RESEARCH LETTER

Activation time at the left ventricular pacing site (QLV) relative to the actual site of latest activation—Implications for response to cardiac resynchronization therapy

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Pacing the latest left ventricular (LV) electrically activated site (LEAS) may be an intraprocedural technique to improve cardiac resynchronization therapy (CRT) efficacy. Thus, a QLV (defined by time interval from the first deflection on a surface electrocardiogram to local intrinsic activation at the LV pacing site) of >95 ms was proposed to distinguish CRT responders.[1] However, the predictive value was modest. In another report, QLV was not associated with optimal acute hemodynamic response at the individual level.[2] This may be because LEAS was not identified in these studies, and empirically delivered leads may have missed it (extent described by the interval between QLEAS [defined by time interval from the first deflection on a surface electrocardiogram to local activation at LEAS] and QLV). Therefore, we compared QLEAS with QLV and assessed the effect of the QLEAS-QLV interval on response to CRT.

We studied patients who had received CRT for class I or class IIa indications, regardless of CRT response, at 5 European sites. The study was approved by the institutional committee on human research at the authors' institutions and adhered to the Declaration of Helsinki. LV lead placement, device programming, and follow-up followed physician preference and site protocol. All patients had clinical follow-up between 6 and 12 months postimplantation, including echocardiographic study. *CRT nonresponse* was defined as an LV end-systolic volume reduction of <15%, assessed echocardiographically. Patients underwent noninvasive 3-dimensional (3D) electrical activation mapping and torso computer tomography scanning 6–24 months postimplantation.[3] QLV (at the LV lead pole used for pacing) and QLEAS were derived from noninvasive 3D electrical activation maps by a core laboratory blinded to clinical data. Logistic regression modeling was conducted for QLV and QLEAS-QLV against CRT response, and optimal cut points were calculated.

Of 111 patients (mean age 64 ± 11 years; 74% male; 98% left bundle branch block; QRS duration 172 ± 21 ms;

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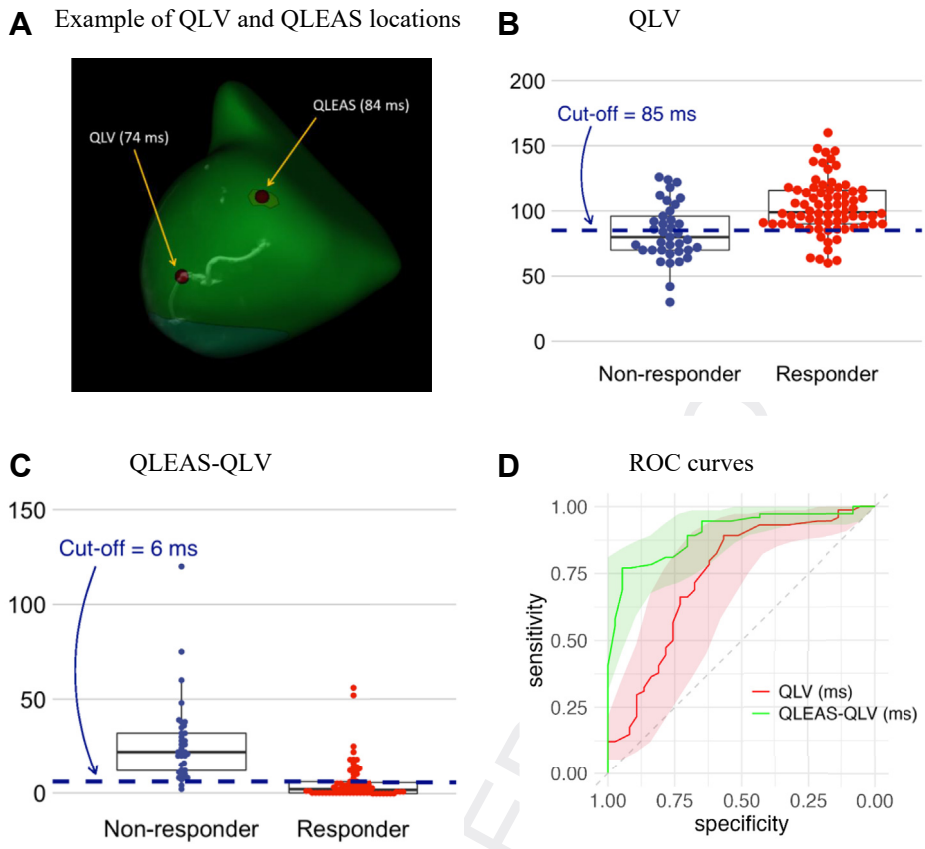

Figure 1 **A:** Example of QLV and QLEAS locations in a patient being a nonresponder (quadripolar spiral lead and pacing from LV ring 2 to RV). **B and C:** Box plots showing QLV with a cut point of 85 ms between responders and nonresponders (panel B) and QLEAS-QLV with a cut point of 6 ms between responders and nonresponders (panel C). **D:** ROC curves of a QLV cut point of 85 ms and a QLEAS-QLV cut point of 6 ms. LV = left ventricular; QLV = time interval from the first deflection on a surface electrocardiogram to local intrinsic activation at the LV pacing site; QLEAS = time interval from the first deflection on a surface electrocardiogram to local activation at the electrically activated site; ROC = receiver operating characteristic; RV = right ventricle.

baseline LV ejection fraction 28% ± 6%; LV end-systolic volume 183 ± 87 mL; implant duration 12 ± 5 months), 31%/69% had New York Heart Association class II/III and 38% had ischemic heart disease. Two-thirds (67% [74 of 111]) of the patients responded at 10 ± 3 months postimplantation.

The mean QLV value was 97 ± 23 ms (range 42–148 ms) overall, 103 ± 21 ms for responders, and 83 ± 22 ms for nonresponders ($P < .001$). QLEAS was 109 ± 19 ms (range 66–150 ms) overall, 109 ± 20 ms for responders, and 110 ± 19 ms for nonresponders ($P = .74$). QLEAS-QLV was 13 ± 18 ms (range 0–120 ms) overall, with larger values indicating LV lead placement in a site activated correspondingly earlier than LEAS. The difference was 6 ± 10 ms for responders and 27 ± 22 ms for nonresponders ($P < .001$) (Figure 1).

The optimal cut point for QLV was 85 ms, with a sensitivity of 0.89, a specificity of 0.57, and an area under the curve (AUC) of 0.742 (95% confidence interval 0.637–0.846). The optimal cut point for QLEAS-QLV was 6 ms, with a sensitivity of 0.77, a specificity of 0.95, and an AUC of 0.901 (95% confidence interval 0.844–0.957) (Figure 1). The AUC for QLV and QLEAS-QLV cut points differed significantly ($P < .001$).

Eighteen of 111 patients (16%) were nonresponders despite a QLV of ≥85 ms, whereas only 2 patients (2%) were nonresponders despite a QLEAS-QLV interval of ≤6 ms.

In summary, a significant nonresponse rate persists in "ideal" CRT patients (ie, left bundle branch block and QRS duration > 150 ms) but this may be mitigated by LV pacing at the site of terminal LV activation. Our data confirm that longer QLV is associated with CRT response.[1] However, QLEAS better discriminates CRT responders from nonresponders; thus, QLV-guided LV lead placement without prior knowledge of LEAS will miss the target LV pacing site in 16% of individuals.

In conclusion, using noninvasive 3D global mapping to identify LEAS pre-CRT implantation and directing LV lead placement to within 6 ms of this site may improve CRT efficacy. However, this strategy may be limited by coronary venous anatomy. These hypotheses merit prospective evaluation.

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