

Do novel noninvasive ECG techniques improve patient selection for CRT?

C. Daubert, P. Mabo, C. Leclercq

► **To cite this version:**

C. Daubert, P. Mabo, C. Leclercq. Do novel noninvasive ECG techniques improve patient selection for CRT?. *Heart Rhythm*, Elsevier, 2017, 14 (3), pp.400–401. 10.1016/j.hrthm.2016.12.019 . hal-01484698

HAL Id: hal-01484698

<https://hal-univ-rennes1.archives-ouvertes.fr/hal-01484698>

Submitted on 27 Mar 2017

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

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

Claude Daubert^{1,2}, MD, Philippe Mabo^{1,2,3}, MD and Christophe Leclercq, MD, PhD^{1,2,3}

¹Faculté de médecine, Université de Rennes 1, France ; ²LTSI INSERM U1099, Rennes, France ; ³Service de cardiologie et maladies vasculaires, CHU Rennes, France

Corresponding author : Claude Daubert, Tel : +33299795034 ; E-mail : jcdaubert@orange.fr

Conflict of interest statement : Nothing to declare

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 CRT³.

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 QRS⁴), 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-dependent⁷

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 group⁷⁻¹¹. In a study in canine LBBB hearts, van Deursen⁸ 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 ECG⁹. 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 trial¹². 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 period¹¹. The value of VCG to predict the 12-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 multi-electrode vest recording BS potentials from 250 sites around the entire torso and a thoracic computed tomography (CT) scan providing epicardial-surface and torso geometries¹². 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 developed to identify arrhythmic sources and showed remarkable

performances¹³. 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 times¹⁵. The system was used first for exploratory studies in CRT candidates to characterize the type and degree of ventricular dyssynchrony according to baseline characteristics : etiology, QRSd and QRS morphology¹⁴⁻¹⁶. The value of BSEM to predict the 6-month clinical response to CRT using a clinical composite score was assessed by Ploux et al¹⁶ 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 patients¹⁸. 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 with 12-lead surface ECG .

Ideally, VCG and BSEM should be evaluated in the same trials to determine which technique

References

1. Tracy CM, Epstein AE, Darbar D, et al. ACCF/AHA/HRS Focused Update of the ACCF/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities. *Circulation* 2012 ; 126 : 1784-1800
2. Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). *Eur Heart J* 2013; 34: 2281-2329
3. Daubert C, Behar N, Martins RP, Mabo P, Leclercq C. Avoiding non-responders to cardiac resynchronization therapy: a practical guide. *Eur Heart J* 2016 DOI: 10.1093/eurheartj/ehw270
4. Gold MR, Thébaud C, Linde C, Abraham WT, Gerritse B, Ghio S, ST John Sutton M, Daubert C. The effect of QRS duration and morphology on cardiac resynchronization therapy outcomes in mild heart failure: results from the REVERSE study. *Circulation* 2012; 126: 822-829
5. De Guillebon M, Thambo JB, Ploux S, Deplagne A, Sacher F, Jais P, Haissaguerre M, Ritter P, Clementy J, Bordachar P. Reliability and reproducibility of QRS duration in the selection of candidates for cardiac resynchronization therapy. *J Cardiovasc Electrophysiol* 2010 ; 21 : 890-89
6. De Pooter, Haddad ML, Timmers L, Van Heuwerswyn F, Jordaens L, Duytschaever M, Stroobandt R.. Different methods to measure QRS duration in CRT patients : impact on the predictive value of QRS duration parameters. *Ann Noninvasive Electrophysiol.* 2015 ; 21 : 305-315
7. Engels EB, Mafi-Rad M, van Stipdonk AMW, Vernooij K, Pinzen FW. Why QRS duration should be replaced by better measures of electrical activation to improve patient selection for cardiac resynchronization therapy. *J Cardiovasc Trans Res* 2016 ; 9 : 257-265
8. van Deursen CJM, Rademakers LM, van Hunnik A, Kuiper M, Wecke L, Crijns HJGM, Prinzen F. Vectocardiography as a tool for easy optimization of cardiac resynchronization therapy in canine left bundle branch block hearts. *Circ Arrhythm Electrophysiol* 2012 ; 5 : 544-552
9. Mafi Rad M, Wijntjens GW, Engels EB, Blaauw Y, Luermans JG, Pison L, Crijns HJ, Prinzen FW, Vernooij K. Vectorcardiographic QRS area identifies delayed left ventricular lateral wall activation determined by electroanatomic mapping in candidates for cardiac resynchronization therapy. *Heart Rhythm*

10. van Deursen CJM, Vernooij K, Dudink E, Bergfeldt, Crijns HJGM, Prinzen FW, Wecke L. Vectorcardiographic QRS area as a novel predictor of response to cardiac resynchronization therapy. *J Electrocardiol* 2015 ; 48 : 45-55
11. Végh EM, Engels EB, van Deursen CJ, Merkely B, Vernooij K, Singh JP, Prinzen FW. T-wave area as biomarker of clinical response to cardiac resynchronization therapy. *Europace* 2016 ; 18 : 1077-1085
12. Tereshchenko LG, Cheng A, Park J, Wold N, Meyer TE, Gold MR, Mittal S, Singh J, Stein KM, Ellenbogen KA. Novel measure of electrical dyssynchrony predicts response in cardiac resynchronization therapy: Results from the SMART-AV Trial. *Heart Rhythm* 2015, 12 :2402-2410
13. Rudy Y, Burnes JE. Noninvasive electrocardiographic imaging. *Ann. Noninvasive Electrocardiol* 1999; 4: 340–358.
14. Shah AJ, Hocini M, Pascale P, Roten L, Komatsu Y, Daly M, Ramoul K, Denis A, Derval N, Sacher F et al. Body surface electrocardiographic mapping for non-invasive identification of arrhythmic sources. *Arrhythmia & Electrophysiology Review* 2013; 2:16–22
15. Ghosh S, Silva JN, Canham RM, Bowman TM, Zhang J, Rhee EK, Woodard PK, Rudy Y. Electrophysiologic substrate and intraventricular left ventricular dyssynchrony in nonischemic heart failure patients undergoing cardiac resynchronization therapy. *Heart Rhythm* 2011 ; 8 : 692-699
16. Ploux S, Lumens J, Whinnett Z, Montaudon M, Strom M, Ramanathan C, Derval N, Zemmoura A, Denis A, De Gillebon M et al. Noninvasive electrocardiographic mapping to improve patient selection for cardiac resynchronization therapy: beyond QRS duration and left bundle branch block morphology. *J Am Coll Cardiol* 2013; 61: 2435-2443.
17. Johnson WB, Vatterott PJ, Peterson MA, Bagwe S, Underwood D, Bank AJ, Gage RM, Ramza B, Foreman BW, Splet V et al. Body surface mapping using an ECG belt to characterize electrical heterogeneity for different left ventricular pacing sites during cardiac resynchronization-Relationships with acute hemodynamic improvement. *Heart Rhythm* DOI : <http://dx.doi.org/10.1016/j.hrthm.2016.11.017>
18. Gage RM, Curtin AE, Burns KV, Ghosh S, Gillberg JM, Bank A. Changes in electrical dyssynchrony by body surface mapping predict left ventricular remodeling in cardiac resynchronization therapy patients. *Heart Rhythm* <http://dx.doi.org/10.1016/j.hrthm.2016.11.019>