Is it time for personalized cardiac resynchronization therapy

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Cardiac resynchronization therapy (CRT) in appropriately selected patients can significantly improve left ventricular function and New York Heart Association (NYHA) class.^{1–3} CRT trials' inclusion criteria have been based solely on QRS duration with left ventricular (LV) lead implantation in the posterolateral branch of the coronary sinus as the preferred location. Using these guidelines, 60–70% of the CRT recipients respond with improvement in symptoms and/or ejection fraction. Response rate is much higher in individuals with typical left bundle branch block (LBBB) QRS morphology, with QRS duration >150 msec and non-ischemic cardiomyopathy. In those who lack these criteria response rate to CRT has been poor. The reason for this poor response rate is multifold including lack of dyssynchrony, presence of scar at the site of lead implantation, and inappropriate LV lead position. To overcome these challenges and improve patient response, implanting physician will benefit from the following information: (1) Is there the presence of significant dyssynchrony? (2) Which is the most dyssynchronous segment of the left ventricle? (3) Can that segment be accessed and used for pacing? This information will be most useful in patients with intraventricular conduction delay (IVCD) and atypical LBBB like QRS pattern rather than typical LBBB. In the presence of typical LBBB, latest activating segment is

posterolateral basal left ventricle (LV) and there is usually significant dyssynchrony.⁴

Several studies have tried to address one or more of these questions using different imaging modalities.^{5–7} Ideal imaging modality will have high spatial and temporal resolution to accurately identify the latest contracting segment, will give the implanting physician information about myocardial viability, coronary venous anatomy, and will have high degree of automation and reproducibility. Single-Photon Emission Computed Tomography (SPECT), Echocardiography, and Cardiac Magnetic Resonance Imaging (CMR) all have been evaluated for this purpose and each has its own limitation. There is disagreement on which echocardiographic parameter to use for dyssynchrony assessment and reproducibility has been poor. The largest trial using echocardiographic dyssynchrony assessment-guided CRT placement was negative⁶ although the inclusion criteria included only narrow QRS patients. Phase analysis from gated SPECT imaging has been proposed as a relatively straightforward way of assessing dyssynchrony.⁸ It uses Fourier harmonic function to approximate change in thickness of myocardium during a cardiac cycle to onset of contraction. This information of phase of onset of contraction is displayed on a polar map. Phase standard deviation and phase histogram bandwidth can then be used to quantify dyssynchrony and also to identify the latest contracting segments. This can then be combined with viability assessment and potentially fused with coronary sinus venograms,⁹ thereby providing a road map for precise and individualized LV lead placement.

The current study¹⁰ by Zhou et al helps in taking personalized CRT one step closer by trying to automate dyssynchrony assessment. In their study, the authors acquired images using 8-frame ECG-gated SPECT in 36 patients predominantly with non-ischemic cardiomyopathy and QRS duration >120 ms. Phase analysis as described above was then used for dyssynchrony assessment. Data from perfusion assessment were used

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to identify scarred segments. The latest contracting, which did not have scarring, was recommended for LV lead placement. Automatic assessment was then compared with the visual integration method by experts. There are three noteworthy findings in this manuscript: (1) There was an excellent agreement between the automatic method by the first operator and the visual integration method by experts. However, inter-operator reproducibility of the segment of choice by automatic method was less than 70%. (2) More than one segment was recommended in close to 45% of the patients as segments whose phase angles were within 10° of the latest phase angle were considered optimal for lead placement. Third and most interesting finding is the recommendation of the anterior lead placement in close to 55% of the patients, which would be a major departure from the current practice in which the posterolateral segment is usually targeted for LV lead placement.

The manuscript is a step in right direction but there are several shortcomings in both the technique and the study, which should be kept in mind for any future work. This is a small study of predominantly non-ischemic patients in which outcomes were not assessed. The temporal resolution of 8-frame ECG SPECT as the authors point out is 5.6°. In other words, it is unable to distinguish the latest activating segments if their phase of onset is within $\pm 5.6^\circ$ of each other. Hence, increasing the resolution of the technique (higher frame rates) is needed to improve accuracy and decrease ambiguity. As the authors mention in the discussion, the extent of baseline dyssynchrony assessment based on phase bandwidth or phase standard deviation should also be incorporated in the recommendation algorithm, as patients may, with minimal dyssynchrony, be unlikely to derive benefit despite accurate lead placement in the segment of latest activation. The current 17-segment model results in a significant overlap given the low resolution and therefore may be confusing for the implanting physician. We need to find an easier way to represent the combined dyssynchrony, viability, and coronary venous anatomy information. Fusion with CT or fluoroscopic venography can provide an excellent visual guide for the implanting physician. Lastly, it is unlikely that precise and personalized CRT will gain much traction unless a prospective randomized outcomes trial comparing dyssynchrony assessment-guided LV lead implant to traditional implant is done. This would be most useful in patients with incomplete LBBB and IVCD in which the latest activating segment can

vary considerably from one patient to another. Given pace of improvement in imaging techniques to non-invasively assess, quantify, and locate dyssynchronous LV segments time of personalized CRT is not far.

Disclosure

The author declare no conflict of interest.

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