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# The Age of Reason for Gated SPECT MPI to Deal With Cardiac Dyssynchrony

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Cardiac synchrony is defined as coordinated distribution of electrical activation through a prescribed path across the heart, leading to a harmonic contraction of contractile elements. The onset of contraction is dependent on two main factors including the pace of electrical waves through the conductive system and the response of contractile segments to the electrical stimulation as mechanical activation. When the propagation of mechanical activation is reasonably uniform, the blood pump is expected to work efficiently and in a synchronous way. Intraventricular and interventricular synchrony is also expressed as spreading the activation in a uniform way across one or the two ventricles, respectively (1). Dyssynchrony, on the other hand, occurs when one of these two essential elements of electrical or mechanical activation fails to work properly (2). The well-known indicator of electrical dyssynchrony, a wide QRS complex, has long been the main criterion for assessment and treatment of cardiac dyssynchrony by different device-based procedures including implantable cardioverter-defibrillator (ICD) and more recently cardiac resynchronization therapy (CRT) (3, 4).

Over a decade ago, CRT was established as a tool to not only improve clinical symptoms but also reverse ventricular remodeling, increase left ventricular (LV) ejection fraction (EF), decrease the severity of mitral regurgitation, reduce hospitalizations and more importantly improve survival of patients with heart failure (5-8). CRT was initially recommended for patients with wide QRS ( $\geq 120$ ms) and depressed LVEF ( $\leq 35\%$) with heart failure symptoms in the New York Heart Association (NYHA) class III or ambulatory class IV as conventional patient selection criteria (4, 5). Recent studies, however, extended the usefulness of CRT in some specific patients with milder degrees of heart failure (class II or even I) (9, 10).

Nevertheless, response to therapy has not been satisfactory as it was supposed to be. About one third of patients who undergo CRT with standard criteria do not benefit clinical and/or LV functional improvement (11-13). On the contrary, CRT could be beneficial in another subset of patients who have mechanical dyssynchrony without a concomitant wide QRS complex. Therefore, electrical dyssynchrony, conventionally determined by a wide QRS, does not necessarily reflect mechanical dyssynchrony (14). Given the fact that direct assessment of mechanical dyssynchrony would be significantly a better marker of CRT success than the comprehensive electrocardiogram (15), different imaging modalities including echocardiography (16, 17), computed tomography (18), magnetic resonance imaging (19) and different types of radionuclide scintigraphy have been proposed. Among all, echocardiography providing several imaging tools for LV dyssynchrony measurement such as speckle tracking two-dimensional (2D) strain analysis, and three-dimensional (3D) echocardiography as well as the most commonly used for the evaluation of mechanical dyssynchrony, tissue Doppler imaging (TDI), have been widely investigated to distinguish responders from non-responders to CRT (16, 17).

In fact, appropriate response to CRT depends on several variables, only one of which is presence and magnitude of LV dyssynchrony. To approximate the extent of scar tissue, particularly in the target segment for pacing and also appropriate delivery of the pacing electrode to the correct site with significant delayed contraction which still is viable and has a proper contractile reserve, are other important factors to achieve desirable results (14).

Gated single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) using phase analysis has literally provided all the mentioned important data in conjunction with myocardial perfusion data in 3D in one single study. This technique measures the onset of mechanical contraction across the LV and represents it as a phase polar map or a phase histogram. The phase standard deviation (PSD) and the phase bandwidth (PHB) encompassing 95% of samples of the phase histogram, have been introduced as main indices of LV synchrony (20, 21). Apart from the major limitation of this method, the limitation to assess only LV dyssynchrony, gated SPECT MPI using phase analysis has the advantage of automatic processing, good reproducibility, being straightforward to calculate, availability as a conjunctive method with perfusion study without any need for additional imaging, enabling to define the location, extent and severity of scar tissue, providing comprehensive information on LV, EF and LV volumes, and also possibility to determine site selection for LV pacing lead placement by defining the latest mechanical activation (1).

In the recent issue of journal, Azizian et al. presented interesting data derived from phase analysis of gated SPECT MPI of 30 consecutive patients with reduced LV ejection fraction (< 35%) and wide QRS (> 120 ms) with severe heart failure (NYHA class III or early IV) who had already been admitted for CRT (22). Before the device implantation, patients underwent gated imaging; they were evaluated for NYHA functional class and 6-min walking test (6-MWT) for clinical assessment and underwent standard 2D echocardiography before and six months after the device implantation. The results represented a remarkable clinical improvement at a 6-month follow-up in 74% of patients; however, according to the echocardiography criteria (>15% decrease in end systolic volume) only 57% of patients were recognized as responders. While there were no significant differences in baseline clinical and echocardiographic characteristics between the responders and non-responders, gated- MPI-derived LV dyssynchrony data were significantly different between the responders and non-responders. Furthermore, cut-off value of 112° for PHB, 21° for PSD, and 52% for Entropy were estimated to predict clinical response to CRT with a good sensitivity and specificity as the most important parameters for determination of LV dyssynchrony. The authors concluded that regarding the good correlation between clinical response to CRT and data of LV dyssynchrony assessed by gated MPI phase analysis, which was closer to the clinical outcomes than 2D-echocardiographic results, PHB and PSD can be used to predict response to CRT.

Nevertheless, as the authors stated, the results need to be verified in a larger patient population from a multicenter study. Different software packages and gamma cameras are prone to yield different results, representing incomparable cut-off values.

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