Do novel non-invasive ECG techniques improve patient selection for CRT?

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Guidelines recommend cardiac resynchronization therapy (CRT) to reduce morbidity and mortality for patients with symptomatic heart failure (HF), a reduced left ventricular ejection fraction and evidence of ventricular dyssynchrony. In the absence of validated markers of mechanical dyssynchrony, the current recommendations are based on surface ECG with a prolonged QRS duration (QRSd)[1,2]. Although none of the landmark studies used QRS morphology as inclusion criteria, guidelines indicate that morphology is an important determinant of response and therefore make a stronger recommendation in patients with typical left bundle branch block (LBBB). QRS duration and QRS morphology by standard 12-lead ECG measures are the current cornerstones of patient selection to CRT[3].

Surface ECG is a simple, cheap and widely available tool to study electrical dyssynchrony but it has limitations. Because of the limited number of leads, it only allows gross approach of the activation process and may not capture the entire activation sequence. Although QRSd measurement had a good reproducibility in controlled studies with core center analysis (mean intra-and inter-observer variability of 1.6% and 1.4% on native QRS[4]), non-controlled studies reported significant variations according to the lead(s) used, a poor reproducibility and a low concordance between manual and computerized measures[5,6]. There is therefore a need for novel non-invasive ECG techniques, more efficient and less investigator-dependent[7]

A first alternative could be the automated vectocardiogram (VCG) that contains 3D information of the cardiac electrical forces. It can easily be derived from the standard 12-lead ECG and analyzed automatically by customized MATLAB software.[7] In the context of CRT, the value of VCG was extensively investigated by the Maastricht group[7-11]. In a study in canine LBBB hearts, van Deursen[8] showed that maximum QRS vector amplitude (VA_{QRS}) was closely correlated with electrical and mechanical ventricular dyssynchrony. They also suggested that VCG may be a reliable and easy tool for individual optimization of CRT. In patients candidate for CRT, they showed that VA_{QRS} and the QRS complex area (QRS_{AREA}) identified delayed LV lateral wall activation (assessed using coronary venous electroanatomic mapping) better than QRSd and/or QRS morphology on standard ECG[9]. In a single-center observational study, QRS_{AREA} [10] but also T-$wave_{AREA}$ [7] were shown to predict the 6-month volumetric response to CRT (decrease>15% in LVESV) better than QRS measures on 12-lead surface ECG. Similar results were observed with SAI QRST, an averaged arithmetic sum of absolute areas under the QRST curve in a retrospective analysis of the SMART AV trial[12]. In the same way, a retrospective analysis of 335 CRT patients showed that T-$wave_{AREA}$ was the better predictor of a combined clinical endpoint of death, HF hospitalization or heart transplant/LVAD implantation over a 36-month follow-up period[11]. The value of VCG to predict the12-month echocardiographic response is currently assessed in a prospective multi-center observational study (ClinicalTrials.gov: NCT01519908)

Another alternative is body surface electrocardiographic mapping (BSEM). The original system uses a multielectrode vest recording BS potentials from 250 sites around the entire torso and a thoracic computed tomography (CT) scan providing epicardial-surface and torso geometries[12]. BS potentials and CT images are merged and processed to reconstruct epicardial potentials, electrograms, and isochrones on the heart surface during a single beat. The system was originally developped to identify arrhythmic sources and showed remarkable performances[13]. By imaging activation sequences and measuring spatial differences in activation times, BSEM also allows precise evaluation of electrical asynchronies. Several ventricular dyssynchrony indices can be derived from intrinsic maps, in particular electrical dyssynchrony index (ED)[14], LV total activation time (LVAT) and ventricular electrical uncoupling (VEU), defined as the difference between LV and RV activation times[15]. The system was used first for exploratory studies in CRT candidates to characterize the type and degree of ventricular dyssynchrony according to baseline characteristics : etiolology, QRSd and QRS morphology[14-16]. The value of BSEM to predict the 6-month clinical response to CRT using a clinical composite score was assessed by Ploux et al[16] in a small series of 33 patients. They showed that VEU was superior to LVAT and QRSd, independent of QRS morphology for predicting CRT response

In studies reported in this issue, Johnson et al and Gage et al used a simplified BSEM system consisting in a single-use disposable ECG belt with 53 anterior and posterior unipolar ECG electrodes without any combined cardiac imaging[17,18]. Electrical dyssynchrony was quantified using standard deviation of activation times (SDAT). The value of baseline SDAT and its change after CRT to predict the 6-month echocardiographic response was assessed in 66 CRT patients[18]. Results showed that SDAT and its changes predicted CRT response better than QRS duration. A native SDAT >35 msec could be the best predictor.

In summary, VCG and BSEM are both candidates to dethrone the 12-lead surface ECG for patient selection to CRT. In small size observational studies, dyssynchrony indices derived from the two techniques better predicted CRT response than QRSd and/or QRS morphology. These preliminary results must now be confirmed in larger multicenter prospective studies evaluating the clinical benefit and cost-effectiveness of these novel non-invasive ECG techniques compared with12-lead surface ECG . Ideally, VCG and BSEM should be evaluated in the same trials to determine which technique is the best

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