Left ventricular non-compaction

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Disclosures

No conflict of interest regarding this talk

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Swiss Cardiologists of Tomorrow
Normal heart

Right Ventricle

Coarse apical trabeculations

Outlet

Inlet

Left Ventricle

Fine apical trabeculations

Outlet

Inlet

Freedom et al, Cardiol Young 2005;15:345
Left ventricular non-compaction (LVNC)
Historical background

- *Spongy appearance of myocardium* 1926 by Grant
- *Persistent isolated myocardial sinusoids* 1967 by Bender
- Echocardiography 1984 by Engberding
- Detailed description 1986 by Jenni
- Term *non-compaction* 1990 by Chin

**Fig. 1.** Two-dimensional echocardiography (apical four-chamber view), end systole: thickened myocardium of the left ventricle, persistent sinusoids in the apex and at the posterolateral wall (arrows). A: apex; LV: left ventricle; LA: left atrium; M: mitral valve; R.A: right atrium; RV: right ventricle; T: tricuspid valve; P: pericardial effusion.

**Fig. 2.** Two-dimensional echocardiography (apical four-chamber view), end systole: markedly thickened myocardium of the right ventricle with persistent sinusoids (arrows).
Historical background

Isolated Noncompaction of Left Ventricular Myocardium
A Study of Eight Cases

Thomas K. Chin, MD, Joseph K. Perloff, MD, Roberta G. Williams, MD,
Kenneth Jue, MD, and Renee Mohrmann, MD

Histological examination disclosed that the deep intertrabecular recesses were lined with endothelium that was continuous with the endocardial endothelium (Figure 6), indicating that the “spongy” appearance of noncompaction was due to the deep intertrabecular recesses per se and not to intramyocardial sinusoids. Accordingly, the term “persistent sinusoids” is not appropriate. The descriptive term “spongy myocardium” has the virtue of precedence,
Embryogenesis of the myocardium

Similar in all vertebrates

1. Early heart tube
2. Emergence of trabeculations
3. Trabecular remodeling
4. Development of multilayered spiral system
Embryology of the myocardium

week 6, 8 - 11 mm
Embryology of the myocardium

At 6 weeks:
Abundant fine trabeculations

At 12 weeks:
Trabeculae start to solidify

The Process of Compaction

Early fetal period:
Compaction almost completed

Sedmera et al. Anat Rec 2000;258:319
Terminology

- Non-compaction
  - Isolated
  - CHD
- Hypertrabeculation
- Sinusoids
Arteriosinusoidal fistulae (Persistent Sinusoids)
Morphology of non-compaction
Diagnostic criteria (Jenni)

Jenni et al.\textsuperscript{13}

Thickened myocardium with a two-layered structure consisting of a thin compacted epicardial layer/band (C) and a much thicker, non-compacted endocardial layer (N) or trabecular meshwork with deep endomyocardial spaces; N/C ratio > 2.0

Predominant location of the pathology: mid-lateral, mid-inferior, and apex

Colour Doppler evidence of deep intertrabecular recesses filled with blood from the left ventricular cavity

Absence of coexisting cardiac abnormalities (in the presence of isolated LVNC)

\textit{Acquisition of the images:} short-axis views, measurements of the N/C ratio at \textbf{end-systole}

Jenni R et al. EHJ, 2011;32:1446
Diagnostic criteria (Jenni)

Jenni R et al. EHJ, 2011;32:1446
Diagnosis of Non-compaction

Jenni R et al. Heart 2001;86:666
Diagnostic criteria (Chin)

Chin et al.\textsuperscript{11}

Two-layered structure of the myocardium (epicardial compacted, endocardial non-compacted layer)

Determination of the $X$-to-$Y$ ratio ($\leq 0.5$)

$X$—Distance between the epicardial surface and through of intertrabecular recess

$Y$—Distance between epicardial surface and peak of trabeculation

\textit{Acquisition of the images:} parasternal short-axis view, measurements of the $X$-to-$Y$ ratio at end-diastole

Jenni R et al. EHJ, 2011;32:1446
Diagnostic criteria (Stöllberger)

Stöllberger et al.\textsuperscript{15,21}

More than three trabeculations protruding from the left ventricular wall, located apically to the papillary muscles and visible in one image plane

Trabeculations with the same echogenicity as the myocardium and synchronous movement with ventricular contractions

Perfusion of the intertrabecular spaces from the left ventricular cavity

Ratio of non-compacted to non-compacted segment $> 2.0$ at end-diastole (this criterion was introduced later)

Acquisition of the images: apical four chamber view; angulation of the transducer and acquisition of pictures in atypical views to obtain the technically best picture quality for differentiation between false chords/aberrant bands and trabeculations

Diagnostic criteria have changed during the last years

Jenni R et al. EHJ, 2011;32:1446
Diagnostic criteria (MRI)

Petersen et al.\textsuperscript{26}

Ratio between the non-compacted and compacted layer $>2.3$

\textit{Measurement: at end-diastole}

Jacquier et al.\textsuperscript{27}

Trabeculated left ventricular mass $>20\%$ of the global left ventricular mass

\textit{Measurement: left ventricular trabeculation and global/compacted LV mass were defined at end-diastole}

Sarma RJ et al Progr Cardiovasc Dis 2010;52:264
Diagnostic criteria

Non-compaction

Normal

Compacta thickness

Compacta thickness

Stähli B et al. unpublished observation
Complications

- Heart failure
- Arrhythmias/SCD
- Embolic events
<table>
<thead>
<tr>
<th><strong>Diagnostic assessment</strong></th>
<th><strong>Therapeutic strategies</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler echocardiography</td>
<td>Normal LV size/systolic function</td>
</tr>
<tr>
<td>Cardiac MRI</td>
<td>Heart failure therapy</td>
</tr>
<tr>
<td></td>
<td>Anticoagulation</td>
</tr>
<tr>
<td>Genetic testing</td>
<td>ICD</td>
</tr>
<tr>
<td>Neurological assessment</td>
<td>Biventricular pacing</td>
</tr>
<tr>
<td>Family screening</td>
<td>Regular follow-up (every 2 years)</td>
</tr>
<tr>
<td>(first-degree relatives)</td>
<td>As per guidelines for heart failure</td>
</tr>
<tr>
<td>Electrophysiology study</td>
<td>LVEF &lt; 40%</td>
</tr>
<tr>
<td></td>
<td>Secondary prevention/primary prevention?</td>
</tr>
<tr>
<td></td>
<td>Advanced heart failure/LVEF &lt; 35%/dyssynchrony (as per guidelines)</td>
</tr>
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</tbody>
</table>

Jenni R et al. EHJ, 2011;32:1446
Clinical Course

LV-EF (%)

Follow up (years)

Stähli B et al. unpublished observation
## Clinical Course

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adverse Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(115 Patients at Risk)</td>
</tr>
<tr>
<td>Cardiovascular death or orthotopic heart transplantation</td>
<td>27 (23%)</td>
</tr>
<tr>
<td>Orthotopic heart transplantation</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>21 (18%)</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
<td>10 (9%)</td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>5 (4%)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Symptomatic splenic infarction</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Sustained ventricular tachycardia</td>
<td>5 (4%)</td>
</tr>
<tr>
<td>Admission with decompensated heart failure</td>
<td>15 (13%)</td>
</tr>
</tbody>
</table>

Fifty-two adverse cardiovascular events occurred in 32 patients; no adverse events occurred in asymptomatic patients.
Predictors of outcome

Predictors of outcome

Predictors of outcome

Stämpfli SF et al. Abstract SGK 2016
Predictors of outcome

- proBNP (log2)
- LVEF (per 10% ↓)
- NYHA (class change)
- PoTP (per 10% ↓)
Predictors of outcome

Normal proBNP
proBNP >2000 ng/l
LVEF >55%
LVEF <30%
LVEF <15%

Hazard ratio

* HR not quantifiable

Stämpfli SF et al. Abstract SGK 2016
HCM & Non-compaction

Genetics & Non-compaction

Beta-myosin heavy chain
Alpha cardiac actin
Cardiac myosin binding protein C
Cardiac troponin T
Cardiac troponin I
Alpha tropomyosin
Lamin A/C
ZASP
63 adult patients with isolated LVNC
18 heterozygous mutations

<table>
<thead>
<tr>
<th></th>
<th>Mutation Positive (n=18)</th>
<th>Mutation Negative (n=45)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female sex, n</td>
<td>13/5</td>
<td>30/15</td>
<td>NS</td>
</tr>
<tr>
<td>Age at diagnosis, y</td>
<td>39.2±16.9</td>
<td>43.3±15.0</td>
<td>NS</td>
</tr>
<tr>
<td>Age at follow-up, y</td>
<td>45.5±16.6</td>
<td>46.8±15.7</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of follow-up, y</td>
<td>6.7±5.5</td>
<td>3.8±4.2</td>
<td>0.046</td>
</tr>
<tr>
<td>At diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac symptoms*</td>
<td>14 (78)</td>
<td>40 (89)</td>
<td>NS</td>
</tr>
<tr>
<td>Heart failure†</td>
<td>10 (56)</td>
<td>28 (62)</td>
<td>NS</td>
</tr>
<tr>
<td>Tachyarrhythmias‡</td>
<td>2 (11)</td>
<td>7 (16)</td>
<td>NS</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDD at diagnosis, mm</td>
<td>60.0±9.2</td>
<td>60.0±12.3</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDD at follow-up, mm</td>
<td>59.7±9.0</td>
<td>58.4±10.2</td>
<td>NS</td>
</tr>
<tr>
<td>LVFS at diagnosis, %</td>
<td>20.0±9.3</td>
<td>22.8±8.9</td>
<td>NS</td>
</tr>
<tr>
<td>LVFS at follow-up, %</td>
<td>22.2±10.3</td>
<td>23.4±11.1</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF at diagnosis, %</td>
<td>36.1±17.1</td>
<td>38.7±16.1</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF at follow-up, %</td>
<td>39.6±14.4</td>
<td>42.3±15.1</td>
<td>NS</td>
</tr>
<tr>
<td>At follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD</td>
<td>3 (17)</td>
<td>7 (16)</td>
<td>NS</td>
</tr>
<tr>
<td>Alive‡</td>
<td>16 (89)</td>
<td>36 (80)</td>
<td>0.048</td>
</tr>
<tr>
<td>HTX or death§</td>
<td>2 (11)</td>
<td>9 (20)</td>
<td></td>
</tr>
</tbody>
</table>

Future perspectives

- Distinct cardiomyopathy vs. phenotype of different diseases
- Diagnostic criteria (methods differ, sensitivity, pitfalls, multimodality)
- Patients at risk (anticoagulation, …)
- Genetics
National Multicenter LVNC Registry

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Felix C. Tanner, MD
Simon Stämpfli, MD MSc
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University Heart Center Zurich
Apéro!

S C T

Today

Ristorante Gina

6 pm
Thank you and have a good congress!
Predictors of outcome

Clinical predictors\textsuperscript{30,51,59}

- Age at initial presentation
- Functional capacity, NYHA class III–IV
- Sustained ventricular arrhythmias

Echocardiographic parameters\textsuperscript{24,30,51,57,63}

- Ratio of non-compacted to compacted layers
- Number of affected segments
- LV end-diastolic diameter
- Abnormal lateral mitral tissue Doppler Ea velocity

Jenni R et al. EHJ, 2011;32:1446
Predictors of outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>1.03</td>
<td>1.002–1.054</td>
<td>0.04*</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.0</td>
<td>0.5–2.8</td>
<td>0.97</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic at diagnosis</td>
<td>32.0</td>
<td>0.6–1,592.3</td>
<td>0.08</td>
</tr>
<tr>
<td>New York Heart Association III or more at diagnosis</td>
<td>8.8</td>
<td>3.2–24.0</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Presented with clinical complication</td>
<td>20.6</td>
<td>4.9–87.5</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Decompensated heart failure</td>
<td>4.5</td>
<td>1.9–10.8</td>
<td>0.001*</td>
</tr>
<tr>
<td>Sustained ventricular arrhythmia</td>
<td>14.3</td>
<td>5.0–41.1</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Systemic embolization</td>
<td>3.2</td>
<td>0.4–24.8</td>
<td>0.26</td>
</tr>
<tr>
<td>Electrocardiographic findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2.4</td>
<td>1.1–5.6</td>
<td>0.03*</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>2.8</td>
<td>1.3–6.1</td>
<td>0.009*</td>
</tr>
<tr>
<td>Echocardiographic findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction at diagnosis</td>
<td>0.96</td>
<td>0.93–0.99</td>
<td>0.004*</td>
</tr>
<tr>
<td>Left ventricular end-diastolic diameter indexed to body surface area</td>
<td>1.7</td>
<td>1.2–2.5</td>
<td>0.002*</td>
</tr>
<tr>
<td>Diastolic left ventricular dysfunction</td>
<td>3.4</td>
<td>0.4–28.1</td>
<td>0.26</td>
</tr>
</tbody>
</table>

CI = confidence interval; HR = hazard ratio.
* Statistically significant.