

EDITORIAL COMMENT

Assessment of LV Systolic Dyssynchrony in Heart Failure Beyond a Snapshot*

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Left ventricular (LV) systolic dyssynchrony, also known as intraventricular dyssynchrony, represents the delay or heterogeneity in the timing of contraction in different myocardial segments within the LV. At the turn of the millennium, since the development of cardiac resynchronization therapy (CRT) for patients with chronic systolic heart failure who have a wide QRS complex, we have witnessed a plethora of research exploring the role of systolic dyssynchrony in assessing the mechanism

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of electromechanical delay, examining CRT benefits on the myocardial mechanical perspective, and defining parameters of dyssynchrony that predict CRT responders (1). Recently, evidence is accumulating in extending the assessment of resting dyssynchrony beyond chronic heart failure patients with a wide QRS complex. In chronic heart failure patients with a narrow QRS complex (usually defined as QRS <120 ms), LV systolic dyssynchrony has been found to be relatively prevalent and is a predictor of poor prognosis (2,3). In this issue of *JACC*, Tanaka et al. (4) in the IMAC2 (Intervention in Myocarditis and Acute Cardiomyopathy II) study described the prevalence of LV systolic dyssynchrony in 216 patients with acute nonischemic cardiomyopathy and narrow QRS complex and reported its improvement after medical therapy for 6 months. Of note, the study was a multicenter

design, and the experienced echocardiographic core laboratory was able to maintain a low intraobserver and interobserver variability for analysis of dyssynchrony and ejection fraction, an issue critical for study of this kind. There are 2 main observations in the IMAC2 study. The prevalence of LV systolic dyssynchrony was relatively high (54%) in the population with acute nonischemic cardiomyopathy, although it decreased dramatically to 12% after a mean follow up of 7 ± 3 months. LV systolic dyssynchrony was consistently reduced by using 3 comprehensive parameters that assessed long-axis velocity of 6 LV walls through velocity vector imaging. This study corroborates with a pioneer study on 50 patients with acute decompensated heart failure (although 56% had a wide QRS complex) in whom LV systolic dyssynchrony improved as early as 48 h after intensive medical therapy (5). Intriguingly, the study found that significant improvement in hemodynamics was only observed in patients who had baseline dyssynchrony. Tanaka et al. (4) also found a relationship between improvement of dyssynchrony and gain in ejection fraction as well as decrease in the ratio of pulse-wave Doppler derived transmitral early diastolic velocity to color tissue Doppler derived early diastolic velocity obtained from lateral mitral annulus, which reflects LV filling pressure. Although this study cannot conclude a causative relationship, it remains possible that LV systolic dyssynchrony plays a role in the pathogenesis of acute decompensated heart failure through its negative impact on systolic and diastolic function. Conversely, factors leading to the development of acute heart failure may increase the vulnerability of the occurrence of dyssynchrony. Other factors that might have played an important role in the relationship between acute heart failure and LV dyssynchrony have not been investigated in the

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current study, which included the adverse LV geometry and the change of mitral regurgitation. One potential concern in the interpretation of the study is related to the use of 2 different software programs for offline analysis of the 2-dimensional (2D) speckle tracking images from multiple vendors. With the use of different vendor-specific algorithms for reconstitution and calculation of 2D speckle signals, it remains crucial to demonstrate that the measured results from the 2 systems were similar when assessed in the same subjects (i.e., a low cross-vendor variability).

The current study provides convincing evidence that LV systolic dyssynchrony occurs beyond electromechanical delay caused by the prolongation of QRS duration. In fact, factors including loading condition, degree of LV adverse geometric remodeling, etiology of heart failure, distribution of myocardial disease, degree of LV hypertrophy, LV diastolic function, myocardial stress, and medications could have played a role. Therefore, the beneficial effect of anti-heart failure therapy and the natural course of recovery from acute cardiomyopathy might have reduced LV dyssynchrony and improved LV function through the aforementioned factors. Assessment of LV systolic dyssynchrony in heart failure patients with a narrow QRS complex also has potential treatment implications. Of note, the previously published RETHINQ (Resynchronization Therapy in Narrow QRS) study did not support the role of CRT in systolic heart failure patients with a narrow complex and coexisting LV systolic dyssynchrony (6). However, in the context of the current study, patients within 6 months of recent-onset cardiomyopathy should have been deferred from consideration of the device study. Similar contraindications should also apply to the ongoing ECHO-CRT (Echocardiography Guided Cardiac Resynchronization) study, which is a study to explore the role of tissue Doppler imaging or 2D speckle tracking strain to identify the presence of dyssynchrony in systolic heart failure patients with a narrow QRS complex receiving CRT.

Apart from dynamic changes of LV systolic dyssynchrony over the course of heart failure, recent studies have also examined dynamic dyssynchrony in the context of myocardial stress. For example, exercise stress-induced systolic dyssynchrony is associated with exacerbation of heart failure symp-

toms, increase in mitral regurgitation, and reduction in exercise capacity (7,8). For patients receiving CRT, a pilot study revealed that mechanical dyssynchrony was present in 63% of patients at rest and 72% at peak exercise, and dyssynchrony index measured at peak exercise was a better predictor of functional improvement and LV reverse remodeling after the therapy (9). Furthermore, the occurrence of reversible systolic dyssynchrony during exercise stress testing has been suggested to play a role in the pathogenesis of acute decompensated heart failure, as its prevalence was as high as 80% when compared with 48% in patients with chronic stable heart failure (10).

Recently, the concept of mechanical dyssynchrony has also been extended to the investigation of patients with diastolic heart failure, also called heart failure with preserved ejection fraction. In this population, systolic and diastolic dyssynchrony was found to be relatively common, although it was less prevalent than patients with systolic heart failure (11). Furthermore, the prevalence of systolic dyssynchrony during pharmacological stress increased dramatically from 36% to 85%, whereas diastolic dyssynchrony increased from 38% to 87% (12). Interestingly, treatment of the condition by medical therapy is associated with improvement of diastolic dyssynchrony, which in turn correlated closely with invasive parameters of LV stiffness and filling pressure (13).

With the accumulated knowledge in the technique and potential applications of measuring mechanical dyssynchrony in heart failure subjects, it appears that there is an expanding role in the assessment of dyssynchrony. However, before measurement of dyssynchrony is contemplated, it is imperative to understand the clinical context of this evolving tool—acute versus chronic heart failure, wide versus narrow QRS complex, impaired versus preserved systolic function, resting versus stress echocardiography, and snapshot versus serial assessment. Of course, these issues can only be addressed with further accumulation of experience and evidence from many more studies.

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REFERENCES

1. Yu CM, Sanderson JE, Gorcsan J, III. Echocardiography, dyssynchrony, and the response to cardiac resynchronization therapy. *Eur Heart J* 2010;31:2326-37.
2. Yu CM, Lin H, Zhang Q, Sanderson JE. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. *Heart* 2003;89:54-60.
3. Cho GY, Song JK, Park WJ, et al. Mechanical dyssynchrony assessed by tissue Doppler imaging is a powerful predictor of mortality in congestive heart failure with normal QRS duration. *J Am Coll Cardiol* 2005;46:2237-43.
4. Tanaka H, Tanabe M, Simon MA, et al. Left ventricular mechanical dyssynchrony in acute onset cardiomyopathy: association of its resolution with improvements in ventricular function. *J Am Coll Cardiol Img* 2011;4:445-56.
5. Mullens W, Borowski AG, Curtin R, Grimm RA, Thomas JD, Tang WH. Mechanical dyssynchrony in advanced decompensated heart failure: relation to hemodynamic responses to intensive medical therapy. *Heart Rhythm* 2008;5:1105-10.
6. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. *N Engl J Med* 2007;357:2461-71.
7. Lafitte S, Bordachar P, Lafitte M, et al. Dynamic ventricular dyssynchrony: an exercise-echocardiography study. *J Am Coll Cardiol* 2006; 47:2253-9.
8. D'Andrea A, Caso P, Cuomo S, et al. Effect of dynamic myocardial dyssynchrony on mitral regurgitation during supine bicycle exercise stress echocardiography in patients with idiopathic dilated cardiomyopathy and 'narrow' QRS. *Eur Heart J* 2007;28:1004-11.
9. Rocchi G, Bertini M, Biffi M, et al. Exercise stress echocardiography is superior to rest echocardiography in predicting left ventricular reverse remodelling and functional improvement after cardiac resynchronization therapy. *Eur Heart J* 2009;30:89-97.
10. Zhang Q, Liu YT, Lee PW, et al. Left ventricular systolic dyssynchrony is more common in acute decompensated than chronic stable heart failure with reduced ejection fraction. *J Am Coll Cardiol* 2010;55:A34.
11. Yu CM, Zhang Q, Yip GW, et al. Diastolic and systolic asynchrony in patients with diastolic heart failure: a common but ignored condition. *J Am Coll Cardiol* 2007;49:97-105.
12. Lee AP, Song JK, Yip GW, et al. Importance of dynamic dyssynchrony in the occurrence of hypertensive heart failure with normal ejection fraction. *Eur Heart J* 2010;31:2642-9.
13. Wang J, Kurrelmeyer KM, Torre-Amione G, Nagueh SF. Systolic and diastolic dyssynchrony in patients with diastolic heart failure and the effect of medical therapy. *J Am Coll Cardiol* 2007;49:88-96.

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