Radionuclide Assessment of Left Ventricular Dyssynchrony

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KEYWORDS

• Left ventricular dyssynchrony • Cardiac resynchronization therapy • Heart failure • Radionuclide • Site of latest activation • Myocardial scar • SPECT • Echo • LBBB • QRS

KEY POINTS

- Phase analysis of GMPS is a widely available and reproducible measure of LV dyssynchrony, which also provides comprehensive assessment of LV function, global and regional scar burden, and patterns of LV mechanical activation.
- Preliminary studies indicate potential use in predicting CRT response and elucidation of mechanisms.
- In contemporary CRT, patients selected for the presence of a wide QRS and LBBB are likely to have a septal to lateral wall activation delay, which is amenable to resynchronization by biventricular pacing. In these patients, imaging may be helpful in identifying scar and extensive LV remodeling, which may suggest lack of potential for functional improvement with CRT.
- Because advances in technology may expand capabilities for precise LV lead placement in the future, identification of specific patterns of dyssynchrony may have a critical role in guiding CRT.

DEFINITION AND PREVALENCE

Dyssynchrony refers to a temporal dispersion in the activation and contraction of the normally coordinate ventricle. Minor differences in the amplitude and timing of left ventricular (LV) contraction exist in normally functioning hearts,[1] thus pathophysiologic dyssynchrony needs to be defined using threshold rarely encountered in the normal population.[2] LV dyssynchrony is not an all-or-nothing phenomenon, but represents a continuum of different grades of severity.[1]

LV dyssynchrony can manifest in several different ways: electrical versus mechanical, systolic versus diastolic, intraventricular versus interventricular, and normal versus pathologic dyssynchrony. Currently the QRS duration on a 12-lead electrocardiogram is used as a surrogate for electromechanical dyssynchrony and a wide QRS duration taken to denote a prolonged ventricular conduction time and nonsimultaneous ventricular wall contraction.[3,4] However, there is increasing evidence about the limitations of using the QRS duration as the sole marker of mechanical dyssynchrony.[5,6] Mechanical dyssynchrony can occur between the atria and the ventricles (atrioventricular dyssynchrony), the left and the right ventricles (interventricular dyssynchrony), or among different myocardial segments of the left ventricle (intraventricular dyssynchrony).[7,8] Intraventricular dyssynchrony has been shown to strongly correlate with cardiac hemodynamic parameters and adverse cardiac events, as opposed to interventricular dyssynchrony,[9] and the term is

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used interchangeably with mechanical dyssynchrony. Much of the current knowledge on LV dyssynchrony comes from echocardiographic studies, which have traditionally quantified LV dyssynchrony as either greater than 60 to 65 millisecond (ms) delay in time to peak systolic contraction between the septum and posterolateral walls of the left ventricle, or by the Yu index, defined as the standard deviation (SD) of the time to peak systolic velocity in a 12-segment LV model (>33 ms represents dyssynchrony).[2] Diastolic dyssynchrony is less clearly defined compared with its systolic counterpart.

The mechanisms underlying LV dyssynchrony are poorly understood, but known to depend on a complex interplay of numerous factors including LV systolic dysfunction, electrical abnormality (QRS widening), and LV scar burden. In general, the prevalence of dyssynchrony increases with worsening systolic dysfunction and increasing QRS duration. Among patients with severely reduced LV systolic function, dyssynchrony has been reported in up to 75% of the patients.[10] Similarly, among patients with systolic heart failure, the prevalence of dyssynchrony reportedly varies from 27% in patients with narrow QRS (<120 ms) to 89% in those with QRS duration greater than 150 ms.[1,11] In diastolic heart failure, however, the prevalence of systolic dyssynchrony is reported to be 33% to 60%, whereas diastolic dyssynchrony is 40% to 58%.[12,13]

PATHOPHYSIOLOGY

Ventricular contraction occurs by a geographically coordinated process where myocardial fibers shorten synchronously and by the same amount throughout the ventricle. This highly coordinated process is maintained by an endocardial electrical conduction system that carries the cardiac action potential from the endocardium to the epicardium and from the apex to the base, facilitating synchronized ventricular myocardial contraction.[14–16] Any disruption of this conduction or contraction pattern leads to dyssynchronous ventricular contraction. A classic example of such pathophysiology is seen in left bundle branch block (LBBB), where the early systolic contraction of the LV septum followed by late systolic activation of the lateral free wall results in dyssynchronous contraction, producing regional heterogeneity in myocardial work load and blood flow.[17–19] These are thought to result in LV remodeling (increased LV end-systolic volume) and increasing wall stress, a rightward shift of the end-systolic pressure-volume relationship,[20] a reduction in net LV ejection pressure,[20,21] an increase in the rate of LV pressure (dP/dt_{max}),[22] and a reduced stroke work and volume.[21] This mechanical inefficiency is further exacerbated by functional mitral regurgitation, which is caused by dyssynchronous papillary muscle contraction, annular dilation, and atrioventricular conduction delay.[17,23] The end result is reduced net cardiac output and symptomatic heart failure that is often refractory to conventional medical therapy.[24,25]

CLINICAL IMPLICATIONS IN HEART FAILURE

An association between LV dyssynchrony and mortality has been demonstrated in patients with heart failure.[26] Sustained LV dyssynchrony has been shown to lead to LV systolic dysfunction,[27] whereas dyssynchrony promotes progression of established heart failure, and is an independent predictor of adverse cardiac events.[26,28,29] Cardiac resynchronization therapy (CRT) improves the net systolic function and cardiac mechanical efficiency by resynchronizing biventricular contraction, without increasing myocardial oxygen consumption.[30–32] Simultaneous biventricular preexcitation by CRT and the associated reduction in dyssynchronous contraction improves functional mitral regurgitation, eventually resulting in smaller LV volumes (reverse remodeling).[33,34] Several large, randomized controlled trials have shown that CRT reduces mortality and morbidity in patients with drug-refractory heart failure, particularly in the presence of LV dyssynchrony.[35–38] However, applying CRT to patients with heart failure with no underlying dyssynchrony may lead to poor clinical outcomes.[39]

Initial guidelines for CRT were based on studies that were performed in patients with New York Heart Association (NYHA) class III or IV heart failure, LBBB, QRS greater than 120 ms, and LV ejection fraction (LVEF) less than or equal to 35%.[40] Subsequent studies have shown benefit in patients with milder heart failure.[41–43] A recent meta-analysis of five randomized clinical trials involving 4317 patients with NYHA class I to II heart failure, LVEF less than 40%, and QRS greater than 120 ms showed that CRT with implantable cardioverter defibrillator (ICD) therapy decreased all-cause mortality, heart failure hospitalizations, and improved LVEF compared with ICD alone.[44] More specifically, in NYHA functional class I patients, heart failure hospitalization risk remained lower with CRT, whereas there was no difference in mortality. Following these new data, the guidelines were updated and CRT is now indicated for patients with NYHA class II heart failure with LVEF less than or equal to 35%, LBBB, and a QRS duration greater than or equal to 150 ms