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Mechanical Dyssynchrony

• Electrical activation in the normal heart typically occurs quickly within 40 ms via conduction through the Purkinje network and is associated with synchronous regional mechanical contraction.

• A variety of myocardial diseases induce alterations in cardiac structure and function that result in regions of early and late contraction, known as dyssynchrony.

• Mechanical dyssynchrony is usually associated with a prolonged QRS duration on the surface ECG, although it may also exist in a subset of patients with heart failure and depressed LV function and narrow QRS by ECG.

Gorcsan et al. *JASE* 2008; 21(3):191-212
Types of Dyssynchrony

- Atrioventricular dyssynchrony
- Interventricular dyssynchrony
- Systolic intraventricular dyssynchrony
The classic type of dyssynchrony resulting from abnormal electrical activation is seen with LBBB - early activation of the interventricular septum and late activation of the posterior and lateral LV walls.

The early septal contraction occurs before normal ejection when LV pressure is low and does not contribute to ejection.

This process generates heterogeneous stress and strain in the LV, with one wall exerting forces on the contralateral wall.

Dyssynchrony results in inefficient LV systolic performance, increases in end-systolic volume and wall stress, and delayed relaxation that is thought to affect biological signaling processes involved in regulating perfusion and gene expression.

Improvements in LV synchrony are associated with LV functional improvements and reduction in MR.

Gorcsan et al JASE 2008; 21(3):191-212
To improve patient selection for CRT by identifying the subset of patients with wide QRS but with absence of mechanical dyssynchrony.

Other reasons for not responding to CRT -
- ischemic disease with too much scar to reverse remodel
- subsequent infarction after CRT
- suboptimal lead placement
Echocardiographic Quantification of Dyssynchrony
M-mode at midventricular level

Technically simplest - significant dyssynchrony (≥130 ms)
PW LVOT – to allow time-velocity analysis

LV ejection interval from pulsed Doppler of outflow tract
Color-coded tissue Doppler

Significant dyssynchrony (≥65 ms)
Color-coded tissue Doppler

2-chamber View

Anterior
Inferior

AVO
AVC
Maximum opposing wall delay was seen in apical long-axis view of 140 ms between septum and posterior wall, c/w significant dyssynchrony (≥65 ms).
Tissue Doppler study from 3 standard apical views demonstrating color coding of time to peak velocity data.

Lateral wall (4-chamber) and posterior wall (apical long-axis) are color-coded yellow-orange, indicating delay in time to peak velocity.
Yu index

12-segment SD model using color TD that integrates information from 3 apical views (4-chamber, 2-chamber, and long-axis). SD of the time-to-peak systolic velocity in the ejection phase 12-site standard deviation. \( \geq 33 \) ms signify mechanical dyssynchrony. 120 to 150 milliseconds, the sensitivity is 83% and specificity is 86%. An alternate method is to calculate the maximal difference
Delayed time to onset systolic velocity in lateral wall, as compared with septum in patient with left bundle branch block before resynchronization therapy.
Strain and strain rate imaging have the theoretic advantage of differentiating active myocardial contraction or deformation from passive translational movement and have been utilized to identify dyssynchrony.

However, TD longitudinal strain can be technically challenging because strain is calculated along scan lines, is Doppler angle dependent, and is difficult in patients with spherical LV geometry, often encountered in severe heart failure.

TD strain rate is restricted by a poor signal-to-noise ratio, which adversely affects reproducibility.
longitudinal strain in healthy synchronous patient

In patient with LBBB before CRT
Radial thickening is a major vector of LV contraction → short-axis dynamics are important markers of dyssynchrony,

Strain has an advantage over M-mode of differentiating active from passive motion and identifying radial mechanical activation.

Speckle tracking applied to routine midventricular short-axis images determines radial strain from multiple points averaged to 6 standard segments.
synchrony of peak segmental radial strain in healthy individual

severe dyssynchrony in patient with heart failure and LBBB
• LV dyssynchrony in reality is a 3-dimensional phenomenon.
• The advantage of real-time 3-dimensional echocardiography is that it allows for a comparison of synchrony between of the segments of the LV together in the same cardiac cycle.
• Regional wall-motion patterns can be visualized and quantified after segmentation of the LV chamber with semiautomatic contour tracing algorithms.
• Systolic dyssynchrony index - dispersion of time to minimum regional volume for all 16 LV segments: predictive of reverse remodeling after CRT in 26 patients.
• Disadvantages include lower spatial and temporal resolution, with frame rates for 3-dimensional wide-sector image acquisition at approximately 20 to 30 frames/s.

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3DE assessment of segmental volume displacement in patient with normal synchrony.

significant dyssyn
Pulsed Doppler from right ventricular outflow tract and left ventricular (LV) outflow tract demonstrating significant delay in LV ejection (40 ms)
Velocity vector images demonstrating synchrony of velocity convergence toward center of left ventricle in healthy individual.

Severe septal-lateral wall dyssynchrony in patient with heart failure and LBBB.
Mitral regurgitation before CRT  One day after CRT
Atrioventricular optimization using mitral inflow velocities in patient with intra-atrial conduction delay
Simplified AV Delay Screening

**Satisfactory AV Delay**

1. E and A Waves Separated
2. Termination of A after QRS onset or Mitral Closure Click Aligned With End of A and QRS Complex.

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**Absent A Wave**

*AV Much Too Short*

**Truncated A Wave**

*AV Too Short*

**Merged E and A**

*AV Too Long*

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**AV Optimization**
Large variability in the analysis of the dyssynchrony parameters. No single echocardiographic measure of dyssynchrony may be recommended to improve patient selection for CRT beyond current guidelines.

Chung ES et al Circulation. 2008;117:2608-2616
<table>
<thead>
<tr>
<th>Index</th>
<th>Method</th>
<th>Normal</th>
<th>Cutoff</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraventricular longitudinal dyssynchrony</strong></td>
<td></td>
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<tr>
<td>Opposing wall delay, two sites(^{12,15,38})</td>
<td>Color tissue Doppler peak velocity (apical 4-chamber or long-axis views)</td>
<td>(&lt;50) ms</td>
<td>(\geq 65) ms</td>
<td>Rapidly applied; offline analysis is possible</td>
<td>Requires color TD equipment; affected by passive motion tethering</td>
</tr>
<tr>
<td>Maximum wall delay, 12 sites(^{43,47})</td>
<td>Color tissue Doppler peak velocity (apical 4-chamber, 2-chamber, and long-axis views)</td>
<td>(&lt;90) ms</td>
<td>(\geq 100) ms</td>
<td>More complete detection of longitudinal dyssynchrony; offline analysis is possible</td>
<td>Requires color TD equipment; affected by passive motion tethering</td>
</tr>
<tr>
<td>Yu index(^{14,31,43})</td>
<td>Color tissue Doppler, 12-segment SD (apical 4-chamber, 2-chamber, and long-axis views)</td>
<td>(&lt;30) ms</td>
<td>(\geq 33) ms</td>
<td>More complete detection of longitudinal dyssynchrony; offline analysis is possible</td>
<td>Requires color TD equipment; more time-consuming; affected by passive motion tethering</td>
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<tr>
<td>Delay in onset of systolic velocity(^{51})</td>
<td>Pulsed tissue Doppler (apical 4-chamber, 2-chamber, and long-axis views; LV and RV)</td>
<td>(&lt;80) ms</td>
<td>(\geq 100) ms</td>
<td>More widely available</td>
<td>Acquisition technically difficult; offline analysis is not possible; affected by passive motion tethering</td>
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<tr>
<td>Delayed longitudinal contraction(^{41,42})</td>
<td>Color tissue Doppler-strain-strain rate (apical views)</td>
<td>None</td>
<td>N/A</td>
<td>Less affected by passive motion or tethering; offline analysis is possible</td>
<td>Requires specialized color TD equipment; technically demanding</td>
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<tr>
<td><strong>Intraventricular radial dyssynchrony</strong></td>
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<tr>
<td>Septal to posterior wall delay(^{54,35})</td>
<td>M-mode (parasternal mid-LV view)</td>
<td>(&lt;50) ms</td>
<td>(\geq 130) ms</td>
<td>Widely available; rapidly applied; no advanced technical requirements</td>
<td>Largely affected by passive motion or tethering; difficulties with segmental akinesis</td>
</tr>
<tr>
<td>Septal to posterior wall delay(^{54,57})</td>
<td>Radial strain (parasternal mid-LV view)</td>
<td>(&lt;40) ms</td>
<td>(\geq 130) ms</td>
<td>Less affected by passive motion or tethering; speckle tracking may be applied to routine images</td>
<td>Requires specialized instrumentation for analysis; assesses only radial dynamics</td>
</tr>
<tr>
<td><strong>Interventricular dyssynchrony</strong></td>
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<tr>
<td>Interventricular mechanical delay(^{62-64})</td>
<td>Routine pulsed Doppler (RVOT and LVOT views)</td>
<td>(&lt;20) ms</td>
<td>(\geq 40) ms</td>
<td>Widely available; no advanced technical requirements; highly reproducible</td>
<td>Nonspecific; affected by LV and RV function</td>
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</table>
Application of Dyssynchrony analysis

• Evidence from large-scale clinical trials and current practice guidelines do NOT include an echocardiographic Doppler dyssynchrony study for patient CRT selection.

• **Patients who meet accepted criteria for CRT should NOT have therapy withheld because of results of an echocardiographic Doppler dyssynchrony study.**

• Echo - an adjunct to assist with clinical decision making for CRT for selected patients who may have borderline inclusion criteria, such as a borderline QRS duration.

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Application of Dyssynchrony analysis

• Enrollment in the CARE-HF randomized CRT trial required patients with **borderline QRS duration between 120 and 149 milliseconds** to meet two of 3 additional criteria for dyssynchrony:
  – an aortic pre-ejection delay longer than 140 milliseconds,
  – An IVMD longer than 40 milliseconds, or
  – delayed activation of the posterolateral LV wall.

• In addition, the subgroup analysis of patients with **QRS 120 to 129 milliseconds and evidence of mechanical dyssynchrony in RethinQ** demonstrated benefit from CRT.

• Other possible clinical settings where dyssynchrony analysis may potentially play a role is
  – in patients with borderline EF or
  – ambiguous clinical histories for NYHA functional class.

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Conclusions

- Echocardiography plays an exciting and evolving role in the care of the patient with CRT, from quantifying improvements in ventricular function and MR to optimizing the device after implantation.
- More work to 1) quantify mechanical dyssynchrony, 2) to refine patient selection and 3) guiding lead placement.
- Technologic improvements in echocardiographic data acquisition and analysis as well as advances in our understanding of the pathophysiology of dyssynchrony and CRT have great potential to impact future clinical practice and improve patient outcome.
John Gorcsan III - I’m staying on the CRT dyssynchrony ship!
Thank you

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