Comparison of UHF-ECG with other noninvasive electrophysiological mapping tools for assessing ventricular dyssynchrony

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Abstract

This paper compares Ultra High Frequency ECG (UHF-ECG) with other techniques in the capacity to assess ventricular dyssynchrony. Ventricular dyssynchrony is important to identify patients that qualify for Cardiac Resynchronization Therapy (CRT) and to measure effects of CRT and other pacing therapies.

Currently used tools are: duration of the QRS complex in the 12-lead ECG, vectorcardiographically determined QRSarea, ECG belt and ECG imaging. QRS duration is crude, QRSarea has been shown to predict CRT response in three large single center studies, ECG belt is a novel approach using 50-60 body surface electrodes and yields (variation in) activation times. ECG imaging requires cardiothoracic imaging and recordings using 150-250 electrodes and results in images of activation, which are converted into inter and intraventricular AT differences. UHF-ECG requires 12-14 lead ECG but provides two measures: (also) a measure of interventricular dyssynchrony (e-DYS) and a marker of width of the activation wavefront that reflects the contribution of rapid conduction. The latter is a unique feature that appears particularly useful in studies on different modes of physiological pacing.

1. Introduction

With the emergence of Cardiac Resynchronization Therapy (CRT) the interest in measuring activation sequences in the ventricles have increased. While invasive mapping tools were available, wider spread clinical application requested noninvasive tools. After the conventional measurement of QRS duration, newer and probably better tools emerged over the last decade. ECG imaging was first reported in 2004 (1). In this technique a multielectrode vest records >200 body-surface electrocardiograms; electrical potentials, electrograms and isochrones are then reconstructed on the heart's surface using geometrical information from computed tomography (CT) and a mathematical algorithm. This technique is now used in at least two commercial applications. A simpler mapping tool is the ECG belt, which uses 50-60 electrodes in a belt wrapped around the chest. The principle is like that of ECG imaging, but without the need of a CT scan (2). Even simpler is the vectorcardiogram, which currently is largely derived from the standard 12-lead ECG followed by application of the Kors matrix (3).

Recently, Ultra High Frequency ECG (UHF-ECG) was developed (4). The technique allows to calculate at least two measures of dyssynchrony: electrical dyssynchrony (e-DYS) and the duration of the amplitude envelope (Vd). (5)

2. Comparison of techniques

2.1. Accuracy of measurement

<u>QRS duration</u>: while this seems a simple measurement, variability can be considerable. The best evaluation in this regard is the one by De Pooter et al. variation in QRS duration turned out to be up to 20 ms for non-paced QRS complexes and even ~40 ms for paced QRS complexes (6). The latter has, among others, to do with the question whether the pacing artefact should be used as start of the QRS complex or the first significant deflection. Another disadvantage of QRS duration as a marker of dyssynchrony is, that all information on the morphology of the complex is lost when using this marker, while specifically a left ventricular (LV) electrical delay is a good substrate for CRT.

<u>QRS area</u> is determined as the sum of the areas under the QRS complex in the X, Y and Z direction of the vectorcardiogram. The measurement of QRS area is considerably more accurate than that of QRS duration, because the timewise uncertain beginning and end of the QRS complex hardly contribute to the area of that complex(3).

<u>ECG imaging</u> provides much more detailed spatial information when compared to QRS duration and QRS area, but at the expense of the need of expensive electrode

vests and equipment, a CT scan and relatively labour-intensive analysis. ECG imaging has been validated against direct contact mapping measurements (7) showing a Pearson correlation coefficient of R=0.82 between actual and reconstructed activation times and a precision of finding the origin of ventricularly paced beat of 10 [7-17] mm. Ventricular Electrical Uncoupling (VEU), calculated as the difference of mean RV and LV activation times is therefore accurately determined (8). Yet, considerable technical challenges remain to obtain more detailed measures, particularly due to the ill-posed character of ECG imaging. (9)

The ECG belt technique has not been compared with actual contact mapping data. Its first publication showed the relation between ECG belt-derived parameters such as SDAT and hemodynamic changes during programming of the CRT device (2) and against a cardiac resynchronization index (10).

Relevant parameters calculated from the UHF-ECG are the electrical interventricular dyssynchrony (e-DYS) and the width of the voltage peak calculated for each lead separately and averaged for all leads (Vd). These are calculated almost fully automatically, so inter and intraindividual variation is likely very low.

2.2. Use for assessing dyssynchrony

At the start of CRT, more than two decades ago, QRS duration was used as the primary measure of dyssynchrony. Later studies showed that this parameter is not a good predictor of CRT response (11) and that morphology of that complex, in particular a left bundle branch block (LBBB) morphology, is more predictive (11). However, there are multiple definitions for defining LBBB from the surface ECG and the extent of benefit of CRT is highly dependent on the LBBB definition used (12).

The ratio behind QRS area is that it expresses non-opposed electrical forces, and high values may therefore indicate dyssynchronous electrical activation. This hypothesis was confirmed in a study showing that a large QRS area corresponds with delayed activation of the LV posterolateral wall, independent of QRS morphology (13). Moreover, at the same QRS duration QRS area is lower in patients with ischemic than non-ischemic heart failure (14) and is inversely related with the size of MRI-determined scar (15). Three single center studies independently showed that QRS area is a good predictor of CRT response (mortality, heart failure hospitalization and echocard-iographic reverse remodeling) (16-18). Moreover, the reduction in QRS area is an additional predictor of clinical CRT response (19). Regarding physiological pacing, a recent study showed that QRS area reduced at least as much during LV septal pacing and HBP as during BiV pacing, which was also reflected by similar hemodynamic effect (20).

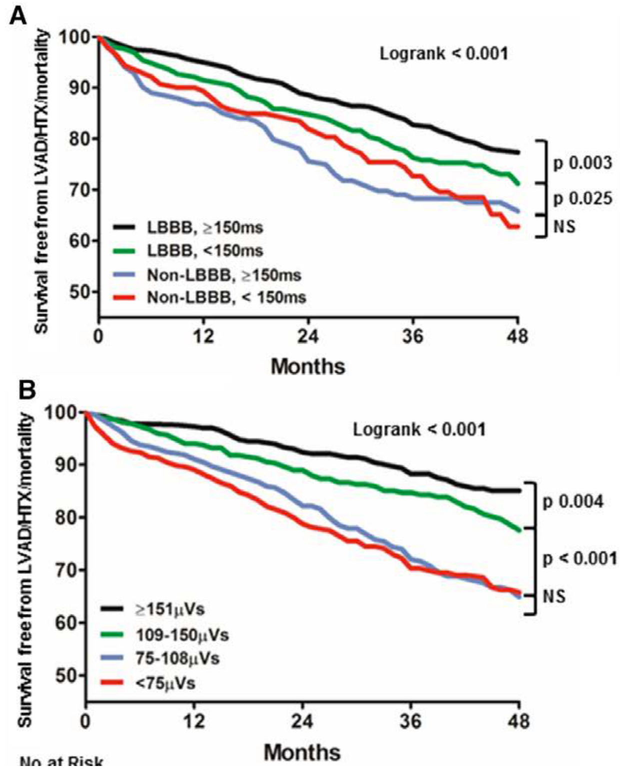

Figure 1: association between the combination of QRS duration and LBBB (A) and QRS area (B) and clinical outcome of CRT (survival free from LVAD implantation, heart transplant or death. Modified from (16).

The ECG belt technique has primarily been used to optimize CRT settings (atrioventricular and interventricular delays) using acute hemodynamic parameters as standard (2) (10).

ECG imaging has been applied to achieve better insight in mechanisms of CRT and finding the best position of the LV pacing lead. In this respect the technique may be useful in combination with CT imaging of the coronary veins and potentially MRI late enhancement to find the latest activated region outside a region of scar as the preferred position of the LV lead (21). Due to the relative complexity of the technique, no large-scale validation of ECG imaging as predictor of CRT response have been performed. Ploux et al. calculated the VEU and showed that this parameter is a good predictor of CRT response. A related parameter (activation delay vector (ADV)) expresses electrical substrate through magnitude and direction of activation. Intrinsic ADV accurately predicted the acute hemo-dynamic (AUC = 0.93) and chronic (AUC = 0.90) response to CRT in a cohort of 79 patients. However, ADV change by CRT only moderately predicted the response (highest AUC = 0.76). Also, LV pacing site optimization had limited effects: +3±4% LVdP/dtmax when compared to conventional basolateral LV pacing (22). In a more recent study the difference between His- (HBP) and biventricular pacing (BiVP) was investigated using ECG imaging (23). This study employed LV activation time and epicardial propagation mapping (figure 2). However, this study did not provide information about a potential hemodynamic benefit of HBP over BiV pacing.

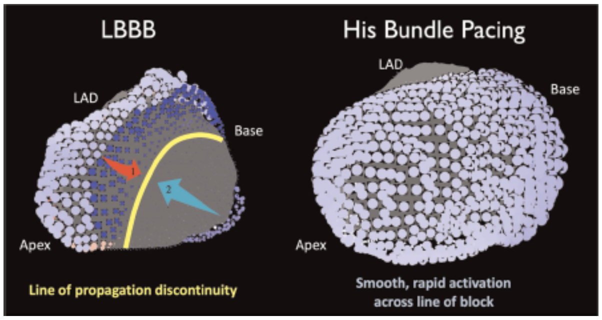

Figure 2. Example of epicardial propagation mapping based on ECG imaging data. The epicardial surface of the LV is shown for intrinsic LBBB (left) and HBP with shortening of LVAT (right) in the same patient. Blue circles are ECGI derived activations. In LBBB, the activation wavefront appears to halt at a line of propagation discontinuity (yellow). During HBP this discontinuity disappeared. HBP, His bundle pacing; LBBB, left bundle branch block; LV, left ventricle; LVAT, left ventricular activation time. Derived from (23).

UHF-ECG studies are relatively recent, due to the recent emergence of this technique (4). In a small study it was shown that BiVp reduces e-DYS, but not Vd, which can be explained by the reduction in ventricular dyssynchrony without influencing mean conduction velocity. In contrast, HBP reduced both e-DYS and Vd, the latter pointing to the contribution of the rapid conduction system to the electrical resynchronization (figure 3, (5)). A more detailed study showed that there were no significant differences between selective and non-selective HBP in terms of e-DYS and Vd (24). In a next study the difference was investigated between left bundle branch (LBBp) and LV septal pacing (LVSp). Interestingly, LBBp (with capture of the rapid conduction system) created a larger (more negative) e-DYS than LVSp, while mean Vd was comparable (25). Future studies are needed to show whether LVSp provides a better hemodynamic outcome than LBBp.

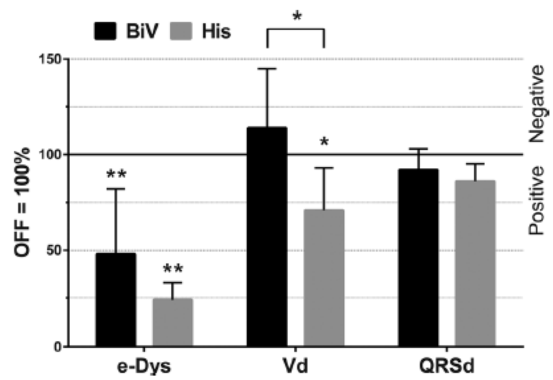

Figure 3. Relative changes of e-DYS, Vd, and QRS duration (QRSd) during BiV and His-bundle pacing (n=5-6) compared to baseline. BiV, biventricular pacing, His: His bundle pacing; e-DYS, electrical dyssynchrony. Derived from (5).

3. Conclusions

Three electrophysiological tools appear to be useful in the evaluation of impulse conduction during LBBB and different pacing modes. QRS area is a single, global parameter that currently requires off-line analysis of a regular 12-lead ECG and has been validated extensively. QRS imaging provides extensive information, but its costs, complexity and requirement of imaging of the patient with the electrode vest is difficult to implement in the normal clinical workflow, though extremely useful for scientific studies. UHF-ECG requires only a ~30 sec high-quality ECG recording and yet yields at least two parameters that seem useful in appreciating the benefits of conventional BiVp as well as the various modes of physiological pacing.

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