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EDITORIAL COMMENT

Electrocardiogram for cardiac resynchronization therapy: A great past, what's its future?

ECG para terapêutica de ressincronização cardíaca: um grande passado, que futuro?

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Thank you for this excellent synthesis, for the first time an exhaustive compilation of the principal works about the role of QRS width and pattern in patient selection for cardiac resynchronization therapy (CRT) has been achieved. Furthermore, the authors, using a rigorous methodology, have extracted the most contributory papers from an incredible body of literature of more than 13 000 articles published on the subject since the early days of this treatment. Sixty-two were selected focusing on preoperative ECG characteristics of future responders, including more parameters than the standard cutoff of 150 ms associated with LBBB pattern, like PR and QT intervals, QRS axis and others.

The authors also focused on more ''contemporary'' electrocardiogram (ECG) parameters, like QRS notching or fragmentation, S waves assessment, intrinsicoid deflection (today called the ''time to peak R wave''), and lead I ratio $\geq$12. The authors confirmed the importance of classical ECG criteria (QRS width >150 ms and LBBB), showing a good reliability in current patient selection, a possible prediction of super-responders, potentially slightly improved by Strauss criteria, unlike other parameters not bringing much. From this work, we also discover interesting findings suggesting that very wide QRS >180 ms take less benefit from standard biventricular (BiV) implantation as it is performed today. Another difficulty the authors had to overcome was the diversity of positive response definitions, suggesting that ECG-based selection offered better results in symptoms improvement rather than volumetric reverse remodelling. However, the discussion about their respective values is still addressed, as well as the status of ''unchanged'' patients in the long-term to be considered as responders or not.

At the end of the game, what do we learn? Not much I am afraid. The role of ECG-based criteria for selection defined from the first world-wide CRT case[1] is once again reassessed, and the members of the medical community following this recommendation reassure them that they are acting in the right way. However, we should remember that since the early days of CRT, the non-response rate has remained stable around 25—30%, of which we should not be proud. Despite one of the fastest recognitions of the validity of a therapy (recognized by the FDA in 2000, only six years after its discovery), despite incredible improvements in technology for left ventricular (LV) lead insertion, stability and therapy delivery, there has been real gain in terms of success rate. Since the beginning of CRT, ECG-based criteria are the basis of patients' selection despite the mechanical nature of the disease (dyssynchrony), and thirty years and several thousands of papers later, confirmation of this point only shows that we are biting our tail...

However, the 30% rate of non-response in these wide QRS patients should lead us to question the electrophysiologists, and the high number of heart failure patients with

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mechanical dyssynchrony missing the ECG criterion (and then implantation) should also question the general cardiologists.

Instead of perpetual confirmation that QRS width with LBBB pattern is a convenient surrogate of dyssynchrony, we should consider how we can improve the success rate of the therapy and find a way to address more patients. We must be reminded that for obtaining a responder, the correct selection of candidates is not sufficient. Two other points must be respected: a correct implantation with leads inserted in the right position and setting the hemodynamic parameters of the device according to patient's dyssynchrony and positioning of the leads.

Let us not forget that initially the 150 ms cutoff was intuitively chosen by the MUSTIC committee in 1995, and this value was only validated a posteriori several years later by many controlled trials.[2] It was then largely adopted because of its simplicity, skipping a major point: the inter and intraobserver variability of QRS width measurement can reach 50 ms.[3] More embarrassing is the demonstrated absence of parallelism between ECG data and mechanical inter and intraventricular dyssynchronies published 20 years ago.[4] In this work, it was shown that >50% of patients with a QRS <120 ms present with a significant mechanical dyssynchrony, although the proportion goes up to 91% in wide QRS LBBB patients. The interest of CRT in narrow QRS patients was then confirmed by the DESIRE study[5] showing a good 70% response rate in 120 ms-QRS patients under the condition that they presented with a mechanical dyssynchrony at enrollment, using the electromechanical parameters suggested by the Prospect trial.[6] Conversely, having a wide QRS is not sufficient a condition to guarantee the success as desperately shown by the fixed 30% non-success rate. This was confirmed by a recent and large mechanical multicenter study showing five different clusters of clinical response (from 50 to 93%) despite a similar QRS width of 161±5 ms at entry.[7] Finally, a small study focusing on left pre-ejection interval reduction (LPEI) after implant, shows a total absence of correlation between QRS narrowing and mechanical improvement.[8] In fact, dyssynchrony is a 3-dimensional mechanical phenomenon involving both atria and ventricles that a simple ECG cannot describe. In that perspective, a complete electromechanical model has been developed for dyssynchrony and resynchrony assessments is still waiting for its clinical validation.[9]

After patient selection, the following step is the implant process. Today CRT is almost synonymous with BiV pacing, although the recent re-discovery of His and LBB area pacing, initially described in the eighties made physicians to reconsider this idea. When the effective delivery of mechanical resynchronization is evaluated, it appears that very few patients are correctly resynchronized with standard BiV pacing. The Meteor study showed only 17% of them, 24% patients needed right ventricular (RV) lead placement optimization and more than 50% of the study group required a triple site stimulation configuration using two RV electrodes.[10] Optimized RV leads placement and numbers depend on LV lead position and on the type of dyssynchrony to correct. Typically, diffuse homogeneous intraventricular dyssynchrony without significant delays between septal and lateral contractions require more complex configurations than standard BiV. This approach is probably the most promising for improving the success rate, the amplitude of the hemodynamic response and the extension of the indications of CRT. Reduction of the LPEI seems to be a simple parameter to use as suggested a long time ago[11] and a 16 ms decrease after implant seems to be the cutoff value for positive outcome.[12]

Finally, questions persist about the real contribution of parameters settings including AV and VV delays. Absence of setting is recognized as a factor of failure of CRT.[13] The difficulty with these time-consuming echo procedures led manufacturers to propose automatic algorithms that, unfortunately never showed a clear superiority compared to ''manual'' procedures, except in sub-groups of potential super-responders. All of these physician guilty-relief functions are based on sensing and processing of endocavitary electrical signals, except one based on a surrogate of LV dp/dt, and are ''black boxes'' for the operator, proposing a standardized solution which is supposed to fit to all patients. Unfortunately, some patients require an optimization of LV filling provided generally by a short AV delay and conversely, some of them require an optimization of contraction provided generally by a certain degree of fusion between leads stimuli and spontaneous activation. These needs are necessarily different from one patient to another according to the type of his preexisting dyssynchrony and to the placement of the electrodes during implantation. In patients requiring ''systolic'' rather than ''diastolic'' optimization, the simplest way to assess the optimal AV/VV intervals is to adapt them to the maximal provided reduction in LPEI, a parameter correlated to the duration of isovolumic contraction.

In conclusion, thanks to Dias Costa[14] et al., the use of QRS width and LBBB pattern in patient selection is confirmed. Will it be worthy to make ECG criteria more sophisticated? I am not sure that more complexity in ECG analysis will dramatically change the CRT success rate unless we further reduce the number of candidates to implantation. Due to the extreme diversity of mechanical dyssynchronies sharing almost the same ECG pattern and the objective of the therapy being to resynchronize mechanically and not electrically, these failing hearts (a task that no drugs can achieve), because of the complexity of interactions between initial dyssynchrony, leads placement and numbers and AV/VV settings, I think that ECG use in CRT is arriving at the end of its journey. Thanks to this technique first published in humans in 1902,[15] it has been very useful to spread CRT out of pioneer laboratories and democratize the technique; however, further improvements with regard to the success rate and to increase the amplitude of the response and extension of the indications will require a mechanical tool.

Conflicts of interest

The author has no conflicts of interest to declare.

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