonstrated the superiority of tailored LV lead placement as compared with empirical pacing site selection, both in terms of CRT response as well as combined death and heart failure hospitalization endpoint. Despite the fact that our experience with video-thoracoscopic left ventricular lead implantation was obtained as part of a preliminary feasibility study that was not designed to investigate the clinical outcome of patients, some technical aspects of QLV-guided implantation can be compared with the echocardiographically-guided technique of LV lead positioning that was investigated in the TARGET trial. In our study, the LV free wall was mapped very precisely with more than 50 mapping points in 16 predefined segments, while 12-segment classification (echocardiography and fluoroscopy-based) was used for the assessment of local mechanical delay and implantation site in the TARGET trial. Selection of the optimum site using echocardiography (ECHO) was done off-line prior to the implantation procedure and LV lead placement was likely dependent on adequate correspondence between echocardiography and fluoroscopy imaging.[20] In our study, epicardial activation mapping was performed during the implantation procedure by a single operator and was limited to the accessible LV free wall. The lack of "bracketing" of QLV intervals in the resulting QLV map in some of our patients might indicate that the posterior-most segments of LV (perhaps even more electrically delayed) may have been missed in our study. We demonstrated considerably high QLV match of the final LV lead position and segment with optimum QLV ratio (99%). On the contrary, transvenous implantation in the TARGET trial was associated with a noticeably lower success rate of implantation into the optimum segment (63%).

Both the distribution of maximal mechanical delay in the TARGET trial and the maximal electrical delay in our study revealed high variability of the spatial distribution of the optimum LV segment. This is in line with original observation of a variable endocardial activation pattern in LBBB, resulting from differently located lines of functional conduction block.[9] There are limited data on correlation of epicardial and endocardial LV activation in such patients, and comparison of these would be an interesting topic of further research, especially taking into account new investigational endocardial LV lead implantation techniques. A study by Spragg *et al.*[21] showed high interindividual variability of optimum LV endocardial pacing sites assessed by acute hemodynamic response to temporary CRT in 11 patients. Overall, these findings could explain why the predictive value of anatomical location of LV lead (except the LV apex) for CRT response was generally low, if any, in previous studies,[22-27] which has resulted in underestimation of the importance of LV lead position. Another technique of LV lead pacing site optimization was published by Dekker using a special conductance catheter and evaluating the pressure-volume relationship.[28] Four to 6 LV free wall positions of temporary LV leads were compared according to pressure-volume loops registered in LV during biventricular pacing. Significant differences were found between various LV lead locations in terms of acute hemodynamic response.

However, such a technically demanding concept does not seem suitable for routine use.

Adjacent segment relationships were not analyzed in our study because of small population size, which was not powered to detect the ANOVA-differences in activation time between individual segments. That is why we pooled the segments "by rows" from anterior-most to posterior-most in order to statistically confirm the presence of overall activation gradient in this direction, which was also depicted in Figure 4 (lower panel). Overall, conduction pattern was homogeneous and physiological meaningful in individual patients, and not completely random in investigated population with aggregation of optimum sites at more posterior segments of LV free wall. A large interindividual variability of activation pattern was caused mainly by inclusion of 2 patients with IVCD (one of them shown in Fig. 3, panel B). But even in LBBB patients the site of the latest LV activation was rather variable (Fig. 4, upper panel) supporting the value of activation mapping for LV lead placement.

Our data clearly suggest that the posterior part of the LV surface is more delayed than the central lateral segment that is typically chosen during stand-alone video-thoracoscopic LV lead implantation also because of implicitly easy access. However, outcome studies are needed in order to demonstrate the clinical value of this strategy.

Study Limitations

This was a small, single-center study that aimed at establishing the feasibility of a new mapping technique for optimization LV lead position. The acute impact of implantation site optimization was not validated by the LV dP/dt measurement. The study was also too small and not designed to evaluate the clinical benefit of this LV lead placement strategy. Despite the fact that QLV has been identified in several studies as a good predictor of clinical outcome, its correlation with measured changes in dP/dt seems to be modest.[29] However, in that acute study the measured hemodynamic response was not associated with long-term clinical outcome.[29] Therefore, the randomized study of empirical versus electrophysiologically-based LV lead implantation with clinical endpoints is warranted as the next step.

From a technical point of view, it is important to emphasize that the operator has rather limited visual control of the tip of the mapping catheter that is introduced through the pericardial incision. In some instances it was not clear whether the tip could reach the borders of LV free wall. This was especially true for very posterior parts of large left ventricles. In this case the map of the LV free wall may be partially incomplete. Only 1 patient after open-heart surgery was enrolled; more experience is needed in order to identify whether this approach is also feasible for such patients.

Conclusions

This study showed that video-thoracoscopic LV lead implantation could be effectively and safely guided by simplified epicardial QLV mapping, which can be implemented in heart centers with advanced experience with thoracoscopic techniques and expertise in clinical cardiac electrophysiology. We demonstrated variable activation patterns of the LV free wall in individual patients with varying spatial distribution of optimal pacing sites. This strategy was highly successful in targeting the selected LV segment. Compared to empirically chosen pacing site in central lateral position, epicardial QLV mapping allowed to achieve significantly longer QLV ratio for the implanted epicardial lead.

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