Καρδιακός ασυγχρονισμός. Το λυκόφως ή η ευκαιρία της ηχοκαρδιογραφίας;

Παναγιώτα Γ. Κωστάκη,
Επιμελήτρια Καρδιολογικής,
Ευρωκλινική Αθηνών.
I have no conflict of interest
Cardiac asynchrony

Types: Electrical and Mechanical cardiac asynchrony

- Atrioventricular asynchrony
  (AV) delays lead to delayed systole and reduced diastolic filling.

- Interventricular asynchrony
  delays in contraction and diastole between RV /LV.

- Intraventricular asynchrony
  delays of the contraction and diastole sequence between different ventricular segments
Electrical disturbances induce mechanical asynchrony in LV at different levels, leading to:

- Ineffective LV contraction,
- Increased LV filling pressure /overload
- Decreased cardiac output
- LV remodeling
- Mitral regurgitation

CRT improves and reverses these abnormalities and results in LV reverse remodelling and reduction of MR. CRT is associated with performance improvement and reduction in mortality in HF patients.

(Leyva F, et al, JACC;64,10,2016)
## Major RCTs Regarding CRT

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients Enrolled</th>
<th>Inclusion Criteria</th>
<th>Comparison</th>
<th>Significant Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MUSTIC</strong></td>
<td>131</td>
<td>LVEF ≤35%</td>
<td>OMT vs OMT + CRT-D or RV pacing in persistent AF vs OMT + CRT-D</td>
<td>Improvement in 6-min walk test Peak VO₂ Quality of life NYHA class</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LVEDD &gt;60 mm</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>NYHA class III</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>6-min walk test &lt;450 m</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>QRS &gt;150 ms</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>or Paced QRS &gt;200 &amp; persistent AF</td>
<td></td>
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</tr>
<tr>
<td><strong>MIRACLE</strong></td>
<td>453</td>
<td>LVEF ≤35%</td>
<td>OMT vs OMT + CRT-D</td>
<td>Decrease in HF hospitalizations Improvement in 6-min walk test Ejection fraction Mitral regurgitation Quality of life NYHA class</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LVEDD &gt;55 mm</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>NYHA class III/IV</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>QRS ≥130 ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>COMPANION</strong></td>
<td>1,520</td>
<td>LVEF ≤35%</td>
<td>OMT vs OMT + CRT-P vs OMT + CRT-D</td>
<td>Decrease in combined endpoint of hospitalizations or death for CRT-P and CRT-D Decrease in mortality for CRT-D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NYHA class III/IV</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>QRS &gt;120 ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CARE-HF</strong></td>
<td>813</td>
<td>LVEF ≤35%</td>
<td>OMT vs OMT + CRT-P</td>
<td>Decrease in combined endpoint of hospitalizations or death for CRT-P Decrease in mortality for CRT-P</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LVEDD &gt;30</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NYHA class III/IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>QRS ≥150 ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>or QRS ≥120 ms and echo dyssynchrony</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MADIT-CRT</strong></td>
<td>1,820</td>
<td>LVEF ≤30</td>
<td>OMT + ICD vs OMT + CRT-D</td>
<td>Decrease in combined endpoint of hospitalization for HF or death</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NYHA class I/II</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>QRS ≥150 ms</td>
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<td></td>
<td></td>
<td>or LVEF &lt;30</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>NYHA class II/III</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>QRS ≥120 ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>or paced QRS ≥200 ms</td>
<td></td>
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</tr>
<tr>
<td><strong>RAFT</strong></td>
<td>1,798</td>
<td>LVEF ≤30</td>
<td>OMT + ICD vs OMT + CRT-D</td>
<td>Decrease in death or hospitalization from HF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NYHA class I/II</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>QRS ≥150 ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>or LVEF &lt;30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; CRT-D, cardiac resynchronization therapy with ICD; CRT-P, cardiac resynchronization therapy with pacing only; HF, heart failure; ICD, implantable cardioverter defibrillator; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; OMT, optimal medical therapy; RV, right ventricle; VO₂, oxygen consumption.
ECG's key role in patient selection for CRT

Meta-analysis of randomised controlled trials:

- CRT is recommended for patients with severe LV systolic dysfunction and QRS $\geq$130 msec.
- CRT is NOT associated with a reduction in mortality or HF hospitalisation in non-LBBB patients.
Permanent AF and CRT

Analysis from RAFT trial:
(N 229) HF, permanent AF, NYHA II-III, EF ≤30%, QRS ≥120 ms. Randomized ICD vs CRT-ICD.

No difference in primary outcome of death or HF hospitalization between CRT-ICD vs ICD.

➢ Patients with HF and permanent AF, otherwise CRT candidates gain minimal benefit from CRT-ICD compared with a standard ICD.

(Healey J. et al, Circ Heart Fail. 2012; 5:566-570)
Responders to CRT

Several CRT Response Definitions used in trials:

- **Clinical criteria** (NYHA class, QOL, 6 MWT, exercise duration, metabolic exercise tests)
- **LV Reverse remodeling** (Acute/ chronic (CO, LVdp/dt max), LVEF, LVESV/LVEDV, MR)
- **Outcome** (Hospitalizations, morbidity, all cause mortality)

Among patients who underwent CRT according to current guidelines 30% are considered non responders to therapy, defined as no hemodynamic response.

Female and nonischemic HF etiology patients had better CRT outcomes.

( Arshad A, et al. , for the MADIT – CRT Executive committee , JACC 2011;57:813-20)
Factors related to CRT response

- **Clinical** characteristics
- **Electrical** substrate
- Timing of electromechanical regional activation
- Complex interaction of **myocardial substrate**
- Presence of **ischemia and viability**
- Concomitant **valvular disease**
- Implant-related factors such as **LV lead position**
Improvement after CRT is related to the magnitude of reverse remodeling.

LVESV reduction of ≥10% signifies clinically relevant reverse remodeling, and is a strong predictor of lower long-term mortality and HF events.

(Yu et al, Circulation. 2005;112:1580-1586.)
Reduction in LVESV may be more important than the increase in LVEF.

(N=286, CRT in HF, NYHA III-IV, LVEF<35%, QRS>120ms)

Super- Responders:
- Non-ischemic HF
- Longer QRS
- Often LBBB
- Less MR
- Extensive dyssynchrony

1- and 2-year hospitalization-free survival rates 90% and 70% in the negative responder group vs 98% and 96% in the super-responder group (p<0.001).

(Ypenburg et al, JACC 2009;53:483-90)
Echocardiographic assessment of mechanical asynchrony predicts responders to CRT…

Fact or fiction?
### Predictors of Response to CRT (PROSPECT) Trial

426 patients: 53 sites observational study.

**Standard CRT indications, HF, NYHA III/IV, LV EF≤35%, QRS ≥130ms, stable medical regimen. 6 mo FU.**

<table>
<thead>
<tr>
<th>Echocardiographic Predictor</th>
<th>Description of Method</th>
<th>Echocardiography Method</th>
<th>Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPWMD&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Septal-posterior wall motion delay; M mode measured by parasternal short-axis view</td>
<td>M mode</td>
<td>≥130 ms</td>
</tr>
<tr>
<td>IVMD&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Interventricular mechanical delay defined as the difference between left and right ventricular pre-ejection intervals</td>
<td>Pulsed Doppler</td>
<td>≥40 ms</td>
</tr>
<tr>
<td>LVFT/RR&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Left ventricular filling time (LVFT) in relation to cardiac cycle length (RR) as measured by transmitral Doppler echo expressed as percentage</td>
<td>Pulsed Doppler</td>
<td>≤40%</td>
</tr>
<tr>
<td>LPEI&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Left ventricular pre-ejection interval defined as the time interval between the beginning of QRS and beginning of left ventricular ejection by Doppler</td>
<td>Pulsed Doppler</td>
<td>≥140 ms</td>
</tr>
<tr>
<td>LLWC&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Intraventricular dyssynchrony left lateral wall contraction defined as the presence of overlap between the end of lateral wall contraction (via M mode) and onset of LV filling (by Doppler echocardiography)</td>
<td>M mode and pulsed Doppler</td>
<td>Any overlap</td>
</tr>
<tr>
<td>Ts-(lateral-septal)&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Delay between time to peak systolic velocity in ejection phase at basal septal and basal lateral segments</td>
<td>TDI</td>
<td>≥60 ms</td>
</tr>
<tr>
<td>Ts-SD&lt;sup&gt;11,13&lt;/sup&gt;</td>
<td>SD of time from QRS to peak systolic velocity in ejection phase for 12 left ventricular segments (6 basal and 6 middle)</td>
<td>TDI</td>
<td>≥32 ms</td>
</tr>
<tr>
<td>PVD&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Peak velocity difference derived from subtracting the maximal from the minimal difference of time to peak velocity (excluding velocities occurring during isovolumic contraction time) for 6 segments at basal level</td>
<td>TDI</td>
<td>≥110 ms</td>
</tr>
<tr>
<td>DLC&lt;sup&gt;17,18&lt;/sup&gt;</td>
<td>Delayed longitudinal contraction measured in the 6 basal left ventricular segments with a systolic contraction component in early diastole by TDI and confirmed with strain rate imaging</td>
<td>TDI+SRI</td>
<td>≥2 basal segments</td>
</tr>
<tr>
<td>Ts-peak displacement</td>
<td>Maximum difference of time to peak systolic displacement for 4 segments</td>
<td>TDI</td>
<td>≥Median</td>
</tr>
<tr>
<td>Ts-peak (basal)</td>
<td>Maximum difference of time to peak systolic velocity for 6 segments at basal level</td>
<td>TDI</td>
<td>≥Median</td>
</tr>
<tr>
<td>Ts-onset (basal)</td>
<td>Maximum difference of time to onset of systolic velocity for 6 segments at basal level</td>
<td>TDI</td>
<td>≥Median</td>
</tr>
</tbody>
</table>

Chung E. et al, Circulation 2008
Echocardiographic predictors of CRT in PROSPECT

- SPWMD ≥ 130ms, Pitzalis index
- IVMD – interventricular mechanical delay ≥ 40ms
- (septal to lateral) time to peak velocity ≥ 60ms
- Yu index, SD OWD 12 segments ≥ 32 msec
Predictors of Response to CRT (PROSPECT) Trial

Response to CRT: 6 months follow-up

Clinical Composite Score
N = 426

- 69% Improved
- 15% Unchanged
- 16% Worsened

Change in LVESV
N = 286

- ≥15% Reduction: 56%
- Other: 35%
- ≥15% Increase: 9%

CCS: all-cause mortality, HF hospitalization, NYHA class, global outcome.

Relative change in LVESV (≥15% reduction)

30% Non-Responders, p=0.02

42% Non-Responders, p<0.005

Chung E. et al, Circulation 2008
Predictors of Response to CRT (PROSPECT) Trial

- Interobserver variability for echocardiographic parameters was HIGH for Ts-peak, Ts-SD, and SPWMD.

<table>
<thead>
<tr>
<th>Measure</th>
<th>CV, %</th>
<th>CV, %</th>
<th>Coefficient*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVESV</td>
<td>3.8</td>
<td>14.5</td>
<td>NA</td>
</tr>
<tr>
<td>LPEI</td>
<td>3.7</td>
<td>6.5</td>
<td>0.67</td>
</tr>
<tr>
<td>SPWMD</td>
<td>24.3</td>
<td>72.1</td>
<td>0.35</td>
</tr>
<tr>
<td>Ts-SD</td>
<td>11.4</td>
<td>33.7</td>
<td>0.15</td>
</tr>
<tr>
<td>Ts-peak (basal)</td>
<td>15.8</td>
<td>31.9</td>
<td>0.25</td>
</tr>
</tbody>
</table>

LPEI indicates left ventricular preejection interval.

*Based on binary predictor variable that indicates if echocardiographic measure is above or below the cutoff.
## Predictors of Response to CRT (PROSPECT) Trial

### Table 5. Sensitivity, Specificity, and Area Under the Curve for Primary End Points

<table>
<thead>
<tr>
<th>Echocardiography Type</th>
<th>Dyssynchrony Measure</th>
<th>Evaluable Echocardiograms, (yield) %</th>
<th>CCS</th>
<th>LVESV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sensitivity, %</td>
<td>Specificity, %</td>
</tr>
<tr>
<td>M mode</td>
<td>SPWMD</td>
<td>71.7</td>
<td>55.4 (48.3–62.3)</td>
<td>50.0 (39.1–60.9)</td>
</tr>
<tr>
<td>Pulsed Doppler</td>
<td>IVMD</td>
<td>92.4</td>
<td>55.2 (48.9–61.4)</td>
<td>66.4 (46.9–65.6)</td>
</tr>
<tr>
<td></td>
<td>LVFT/RR</td>
<td>85.3</td>
<td>36.3 (30.2–42.7)</td>
<td>76.6 (67.5–84.3)</td>
</tr>
<tr>
<td></td>
<td>LPEI</td>
<td>94.6</td>
<td>66.3 (60.2–72.0)</td>
<td>47.1 (38.0–56.4)</td>
</tr>
<tr>
<td>M mode +</td>
<td>LLWC</td>
<td>60.7</td>
<td><strong>6.3 (3.2–11.0)</strong></td>
<td><strong>91.7 (82.7–96.9)</strong></td>
</tr>
<tr>
<td>TDI, published</td>
<td>Ts (Lat-Sep)</td>
<td>66.8</td>
<td>42.4 (34.4–50.7)</td>
<td>56.9 (44.7–68.6)</td>
</tr>
<tr>
<td></td>
<td>Ts-SD</td>
<td>50.0</td>
<td>74.1 (65.2–81.8)</td>
<td>35.3 (22.4–49.9)</td>
</tr>
<tr>
<td></td>
<td>PVD</td>
<td>81.4</td>
<td>67.6 (60.3–74.3)</td>
<td>37.8 (27.8–48.6)</td>
</tr>
<tr>
<td>TDI + SRI</td>
<td>DLC</td>
<td>81.1</td>
<td>41.7 (34.4–49.2)</td>
<td>60.4 (49.6–70.5)</td>
</tr>
<tr>
<td>TDI, median value used as cutoff</td>
<td>Ts-peak displacement</td>
<td>37.4</td>
<td>54.8 (43.5–65.7)</td>
<td>56.1 (39.7–71.5)</td>
</tr>
<tr>
<td></td>
<td>Ts-peak basal</td>
<td>82.0</td>
<td>51.9 (44.4–59.3)</td>
<td>53.8 (43.1–64.4)</td>
</tr>
<tr>
<td></td>
<td>Ts-onset basal</td>
<td>82.0</td>
<td>54.1 (46.6–61.5)</td>
<td>60.4 (49.6–70.5)</td>
</tr>
</tbody>
</table>

Chung E. et al, Circulation 2008
Given the modest sensitivity and specificity in this multicenter setting despite training and central analysis, NO single echocardiographic measure of dyssynchrony may be recommended to improve patient selection for CRT beyond current guidelines.
Can mechanic asynchrony exist independently of the QRS duration?

- Among patients with HF, EF≤45%, QRS <120 ms, 56% presented with major intra-LV and 12% of inter-LV asynchrony.
- Intra-LV asynchrony was present in 84% of LBBB and 83% of RBBB patients.

*Intra-LV asynchrony was independent predictor of severe cardiac events. (independent of the LVEF and QRS width).*

Bader H, et al, Intra-Left Ventricular Electromechanical Asynchrony. A New Independent Predictor of Severe Cardiac Events in Heart Failure Patients JACC, 2004
**Echo**cardiography Guided **Cardiac** **Resynchronization** **Therapy** in Patients with Symptomatic Heart Failure and Narrow QRS Complex

- Randomized Controlled Trial, 115 centers
- N=809 patients, HF NYHA III-IV, EF≤35%, **QRS < 130ms**.
- Randomized (1:1), CRT-ON vs CRT-OFF.

**Primary end point** : combined death-any cause or first hospitalization for worsening HF.

**Selected by Echo dyssynchrony – Intraventricular delay**

- **Tissue Doppler** – 2 site opposing wall delay ≥ 80ms
- **Speckle Tracking Radial Strain** - Anteroseptal- posterior wall delay ≥ 130ms

Ruschitzka F, et al, NEJM 2013
Selecting patients for CRT in EchoCRT

➢ **Tissue Doppler** – 2 site OW delay ≥ 80ms

➢ **Speckle Tracking Radial Strain** - Anteroseptal-posterior wall delay ≥ 130ms

Ruschitzka F, et al, NEJM 2013
Echo\textit{cardiography Guided Cardiac Resynchronization Therapy} in Patients with Symptomatic Heart Failure and Narrow QRS Complex

On multivariable analysis, a higher risk for the primary endpoint was observed in patients with a QRS duration of 120–130 ms randomized to CRT-ON vs. CRT-OFF (hazard ratio 2.18, 95% CI)

(Steffel J, et al, European Heart Journal 2015)
Inter-observer variability in EchoCRT

➢ Tissue Doppler:
Opposing wall delay (4Ch) 96.2% (Kappa coefficient 0.92).
Opposing wall delay apical long axis 92% (Kappa coefficient 0.84).

➢ Speckle Tracking Radial Strain:
Anteroseptal- posterior wall delay 90.5% (Kappa coefficient 0.79).
What do guidelines say?

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
ESC guidelines on HF 2016
CRT therapy

QRS ≥150ms (IA)
or ≥130-149ms (IB)
SR
LBBB
AV block
LVEF ≤35%

QRS ≥130ms
SR/AF
Non-LBBB
Upgrade
LVEF ≤35%

QRS <130ms

YES
CONSIDER
NO
Question 1:

Can echocardiography contribute for a more appropriate patient selection for CRT and:

a) Identify RESPONDERS?

b) Identify NON-RESPONDERS?
Strain delay index (SDI) and the WAISTED WORK

In dyssynchronous ventricles delayed segments do NOT contribute fully to end-systolic function.

- Wasted energy per segment: Difference of peak ($\varepsilon_{\text{peak}}$) strain and end-systolic ($\varepsilon_{\text{ES}}$) strain.
- Wasted energy is greater in the segment with PRESERVED contractility.

$$\text{SDI}_{(n16\text{seg})} = \sum (\varepsilon_{\text{peak}}) - (\varepsilon_{\text{ES}})$$

SDI >25% identified responders to CRT
(positive predictive value 80%, negative predictive value 84%, intra-observer variability 6%)

(Longitudinal SDI by speckle tracking)

Torsional mechanics in LV dyssynchrony
assessed by 3D speckle tracking

- LV dyssynchrony may negatively affect LV torsional mechanics.
- LV torsion may improve after CRT.

Limitation:
Image acquisition:
Low Vol rate 18-25/s.

Septal Flash (SF) and Apical Rocking (ApRock) and cardiac asynchrony

SF, a “New” Pitzalis index?
Visually assessed echocardiographic parameters to assess response and survival after CRT.

Relationship of visually assessed apical rocking and septal flash to response and long-term survival following cardiac resynchronization therapy (PREDICT-CRT)

Ivan Stankovic1,2,†, Christian Prinz3,4,‡, Agnieszka Ciarka1, Ana Maria Daraban1,3,†, Martin Kotrc4,10, Marit Aarones5, Mariola Szulik6, Stefan Winter7, Ann Belmans8, Aleksandar N. Neskovic7, Tomasz Kukulski6, Svend Aakhus5, Rik Willems1, Wolfgang Fehske7, Martin Penicka4, Lothar Faber3, and Jens-Uwe Yoigt1†

1Department of Cardiovascular Diseases, University Hospital Gasthuisberg, Catholic University Leuven, Herestraat 49, Leuven 3000, Belgium; 2Department of Cardiology, Clinical Hospital Centre Zemun, Faculty of Medicine, University of Belgrade, Belgrade, Serbia; 3Department of Cardiology, Heart and Diabetes Centre of North-Rhine Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany; 4Cardiovascular Center Aalst, OLV Clinic, Aalst, Belgium; 5Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway; 6Department of Cardiology, Congenital Heart Diseases and Electrophysiology, Silesian Center for Heart Diseases, Silesian University of Medicine, Silesia, Poland; 7Klinik für Innere Medizin und Kardiologie, St. Vinzenz Hospital, Cologne, Germany; and 8Leuven Biostatistics and Statistical Bioinformatics Centre, Catholic University Leuven, Leuven, Belgium

Received 10 July 2015; accepted after revision 4 October 2015; online publish-ahead-of-print 20 November 2015
In asynchronously contracting ventricles

**ApRock and SF:**

- corrected by CRT were associated with **reverse remodelling** (reduction LVESV ≥ 15%).
  (Sens. 84 and 79%, spec. 79 and 74%, accuracy 82 and 77%, respectively).
- were independently associated with **lower all-cause mortality after CRT** and had an
  incremental value over clinical variables and QRS width for identifying CRT responders.

(Stankovic I et al, Eur. Heart Journal, Cardiovascular Imaging (2016))
Question 1:

Can echocardiography contribute for a more appropriate patient selection for CRT and:

a) Identify RESPONDERS?
b) Identify NON-RESPONDERS?
NON-RESPONSE to CRT may be affected by:

- Dyssynchrony patterns (electrical-mechanical).
- "Non reversible" myocardium.
- Lack of myocardial viability.
- Need for post-CRT implantation optimization.
Impact of LV size on CRT response

N=668, NDCM/SDCM, HF NYHAII-III, EF≤40%

The degree of baseline LV dilatation before CRT is an independent predictor of change in LVEF and survival.
Global Longitudinal strain and CRT outcome

(N=205), candidates to CRT, HF NYHA II - IV on OMT, QRS ≥120 ms, LVEF ≤35%.
Risk of HF or death.

GLS >−9%, and also GCS >−9% were associated with increased risk of unfavourable events.

Variability: GLS intraobserver agreement was 0.97, GLS interobserver agreement 0.92; intraclass correlation coefficients for GCS intraobserver agreement was 0.96 and for GCS interobserver agreement 0.92.

Echocardiography to guide lead placement in CRT

- The **TARGET Study** (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy), randomized controlled study.
- (N=220) (SR, NYHA III-IV EF≤35%, QRS ≥120 ms)
- Randomized 1:1: Targeted vs standard unguided LV Lead Placement.
- **AIM** stimulation of the latest activated segment, **AVOID** sites with low RS peak amplitude < 10% (scar).

---

**Speckle-tracking 2-D radial strain**
Mid short-axis, LV in previous MI.

**Combined Endpoint of Death and Heart Failure Related Hospitalization**
According to the Presence of Scar at the LV Pacing Site

LV reverse remodelling ≥15% LVESV decrease, 6 Mo FU, (70% vs. 55%)
Inotropic contractile reserve (ICR) and viability of the segment targeted for pacing (inferolateral) assessed with LD-DSE adds incremental value to dyssynchrony indices.

- Presence of viability of the inferolateral wall: sensitivity for the prediction of response 98.1%.
- Absence of either ICR or viability of the inferolateral wall was associated with a negative predictive value of 91.9%.

### Predictive ability for late response and 6-month clinical response

<table>
<thead>
<tr>
<th>Response Parameter</th>
<th>Late response AUC</th>
<th>Late response p value</th>
<th>Clinical response AUC</th>
<th>Clinical response p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS</td>
<td>0.514</td>
<td>0.546</td>
<td>0.433</td>
<td>0.527</td>
</tr>
<tr>
<td>LBBB</td>
<td>0.603</td>
<td>0.029</td>
<td>0.619</td>
<td>0.019</td>
</tr>
<tr>
<td>SPWMD</td>
<td>0.761</td>
<td>&lt;0.001</td>
<td>0.645</td>
<td>0.004</td>
</tr>
<tr>
<td>SLD</td>
<td>0.482</td>
<td>0.877</td>
<td>0.466</td>
<td>0.660</td>
</tr>
<tr>
<td>IVMD</td>
<td>0.634</td>
<td>0.093</td>
<td>0.612</td>
<td>0.295</td>
</tr>
<tr>
<td>TmaxCS</td>
<td>0.830</td>
<td>&lt;0.001</td>
<td>0.754</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ApR</td>
<td>0.720</td>
<td>&lt;0.001</td>
<td>0.715</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF</td>
<td>0.652</td>
<td>0.080</td>
<td>0.614</td>
<td>0.720</td>
</tr>
<tr>
<td>ApR/SF</td>
<td>0.754</td>
<td>&lt;0.001</td>
<td>0.726</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICR</td>
<td>0.791</td>
<td>&lt;0.001</td>
<td>0.788</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Viability</td>
<td>0.617</td>
<td>&lt;0.001</td>
<td>0.649</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICR+viability</td>
<td>0.802</td>
<td>&lt;0.001</td>
<td>0.810</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LBBB left bundle branch block, SPWMD septal to posterior wall motion delay, SLD septal to lateral delay, IVMD interventricular mechanical delay, TmaxCS time to maximum circumferential strain, ApR apical rocking, SF septal flash, ICR inotropic contractile reserve.

(Poulidakis E, et al, Int J of Cardiovascular Imaging, Jan 2019)
Question 2:

Is there a place for echocardiography in post-CRT optimization?
Echocardiography for post-CRT optimization of AV and VV delay

AIM for:
✓ Diastolic filling time: >40% R-R, separation E/A
✓ LV Contractility index:
✓ dP/dt, on MR
✓ Increase VTI at LVOT
✓ Reduce intraventricular delay (<55-60ms) QRS-S (4 basal segments)
✓ Interventricular delay (<40ms), QRS-S basal RV free wall RV-basal IVS.
✓ Presystolic aortic ejection time (IVCT <140ms)
✓ Decrease MR (shorter AV delay)
✓ Measure RVSP
Echocardiography for CRT optimization of AV and VV delay

Current evidence does NOT support AV/VV routine optimization

- **No clear difference** was found among studies between automatic electrocardiographic algorithms and echocardiographic post-CRT optimization (eg. SMART-AV study).

- In NON-responders to CRT, optimization may be recommended.

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*2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.*
In everyday practice echocardiography remains the cornerstone in patient selection for CRT according to LVEF calculation.

Echocardiography STILL maintains its central role in the follow-up of patients post CRT implantation. Looking for reverse remodeling, measuring LV dimensions and volumes, LVEF, assessing residual MR and other valvular disease, estimating pressures.

After CRT implantation, device algorithms are used for optimization of cardiac resynchronization - Often setting “Blindly” V-V delay either synchronous or at 40ms (LV preceding RV activation).
Role of echocardiography in cardiac dyssynchrony

- Echocardiography can identify **NON-RESPONDERS** to CRT.

- Echocardiographic **post-CRT optimization** is under investigation.

- Echocardiography is rather weak to predict **RESPONSE** to CRT.
Comparison of Eight Echocardiographic Methods for Determining the Prevalence of Mechanical Dyssynchrony and Site of Latest Mechanical Contraction in Patients Scheduled for Cardiac Resynchronization Therapy

Francesco F. Faletra, MD; Cristina Conca, MD; Catherine Klersy, MD; Julija Klimusina, MD; François Regoli, MD, PhD; Antonio Mantovani, MD; Elena Pasotti, MD; Giovanni B. Pedrazzini, MD; Stefano De Castro, MD; Tiziano Moccetti, MD; and Angelo Auricchio, MD, PhD.

### Pairwise agreement between methods in detecting mechanical dyssynchrony (kappa statistic)

<table>
<thead>
<tr>
<th>Kappa</th>
<th>TDI</th>
<th>3D Echocardiography</th>
<th>Longitudinal Strain</th>
<th>Radial ST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S-L Delay</td>
<td>TSI</td>
<td>Te-SD</td>
<td>SDI</td>
</tr>
<tr>
<td>Ts-SD by TDI</td>
<td>0.51</td>
<td>0.15</td>
<td>0.07</td>
<td>0.00</td>
</tr>
<tr>
<td>S-L delay by TDI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSI by TDI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Te-SD by TDI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDI by 3D echocardiogram</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDt18s by longitudinal ST</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD6s by radial ST</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Agreement is poor when the kappa statistic 0.61 to 0.8, and almost perfect for values >1.

**Figure 3.** (A) Single most delayed region of mechanical contraction in the study population according to 4 different echocardiographic methods. (B) Agreement among different methods in detecting the same most delayed region of LV contraction. Abbreviations as in Figure 1.