New insights in the assessment of left ventricular dyssynchrony: Laying the foundations for phase analysis by cardiac SPECT

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Chronic heart failure still poses major challenges for the patient, the healthcare system, and the treating physician despite the fact that novel pharmacological (e.g., angiotensin-neprilysin inhibitor) and interventional treatments (e.g., cardiac resynchronization therapy or transcatheter mitral-valve repair) battle the high morbidity and mortality with great promise.^{1–3} Therefore, careful and comprehensive analysis of these patients is needed to help the treating physician making the right decision on the optimal allocation of the available resources.

One of these resources is cardiac resynchronization therapy (CRT). Since intraventricular dyssynchrony may depress cardiac contractility further in some patients with chronic heart failure, the CRT device coordinates the contraction of the left ventricle, demonstrating improved quality of life as well as outcome.^{1,4} Consequently, current guidelines recommend CRT in symptomatic patients with left ventricular ejection fraction (LVEF) $\leq 35\%$ and QRS duration ≥ 130 milliseconds (with left bundle branch block morphology).⁵ However, a substantial number of patients who meet

guideline indication fail to benefit from CRT.⁴ Therefore, better tools to identify candidates for CRT are needed in order to optimize resource allocation.

Cardiac single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) may be such a tool. It provides valuable information on two major pathophysiological determinants of CRT response. On one hand, cardiac SPECT MPI detects the *extent and localization of LV scar tissue*. It has been shown that the extent of scar tissue and viable myocardium is directly related to the response to CRT.⁶ On the other hand, *LV mechanical dyssynchrony* can be evaluated in gated cardiac SPECT MPI by phase analysis. Thereby, the onset of mechanical contraction is measured at multiple points across the LV myocardium and its distribution is visualized by either a polar map or a histogram. With increasing mechanical dyssynchrony, the phase standard deviation and the bandwidth of the histogram are widened. Most importantly, CRT response is associated with larger histogram bandwidth and phase standard deviation.⁷ In addition, LV dyssynchrony assessed by phase analysis from cardiac SPECT MPI could predict major adverse cardiac events independent of other known predictors such as perfusion defects or decreased LV ejection fraction.⁸ Despite its promising evidence and clinical relevance, these parameters of imaging-derived LV dyssynchrony have been adopted restrainedly. One explanation may originate in its terminology, and the fact that the mechanical dyssynchrony in cardiac SPECT MPI is given in degrees of cardiac cycle while cardiologist are experienced readers of electrocardiograms (ECG) and, thus, more familiar with milliseconds.

In the current issue of the Journal, *Barron et al.* investigated the influence of degrees and time of cardiac

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cycle in a retrospective analysis of 399 patients with normal perfusion and function on gated post-stress cardiac SPECT images. Using these images, phase analysis—in degrees and in milliseconds—was performed across the LV myocardium and distribution of mean phase (i.e., the onset of mechanical contraction within the cardiac cycle) was visualized on a polar map and a phase histogram. While standard deviation and bandwidth were not affected by heart rate when expressed in degrees of the cardiac cycle, there was a significant correlation between heart rate and the two values when phase analysis was expressed in milliseconds. Among the latter, a rising heart rate led to a decreasing bandwidth and standard deviation. The authors concluded that although less intuitive to cardiologists, phase analysis is more robust when measured in degrees than in milliseconds.

The authors should be congratulated for this elegantly and properly performed study highlighting the necessity to measure parameters of mechanical dyssynchrony (i.e., bandwidth and standard deviation) in degrees of the cardiac cycle rather than in milliseconds. The study, furthermore, offers valuable insights into the physiological response of mechanical dyssynchrony to changes in heart rate. Nevertheless, as for every study, there are certain weaknesses and limitations that deserve closer attention. First, the study is limited to a homogeneous population with normal perfusion and function, and, as recognized by the authors, did not include “the patients that phase analysis will be clinically applied to.” The present findings need to be confirmed in a population with reduced LVEF and electrical dyssynchrony. Second, mechanical dyssynchrony was assessed in post-stress instead of rest gated SPECT images. In view of the long interval between stress testing and image acquisition (i.e., 30–60 minute), however, relevant confounding is unlikely.⁹ Last but not least, the problematic influence of heart rate on timing values in milliseconds had been recognized over a decade ago and, although clinically less appealing, it was considered more appropriate to express all timing values in degrees or percentages of the averaged cardiac cycle duration.^{7,10} In line with those studies, the current study specifies the correct way to measure mechanical dyssynchrony in cardiac SPECT MPI.

Considering its high reproducibility, even in comparison to ECG,^{11,12} the present study lays the foundation for phase analysis by cardiac SPECT MPI in clinical routine—a technique complementary to perfusion and viability assessment without any extra costs or risks.¹³ In view of the emerging evidence that LV dyssynchrony can be accurately assessed by phase analysis from cardiac SPECT MPI and may predict CRT response, it brings new hope for the challenges that

physicians face in the management of patients with chronic heart failure.^{14,15}

Disclosure

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