Imaging in dilated cardiomyopathy: factors associated with a poor outcome

Johan De Sutter, MD, PhD, FESC
AZ Maria Middelares Gent
and University Gent - Belgium
Dilated cardiomyopathy

• Cardiomyopathy with many causes in which the extent of myocardial dysfunction cannot be explained exclusively by abnormal loading or ischaemic damage

• Epidemiology
  – Men>women
  – Prevalence : 1/2500
  – Incidence : 7/100,000/year (could be underdiagnosed)
  – Familial : 20-49% of all causes

Jefferies and Towbin, Lancet 2010;375:752-62
Panel: Mechanisms responsible for dilated cardiomyopathy

- Disturbed cytoskeletal-sarcomeric link:
  - Genetic mutation (sarcolemma-sarcomere genes)
  - Viral infection (coxsackievirus myocarditis)
  - Non-viral infection (Chagas disease)
  - Toxicity (adriamycin and alcohol)
- Apoptosis
- Autoantibodies and autoimmune disease
- Metabolic disturbance storage disease
- Mitochondrial dysfunction
- Ion-channel disruption
- Chronic incessant tachyarrhythmias
- Peripartum
- Infiltrative disease
- Endomyocardial disease
- Endocrinopathies
- Nutritional deficiencies
- Electrolyte disturbance
Prognosis in dilated cardiomyopathy

- Familial dilated cardiomyopathy
- Acute/recent onset dilated cardiomyopathy
- Imaging in chronic dilated cardiomyopathy
Familial dilated cardiomyopathy

• Clinical screening (ECG + echo) of first degree relatives will reveal familial dilated CMP in at least 20-35% of those family members

• A genetic causes is detected in only 30-35% of familial dilated CMP
  – 2011: point mutations in 33 genes (31 autosomal and 2 X-linked) representing disease gene ontology

Hershberger and Siegfried, JACC 2011;57:1641-1649
# Dilated cardiomyopathy gene ontology

## Table 2: Dilated Cardiomyopathy Gene Ontology

<table>
<thead>
<tr>
<th>Sarcomere</th>
<th>Z-Disc</th>
<th>Cytoskeleton</th>
<th>Mitochondrial</th>
<th>RNA Binding</th>
<th>Ion Channel</th>
<th>Gamma Secretase Activity</th>
<th>Sarcoplasmic Reticulum</th>
<th>Transcription Factor</th>
<th>Nuclear Envelope</th>
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</thead>
<tbody>
<tr>
<td>ACTC</td>
<td>TCAP</td>
<td>DMD</td>
<td>TAZ/G4.5</td>
<td>RBM20</td>
<td>ABCC</td>
<td>PSEN1</td>
<td>PLN</td>
<td>EYA4</td>
<td>LMNA</td>
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<tr>
<td>MYH7</td>
<td>CSRP3</td>
<td>DES</td>
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<td>SCN5A</td>
<td>PSEN2</td>
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<td>TMPO</td>
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<td>MYH6</td>
<td>ACTN2</td>
<td>LDB3</td>
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<tr>
<td>MYBPC3</td>
<td>MYPN</td>
<td>SGCD</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNN1</td>
<td>ANKRD1</td>
<td>PDLIM3</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>TNNC1</td>
<td>VCL</td>
<td></td>
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<tr>
<td>TNNI3</td>
<td>RYAB</td>
<td>ILK</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TPM1</td>
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<td></td>
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<td></td>
<td></td>
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<td>TTN</td>
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</tbody>
</table>

Hershberger and Siegfried, JACC 2011;57:1641-1649
Familial dilated cardiomyopathy

- Clinical screening (ECG + echo) of first degree relatives will reveal familial dilated CMP in at least 20-35% of those family members

- A genetic causes is detected in only 30-35% of familial dilated CMP
  - 2011: point mutations in 33 genes (31 autosomal and 2 X-linked) representing disease gene ontology

- The genotype/phenotype relationship with outcome is only documented for some mutations in small sample size studies

Hershberger and Siegfried, JACC 2011;57:1641-1649
Dilated cardiomyopathy
Troponin T2 gene
novel mutation exon 11
(Int J Cardiol 2010)
Prognosis in dilated cardiomyopathy

• Familial dilated cardiomyopathy

• Acute/recent onset dilated cardiomyopathy

• Imaging in chronic dilated cardiomyopathy
Clinical and Demographic Predictors of Outcomes in Recent Onset Dilated Cardiomyopathy

Results of the IMAC (Intervention in Myocarditis and Acute Cardiomyopathy)-2 Study

Dennis M. McNamara, MD, MSc,* Randall C. Starling, MD,† Leslie T. Cooper, MD,‡ John P. Boehmer, MD,§ Paul J. Mather, MD,|| Karen M. Janosko, MSN, MBA,* John Gorcsan III, MD,* Kevin E. Kip, PhD,¶ G. William Dec, MD,# for the IMAC Investigators

Pittsburgh, Hershey, and Philadelphia, Pennsylvania; Cleveland, Ohio; Rochester, Minnesota; Tampa, Florida; and Boston, Massachusetts
IMAC-2 study

• 373 patients with recent onset dilated CMP
  – < 6 months ideopathic dilated CMP or myocarditis
  – Age : 45±14 years, LVEF 24±8 %
  – Therapy
    • ACE/ARB : 92% ; Beta blockers : 94%
    • ICD : 20%

• Follow-up
  – Cardiovascular events – heart transplantation
  – Changes in LVEF

McNamara, JACC 2011
Transplant-free survival according to baseline NYHA class

McNamara, JACC 2011
Survival free from HF hospitalization according to race

McNamara, JACC 2011
Improvement in LVEF in acute onset dilated CMP under medical treatment

> 10% increase in LVEF

%

<table>
<thead>
<tr>
<th></th>
<th>Steimle-1994</th>
<th>IMAC I - 2001</th>
<th>IMAC II - 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>33</td>
<td>50</td>
<td>70</td>
</tr>
</tbody>
</table>

McNamara, JACC 2011
### Table 2

**Predictors of LVEF and Change in LVEF at 6 Months (n = 292)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>t Value</th>
<th>Standardized Coefficient</th>
<th>Semipartial $^2$ Correlation</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDD</td>
<td>-6.98</td>
<td>-0.41</td>
<td>0.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>3.30</td>
<td>0.18</td>
<td>0.03</td>
<td>0.001</td>
</tr>
<tr>
<td>Black race</td>
<td>-2.39</td>
<td>-0.12</td>
<td>0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>-2.10</td>
<td>-0.11</td>
<td>0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Age</td>
<td>-1.25</td>
<td>-0.07</td>
<td>0.004</td>
<td>0.21</td>
</tr>
<tr>
<td>Baseline LVEF</td>
<td>1.00</td>
<td>0.06</td>
<td>0.003</td>
<td>0.32</td>
</tr>
<tr>
<td>Female</td>
<td>0.32</td>
<td>0.02</td>
<td>0.0003</td>
<td>0.75</td>
</tr>
<tr>
<td>Adjusted $R^2$ = 0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Change in LVEF            |         |                          |                              |         |
| Baseline LVEF             | -10.91  | -0.59                    | 0.28                         | <0.0001 |
| LVEDD                     | -6.98   | -0.39                    | 0.11                         | <0.0001 |
| Systolic BP               | 3.30    | 0.17                     | 0.03                         | 0.001   |
| Black race                | -2.39   | -0.12                    | 0.01                         | 0.02    |
| NYHA functional class     | -2.10   | -0.11                    | 0.01                         | 0.04    |
| Age                       | -1.25   | -0.06                    | 0.004                        | 0.21    |
| Female                    | 0.32    | 0.02                     | 0.0002                       | 0.75    |
| Adjusted $R^2$ = 0.32     |         |                          |                              |         |

*LVEDD = left ventricular end-diastolic diameter; other abbreviations as in Table 1.*
Myocardial recovery at 6 months by baseline LVEDD

McNamara, JACC 2011
Prognosis in dilated cardiomyopathy

- Familial dilated cardiomyopathy
- Acute/recent onset dilated cardiomyopathy
- Imaging in chronic dilated cardiomyopathy
Assessment of prognosis in heart failure patients

• The likelihood of survival can be determined reliably only in populations and not in individuals

• Some attempt at prognostication in HF
  – may provide better information for patients and their families
  – helps to identify patients in whom cardiac transplantation or mechanical device therapy should be considered

ACC/AHA heart failure guidelines update 2009
Prognostic risk factors in heart failure

• Clinical
  – Age – NYHA class - Diabetes
  – Chronic hypotension, resting tachycardia
  – Intolerance to conventional therapy
  – Refractory volume overload
  – Renal insufficiency
  – Hyponatremia, low hematocrit

• Functional/ECG markers
  – LVEF
  – Peak exercise oxygen uptake
  – LBBB – QRS duration

• Biomarkers
  – Elevated BNP – NT-proBNP
  – Elevated troponine

• ...

ACC/AHA heart failure guidelines update 2009
# Risk stratification in chronic heart failure

<table>
<thead>
<tr>
<th>STUDY</th>
<th>N</th>
<th>CAD</th>
<th>AGE</th>
<th>LVEF</th>
<th>Independent predictors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seattle HF Circ 2006</td>
<td>11067 (D+V)</td>
<td>~62%</td>
<td>~64±12</td>
<td>~27±9 % &gt;45% : ~5%</td>
<td>N=15 (+ 9 modulators)</td>
</tr>
<tr>
<td>CHARM EHJ 2006</td>
<td>7599</td>
<td>70%</td>
<td>68±11</td>
<td>38±15 % &gt;45% : 37%</td>
<td>N=21</td>
</tr>
<tr>
<td>MUSIC EHJ 2009</td>
<td>992</td>
<td>46%</td>
<td>65±12</td>
<td>37±14 % &gt;45% : 25%</td>
<td>N=10 (+ NT-proBNP)</td>
</tr>
<tr>
<td>SENIORS EJHF 2011</td>
<td>2128 (D+V)</td>
<td>68%</td>
<td>76±5</td>
<td>36±12% &gt;40% : 33%</td>
<td>N=10</td>
</tr>
</tbody>
</table>

D+V = derivation + validation set
## Risk stratification in chronic heart failure

<table>
<thead>
<tr>
<th>STUDY</th>
<th>N</th>
<th>CAD</th>
<th>AGE</th>
<th>LVEF</th>
<th>CAD as predictor?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seattle HF 2006</td>
<td>11067 (D+V)</td>
<td>~62%</td>
<td>~64±12</td>
<td>~27±9%  &gt;45% : ~5%</td>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>CHARMM 2006</td>
<td>7599</td>
<td>70%</td>
<td>68±11</td>
<td>38±15%  &gt;45% : 37%</td>
<td>Previous MI</td>
</tr>
<tr>
<td>MUSIC 2009</td>
<td>992</td>
<td>46%</td>
<td>65±12</td>
<td>37±14%  &gt;45% : 25%</td>
<td>Previous atherosclerotic vascular event</td>
</tr>
<tr>
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<th>ECHO</th>
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<td>7599</td>
<td>70%</td>
<td>68±11</td>
<td>38±15 % &gt;45% : 37%</td>
<td>LVEF &lt; 45% Mitral regurgitation</td>
</tr>
<tr>
<td>MUSIC EHJ 2009</td>
<td>992</td>
<td>46%</td>
<td>65±12</td>
<td>37±14 % &gt;45% : 25%</td>
<td>LVEF &lt; 35% LA &gt; 26 mm/m²</td>
</tr>
<tr>
<td>SENIORS EJHF 2011</td>
<td>2128 (D+V)</td>
<td>68%</td>
<td>76±5</td>
<td>36±12% &gt;40% : 33%</td>
<td>LA size (cm)</td>
</tr>
</tbody>
</table>

D+V = derivation + validation set
Imaging and outcome in dilated cardiomyopathy

- LV function and volumes
  - Strain
  - Dyssynchrony
  - Late enhancement

- Filling pressures

- Mitral regurgitation

- RV function and volumes
LVEF and all-cause mortality in HF

MAGGIC meta-analysis Eur Heart J 2011
(50991 patients with heart failure)
Determinants of outcome in HF

**Table 2**  Cox’s proportional adjusted hazards ratios for all-cause death and cardiovascular death

<table>
<thead>
<tr>
<th>Variable</th>
<th>Death from any cause</th>
<th>Cardiovascular death</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio (95% CI)</td>
<td>Hazard ratio (95% CI)</td>
</tr>
<tr>
<td>HF-PEF</td>
<td>0.68 (0.64, 0.71)</td>
<td>0.55 (0.49, 0.61)</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.23 (1.18, 1.28)</td>
<td>1.23 (1.14, 1.33)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.04 (1.04, 1.04)</td>
<td>1.03 (1.03, 1.04)</td>
</tr>
<tr>
<td>Ischaemic aetiology</td>
<td>1.07 (1.02, 1.12)</td>
<td>1.11 (1.03, 1.19)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.93 (0.89, 0.97)</td>
<td>0.94 (0.88, 1.00)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.41 (1.35, 1.47)</td>
<td>1.51 (1.41, 1.62)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.10 (1.05, 1.16)</td>
<td>1.28 (1.16, 1.41)</td>
</tr>
</tbody>
</table>
Relationship between drug/device effects of LVEF/volumes and mortality in patients with HF and LV dysfunction

Kramer et al, JACC 2010
Relationship between drug/device effects of LVEF/volumes and mortality in patients with HF and LV dysfunction

Kramer et al, JACC 2010
Prevalence and Prognostic Significance of Left Ventricular Reverse Remodeling in Dilated Cardiomyopathy Receiving Tailored Medical Treatment

Marco Merlo, MD,* Stylianos A. Pyxaras, MD,* Bruno Pinamonti, MD,* Giulia Barbati, PhD,† Andrea Di Lenarda, MD,‡ Gianfranco Sinagra, MD*  

Trieste and Padua, Italy
LV reverse remodeling in dilated CMP

• 242 patients with dilated CMP (duration 13±25 months)
  – Age: 43±13 years, LVEF 31±10%
  – Therapy
    • ACE/ARB: 91%
    • Beta blockers: 85%

• Follow-up
  – Cardiovascular events
  – LV reverse remodeling after 2 years
    • 1) increase in LVEF of at least 10 U or LVEF > 50% and
    • 2) Indexed LVEDD increase of at least 10% or < 33 mm/m²

Merlo et al, JACC 2011
LV reverse remodeling in dilated CMP

• LV reverse remodeling at 24 months = 37%

• Independent predictors of LV reverse remodeling
  – Higher systolic blood pressure
  – Absence of LBBB

Merlo et al, JACC 2011
LV reverse remodeling in dilated CMP

Figure 2: Long-Term Prognostic Impact of LVRR in Idiopathic Dilated Cardiomyopathy Patients

Merlo et al, JACC 2011
Impact of Longitudinal Myocardial Deformation on the Prognosis of Chronic Heart Failure Patients

Julien Nahum, MD; Alexandre Bensaid, MD; Caroline Dussault, PhD; Laurent Macron, MD; Darrort Clémence, MD; Belaid Bouhemad, MD, PhD; Jean-Luc Monin, MD, PhD; Jean-Luc Dubois Rande, MD, PhD; Pascal Gueret, MD; Pascal Lim, MD

Background—Longitudinal myocardial deformation indexes appear superior to left ventricular ejection fraction (LVEF) in assessing myocardial contractility. However, few studies have addressed the prognostic value of longitudinal motion markers (velocity, strain, and strain rate) in predicting outcome in heart failure patients.

Methods and Results—The study included 125 consecutive symptomatic heart failure patients (63±16 years, 77% male, LVEF=31±10%). All patients underwent a complete echocardiographic and clinical examination, and brain natriuretic peptide level was assessed in 93 patients. Longitudinal myocardial velocity by tissue Doppler imaging, global-\(e\), and strain rate by speckle tracking were computed from apical views (4-, 3-, and 2-chambers views) and compared with the occurrence of major adverse cardiac events. On the whole, peak longitudinal velocity, global-\(e\), and strain rate averaged 5±2 cm/s (range, 1 to 9), \(-8±3\%\) (range, \(-3\) to \(-18\)), and \(-0.33±0.16\) s\(^{-1}\) (range, \(-0.83\) to \(-0.05\)), respectively. During the follow-up period (266±177 days), major adverse cardiac events occurred in 47 (38%) patients (15 deaths, 29 recurrent heart failure, and 4 heart transplantations). By univariable analysis using Cox model global-\(e\), strain rate, and LVEF were associated with the occurrence of major adverse cardiac events, whereas only global-\(e\) remained independently predictive of outcome by multivariate analysis.

Conclusions—In the heart failure population, longitudinal global strain by speckle tracking is superior to LVEF and other longitudinal markers in identifying patients with poor outcome. (Circ Cardiovasc Imaging. 2010;3:249-256.)

Key Words: heart failure ■ prognosis ■ longitudinal function ■ global strain
Longitudinal myocardial deformation in chronic heart failure

Nahum et al, Circ Cardiovasc Imaging 2010
Results of the Predictors of Response to CRT (PROSPECT) Trial

Eugene S. Chung, MD; Angel R. Leon, MD; Luigi Tavazzi, MD; Jing-Ping Sun, MD; Petros Nihoyannopoulos, MD; John Merlino, MD; William T. Abraham, MD; Stefano Ghio, MD; Christophe Leclercq, MD; Jeroen J. Bax, MD; Cheuk-Man Yu, MD, FRCP; John Gorcsan III, MD; Martin St John Sutton, FRCP; Johan De Sutter, MD, PhD; Jaime Murillo, MD

**Background**—Data from single-center studies suggest that echocardiographic parameters of mechanical dyssynchrony may improve patient selection for cardiac resynchronization therapy (CRT). In a prospective, multicenter setting, the Predictors of Response to CRT (PROSPECT) study tested the performance of these parameters to predict CRT response.

**Methods and Results**—Fifty-three centers in Europe, Hong Kong, and the United States enrolled 498 patients with standard CRT indications (New York Heart Association class III or IV heart failure, left ventricular ejection fraction ≤35%, QRS ≥130 ms, stable medical regimen). Twelve echocardiographic parameters of dyssynchrony, based on both conventional and tissue Doppler–based methods, were evaluated after site training in acquisition methods and blinded core laboratory analysis. Indicators of positive CRT response were improved clinical composite score and ≥15% reduction in left ventricular end-systolic volume at 6 months. Clinical composite score was improved in 69% of 426 patients, whereas left ventricular end-systolic volume decreased ≥15% in 56% of 286 patients with paired data. The ability of the 12 echocardiographic parameters to predict clinical composite score response varied widely, with sensitivity ranging from 6% to 74% and specificity ranging from 35% to 91%; for predicting left ventricular end-systolic volume response, sensitivity ranged from 9% to 77% and specificity from 31% to 93%. For all the parameters, the area under the receiver-operating characteristics curve for positive clinical or volume response to CRT was ≤0.62. There was large variability in the analysis of the dyssynchrony parameters.

**Conclusion**—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. Efforts aimed at reducing variability arising from technical and interpretative factors may improve the predictive power of these echocardiographic parameters in a broad clinical setting. *(Circulation. 2008;117: 2608-2616.)*

**Key Words:** dyssynchrony ■ echocardiography ■ echocardiography, Doppler ■ heart failure ■ pacemakers
Factors associated with higher response to CRT in advanced heart failure

- Non-ischemic cardiomyopathy
- Female sex
- QRS width > 150 ms
- LBBB on the baseline ECG
- Lower scar burden – preserved posterolateral function
- Posterolateral lead position
- Adequate AV-VV optimization

Bozkurt et al, JACC 2011
Predictors of Response to Cardiac Resynchronization Therapy in the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT)

Ilan Goldenberg, MD; Arthur J. Moss, MD; W. Jackson Hall, PhD; Elyse Foster, MD; Jeffrey J. Goldberger, MD; Peter Santucci, MD; Timothy Shinn, MD; Scott Solomon, MD; Jonathan S. Steinberg, MD; David Wilber, MD; Alon Barsheshet, MD; Scott McNitt, MA; Wojciech Zareba, MD; Helmut Klein, MD; on behalf of the MADIT-CRT Executive Committee

Background—We hypothesized that combined assessment of factors that are associated with favorable reverse remodeling after cardiac resynchronization-defibrillator therapy (CRT-D) can be used to predict clinical response to the device.

Methods and Results—The study population comprised 1761 patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT). Best-subset regression analysis was performed to identify factors associated with echocardiographic response (defined as percent reduction in left ventricular end-diastolic volume 1 year after CRT-D implantation) and to create a response score. Cox proportional hazards regression analysis was used to evaluate the CRT-D versus defibrillator-only reduction in the risk of heart failure or death by the response score. Seven factors were identified as associated with echocardiographic response to CRT-D and made up the response score (female sex, nonischemic origin, left bundle-branch block, QRS ≥150 milliseconds, prior hospitalization for heart failure, left ventricular end-diastolic volume ≥125 mL/m², and left atrial volume <40 mL/m²). Multivariate analysis showed a 13% \( (P<0.001) \) increase in the clinical benefit of CRT-D per 1-point increment in the response score (range, 0–14) and a significant direct correlation between risk reduction associated with CRT-D and response score quartiles: Patients in the first quartile did not derive a significant reduction in the risk of heart failure or death with CRT-D (hazard ratio=0.87; \( P=0.52 \)); patients in the second and third quartiles derived 33% \( (P=0.04) \) and 36% \( (P=0.03) \) risk reductions, respectively; and patients in the upper quartile experienced a 69% \( (P<0.001) \) risk reduction \( P \) for trend=0.005).

Conclusion—Combined assessment of factors associated with reverse remodeling can be used for improved selection of patients for cardiac resynchronization therapy.

Factors associated with reverse remodeling in the CRT-arm of MADIT-CRT

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>High response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Woman</td>
<td>2</td>
</tr>
<tr>
<td>CMP origin</td>
<td>Nonischemic</td>
<td>2</td>
</tr>
<tr>
<td>QRS</td>
<td>≥ 150 ms</td>
<td>2</td>
</tr>
<tr>
<td>QRS pattern</td>
<td>LBBB</td>
<td>2</td>
</tr>
<tr>
<td>Prior HF hospitalization</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>Baseline LVEDV</td>
<td>≥ 125 ml/m²</td>
<td>2</td>
</tr>
<tr>
<td>Baseline LAV</td>
<td>&lt; 40 ml/m²</td>
<td>3</td>
</tr>
</tbody>
</table>

Remark: similar findings for LVEDD > 3 cm/m² and LA diameter < 2 cm/m²

Goldenberg et al, Circulation 2011
Factors associated with reverse remodeling in the CRT-arm of MADIT-CRT

Goldenberg et al, Circulation 2011
Goldenberg et al, Circulation 2011
300 patients with suspected dilated CMP

37% showed late enhancement

LE associated with
- Higher LV volumes
- Higher LV mass
- Higher LV wall stress

Alter et al, Eur J Heart Failure 2011
Electrocardiographic and cardiac magnetic resonance imaging parameters as predictors of a worse outcome in patients with idiopathic dilated cardiomyopathy

Vinzenz Hombach¹*, Nico Merkle¹, Jan Torzewski¹, Johann M. Kraus², Markus Kunze¹, Oliver Zimmermann¹, Hans A. Kestler²†, and Jochen Wöhrle¹†

141 HF patients with non-ischaemic dilated CMP
EF 32±14% - 76% NYHA class III-IV
MRI (LV and RV function, late enhancement)

Multivariate analysis for cardiac death and sudden death (44 months follow-up)
MRI and outcome in dilated CMP

Figure 1 Kaplan–Meier curves for the primary endpoint according to QRS duration, late gadolinium enhancement, and diabetes mellitus (panels from left to right). Survival curves were significantly different for QRS duration ≤110 vs. >110 ms ($P = 0.010$), the presence or absence of late gadolinium enhancement ($P = 0.037$), and the presence or absence of diabetes mellitus ($P < 0.001$).

Hombach et al, Eur Heart J 2009
MRI and outcome in dilated CMP

- Total study cohort (n=184)
  - LGE$_{neg}$ (n=112)
  - LGE$_{pos}$ (n=72) (39%)

  - 45 non-midwall LGE (n=45)
    - Epicardial (n=21)
    - Patchy foci (n=16)
    - Diffuse (n=8)

  - Midwall LGE (n=27)

Lehrke et al, Heart 2011
MRI and outcome in dilated CMP

Lehrke et al, Heart 2011
Imaging and outcome in dilated cardiomyopathy

- LV function and volumes
  - Strain
  - Dyssynchrony
  - Late enhancement

- Filling pressures

- Mitral regurgitation

- RV function and volumes
Estimation of Filling Pressures in Patients with Depressed EF

Mitral E/A

- E/A < 1 and E ≤ 50 cm/s
  - Normal LAP
- E/A ≥ 1 - < 2, or
  - E/A < 1 and E > 50 cm/s
  - Normal LAP
- E/A ≥ 2, DT < 150 ms
  - ↑ LAP

E/e’ (average e’)< 8
- E/Vp < 1.4
- S/D > 1
- Ar – A < 0 ms
- Valsalva ∆ E/A < 0.5
- PAS <30 mmHg
- IVRT/T_{E-e’} >2

E/e’ (average e’)> 15
- E/Vp ≥ 2.5
- S/D < 1
- Ar – A ≥ 30 ms
- Valsalva ∆ E/A ≥ 0.5
- PAS >35 mmHg
- IVRT/T_{E-e’} <2

ASE/EAE recommendations JASE 2009
and Eur J Echo 2009
Event-free survival in patients with restrictive and nonrestrictive filling patterns after AMI

Meta-Analysis Research Group in Echocardiography (MeRGE) AMI Collaborators, Circulation 2008;117:2591-2598
<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Population</th>
<th>Outcome</th>
<th>Results</th>
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<tbody>
<tr>
<td>Yamamoto et al</td>
<td>96</td>
<td>ICM + DCM</td>
<td>Cardiac death + Hospitalisation CHF</td>
<td>Mitral E/E’ (lateral)</td>
</tr>
<tr>
<td>JASE 2003</td>
<td></td>
<td>EF &lt; 40%</td>
<td></td>
<td></td>
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<tr>
<td>Wang et al</td>
<td>182</td>
<td>ICM + DCM</td>
<td>Cardiac death</td>
<td>Mitral E/E’ (colour, 4sites)</td>
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<tr>
<td>JACC 2005</td>
<td></td>
<td>EF&lt;50%</td>
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<td></td>
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<tr>
<td>Dokainish et al</td>
<td>110</td>
<td>ICM + DCM</td>
<td>Cardiac death + Hospitalisation CHF</td>
<td>DT E/E’ (averaged)</td>
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<tr>
<td>JACC 2005</td>
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<tr>
<td>Throughton et al</td>
<td>225</td>
<td>ICM + DCM</td>
<td>Death / Heart Tx + Hospitalisation CHF</td>
<td>DT, S/D, Vp E/E’ (septal)</td>
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<tr>
<td>AJC 2005</td>
<td></td>
<td>EF&lt;35%</td>
<td></td>
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<tr>
<td>Bruch et al</td>
<td>372</td>
<td>ICM + DCM</td>
<td>Death + Hospitalisation CHF</td>
<td>DT E/E’ (averaged)</td>
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<td>AJC 2007</td>
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<tr>
<td>Rossi et al</td>
<td>49</td>
<td>ICM + DCM</td>
<td>Cardiac death + Urgent Tx</td>
<td>E/E ‘ (averaged)</td>
</tr>
<tr>
<td>Eur J Echo 2011</td>
<td></td>
<td>Tx waiting list</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Diastolic function in acute onset cardiomyopathy – IMAC-2 study

Figure 5. Diastolic Function at Baseline and After 6-Month Follow-Up

Tanaka et al, JACC-cardiovasc imaging 2011
Pulmonary artery pressure in HF

\[ \text{PSAP} = \text{TI gradient} + \text{RA pressure} \]
Determinants and prognostic value of pulmonary arterial pressure in patients with chronic heart failure

Thibaud Damy¹,²,³,⁴*, Kevin M. Goode¹, Anna Kallvikbacka-Bennett¹, Christian Lewinter¹, James Hobkirk¹, Nikolay P. Nikitin¹, Jean-Luc Dubois-Randé²,³,⁴, Luc Hittinger²,³,⁴, Andrew L. Clark¹, and John G.F. Cleland¹

¹Department of Cardiology, University of Hull, Castle Hill Hospital, Kingston-upon-Hull, UK; ²Fédération de cardiologie at the AP-HP, Groupe Henri-Mondor Albert-Chenevier, Créteil F-94010, France; ³INSERM, Unité U955, Créteil F-94010, France; and ⁴Université Paris-Est 12, Faculté de Médecine, UMR-S 9555, Créteil F-94010, France
TI gradient and all-cause mortality in heart failure

1380 CHF out patients
- 1026 reduced EF (50% IHD)
- 354 normal EF

TI gradient measurable in only 37% of patients

Determinants TI gradient:
- LV volumes
- Severity of functional MR
- LV filling pressures

Damy T et al, Eur Heart J 2010
Imaging and outcome in dilated cardiomyopathy

• LV function and volumes
  – Strain
  – Dyssynchrony
  – Late enhancement

• Filling pressures

• Mitral regurgitation

• RV function and volumes
Severe functional MR in dilated CMP

1256 HF patients
424 dilated CMP

Severe FMR =
- RV > 30 ml
- ERO > 0.2 cm²
- VC > 0.4 cm

Rossi et al, Heart 2011
Severe functional MR in dilated CMP

Figure 4  Hazard ratio and interval confidence of severe functional mitral regurgitation (FMR) in different subgroups of patients. CAD, coronary artery disease; EF, ejection fraction, NYHA, New York Heart Association; RMP, restrictive mitral filling.

Rossi et al, Heart 2011
Tenting area and outcome in dilated CMP

**Figure 2** Kaplan–Meier plots showing (A) survival free from all-cause mortality and (B) event-free survival (free of death or heart failure-related hospitalizations) according to groups based on tenting area (TA) > 3.4 cm² (n = 45) or TA ≤ 3.4 cm² (n = 45).

Karaca et al, Eur J Heart Failure 2011
Imaging and outcome in dilated cardiomyopathy

- LV function and volumes
  - Strain
  - Dyssynchrony
  - Late enhancement

- Filling pressures

- Mitral regurgitation

- RV function and volumes
<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit</th>
<th>Abnormal</th>
<th>Illustration</th>
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<tbody>
<tr>
<td><strong>Chamber dimensions</strong></td>
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<td></td>
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<tr>
<td>RV basal diameter</td>
<td>cm</td>
<td>&gt;4.2</td>
<td>Figure 7</td>
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<tr>
<td>RV subcostal wall thickness</td>
<td>cm</td>
<td>&gt;0.5</td>
<td>Figure 5</td>
</tr>
<tr>
<td>RVOT PSAX distal diameter</td>
<td>cm</td>
<td>&gt;2.7</td>
<td>Figure 8</td>
</tr>
<tr>
<td>RVOT PLAX proximal diameter</td>
<td>cm</td>
<td>&gt;3.3</td>
<td>Figure 8</td>
</tr>
<tr>
<td>RA major dimension</td>
<td>cm</td>
<td>&gt;5.3</td>
<td>Figure 3</td>
</tr>
<tr>
<td>RA minor dimension</td>
<td>cm</td>
<td>&gt;4.4</td>
<td>Figure 3</td>
</tr>
<tr>
<td>RA end-systolic area</td>
<td>cm²</td>
<td>&gt;18</td>
<td>Figure 3</td>
</tr>
<tr>
<td><strong>Systolic function</strong></td>
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<tr>
<td>TAPSE</td>
<td>cm</td>
<td>&lt;1.6</td>
<td>Figure 17</td>
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<tr>
<td>Pulsed Doppler peak velocity at the annulus</td>
<td>cm/s</td>
<td>&lt;10</td>
<td>Figure 16</td>
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<tr>
<td>Pulsed Doppler MPI</td>
<td>—</td>
<td>&gt;0.40</td>
<td>Figure 16</td>
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<tr>
<td>Tissue Doppler MPI</td>
<td>—</td>
<td>&gt;0.55</td>
<td>Figures 16 and 18</td>
</tr>
<tr>
<td>FAC (%)</td>
<td>%</td>
<td>&lt;35</td>
<td>Figure 9</td>
</tr>
<tr>
<td><strong>Diastolic function</strong></td>
<td></td>
<td></td>
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<tr>
<td>E/A ratio</td>
<td>—</td>
<td>&lt;0.8 or &gt;2.1</td>
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<tr>
<td>E/E' ratio</td>
<td>—</td>
<td>&gt;6</td>
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<tr>
<td>Deceleration time (ms)</td>
<td>ms</td>
<td>&lt;120</td>
<td></td>
</tr>
</tbody>
</table>

ASE guidelines, JASE 2010
Effects of RVEF on outcomes in systolic heart failure – report from the BEST trial

2008 patients with systolic HF (EF < 35%)

30% dilated CMP

RVEF evaluated by gated equilibrium Radionuclide ventriculography

Meyer et al, Circulation 2010
Effects of RVEF on outcomes in systolic heart failure – report from the BEST trial

RVEF < 20% independent predictor of all-cause mortality and HF hospitalization

Meyer et al, Circulation 2010
380 HF patients with LVEF < 45% (13% dilated CMP)
80 healthy controls
MRI for evaluation of LV and RV volumes and EF
Multivariate analysis for outcome (5 years follow-up)
RV dilatation and outcome in systolic heart failure

RVESVI > 49 ml/m² : 25%

Figure 2 Kaplan–Meier curves showing 5 year survival in the studied population.

Bourantas et al, Eur J Heart Failure 2011
Who has a poor outcome?

- Etiology and familial/genetic background
- High clinical risk score

**Imaging parameters**
- (persistent) low LVEF, (persistent) high LV volumes
- High burden of scar tissue
- (persistent) severe functional mitral regurgitation
- (persistent) high left/right filling pressures
- Low RVEF, high RV volumes
Thank you for your attention!