THE LEFT VENTRICULAR NONCOMPACATION SYNDROME IN 50 ADULTS: clinical variants, follow-up and outcomes

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The myocardial noncompaction is a genetically heterogeneous cardiomyopathy characterized by a pattern of prominent trabecular meshwork and deep intertrabecular recesses not connected with coronary blood flow and predisposing to thrombosis.

**Noncompaction cardiomyopathy** – myocardial noncompaction with LV systolic dysfunction

- 0.05%; 141 patients - C. Stöllberger (Vienna, 1995-2011), 210 papers in this problem
- 100 patients from 36,933 who was examined using Echo-CG (1994-2006)
- 3% from 960 patients with CHF
- 1330 papers in Medline (1990-2015)
- 229 patients – SIEG-register (Sicilia)
- 73 patients (incl. children) – Bologna (1994-2006)
- 58 patients (incl. 9 children) – Rotterdam
- 63 patients – Berlin (2008)
OBJECTIVE

to study clinical variants, follow-up and outcomes of the left ventricular noncompaction (LVN) syndrome in adult patients
INCLUSION CRITERIA

mistake initial diagnosis in 82%

- two layers of the myocardium with a ratio of non-compact and compact parts 2:1 (Echo-CG) or 2.3:1 (MRI / MSCT)
- a synchronous motion of non-compact and compact layers
- end-diastolic visualization more than 3 trabeculae in the left ventricle
- end-diastolic blood flow into the intertrabecular spaces
**STUDY GROUP**

n=50, 28 male, mean age 42.8±14.9 (18 - 76) years
family history in 9 patients (18%)

**additional studies**

morphological study of the myocardium (n=14, incl. EMB in 10 patients)
anti-heart antibodies and viral genome (real-time PCR) study
genetic examination with mutations detection in 10% of patients

- *MyBPC3* (n=3)
- *DSP* (n=1)
- *LAMP* (n=1)
ECHOCARDIOGRAPHIC PARAMETERS

LV end-diastolic diameter 6.1±0.8 cm
LV end-diastolic volume 160.7±76.3 (61-501) ml
LV end-systolic volume 108.6±70.1 (19-386) ml
LV ejection fraction 34.6±14.0%
LA diameter 4.3±0.8 cm
LA volume 95.1±37.4 (43-180) ml
RA volume 72.5±40.7 (34-255) ml
RV diameter 2.9±0.6 cm
PA systolic pressure 37.0±17.8 Hg mm
IVS 10.1±3.0 mm
LV back well 9.9±1.9 mm
mitral annulus diameter 3.5±0.4 cm
mitral regurgitation 1.0 [0.5; 2.0] degree
tricuspid regurgitation 1.0 [0.5; 1.0] degree
dp/dt 745.8±244.9 Hg mm
VTI 11.1±4.1 cm
CLINICAL MANIFESTATIONS OF VENTRICULAR NONCOMPACTATION

- CHF (degree I-IIIB)
- NYHA (1-4)
- PVBs: < 1 ts., < 5 ts., < 10 ts., < 20 ts.
- VT/VF: unsustained, sustained
- Sick sinus syndrome
- AV block II-III
- AF: paroxysmal, pers. chronic
- Angina pectoris (1-3)
- Myocardial infarction
- Embolism
ATRIAL FIBRILLATION in MYOCARDIAL NONCOMPACTION

- **frequency is 30%**
- sustained forms (persistent and chronic) are most frequent than paroxysmal form (3 : 2)
- embolic events had 13.3% patients with AF (versus 8.6% without AV, \( p > 0.05 \))
- amiodarone received 73.4% of patients
- RF ablation in one patients was not effective

<table>
<thead>
<tr>
<th>AF</th>
<th>associated factors</th>
<th>( p )</th>
<th>not AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.6 ( \pm ) 0.8 cm</td>
<td>LA diameter</td>
<td>0.107</td>
<td>4.2 ( \pm ) 0.8 cm</td>
</tr>
<tr>
<td>108.9 ( \pm ) 46.9 ml</td>
<td>LA volume</td>
<td>0.077</td>
<td>87.9 ( \pm ) 29.9 ml</td>
</tr>
<tr>
<td>93.9 ( \pm ) 16.0 ml</td>
<td>RA volume</td>
<td>0.015</td>
<td>61.9 ( \pm ) 4.0 ml</td>
</tr>
<tr>
<td>20.0%</td>
<td>sick sinus syndrome</td>
<td>0.047</td>
<td>2.9%</td>
</tr>
<tr>
<td>60.0%</td>
<td>myocarditis</td>
<td>&gt; 0.05</td>
<td>58.8%</td>
</tr>
</tbody>
</table>

**frequency of AF in different clinical variants of myocardial noncompaction**

![Graph showing frequency of AF in different clinical variants of myocardial noncompaction](image-url)
VT/VF in MYOCARDIAL NONCOMPACTION

- **frequency of nonsustained VT is 64%** (incl. «torsade de pointe» in one patient)
- **frequency of sustained VT is 14%, rate of VF is 5%** (only in the patients with variants «DCM + myocarditis» and NCM in association with other cardiomyopathy
  - amiodarone received 92.9% of patients
  - RFA of VT in one patient was not effective

<table>
<thead>
<tr>
<th>VT/VF</th>
<th>associated factors</th>
<th>p</th>
<th>no VT/VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.75 [2; 3]</td>
<td>NYHA functional class</td>
<td>0.018</td>
<td>1 [0.25; 2.75]</td>
</tr>
<tr>
<td>9.4%</td>
<td>AB block II-III degree</td>
<td>0.211</td>
<td>0</td>
</tr>
<tr>
<td>119.7 ± 25.8 ms</td>
<td>QRS duration</td>
<td>0.010</td>
<td>101.4 ± 19.0 ms</td>
</tr>
<tr>
<td>31.8 ± 14.2%</td>
<td>LV ejection fraction</td>
<td>0.042</td>
<td>40.4 ± 12.6%</td>
</tr>
<tr>
<td>3.1 ± 0.6 cm</td>
<td>RV diameter</td>
<td>0.046</td>
<td>2.7 ± 0.6 cm</td>
</tr>
<tr>
<td>71.9%</td>
<td>myocarditis</td>
<td>0.008</td>
<td>31.3%</td>
</tr>
<tr>
<td>15.6%</td>
<td>mortality</td>
<td>0.098</td>
<td>0</td>
</tr>
</tbody>
</table>

**frequency of VT/VF in different clinical variants of myocardial noncompaction**
MYOCARDIUM NONCOMPACtion, RESTRICTive and HYPERTROphic CARDIOMYOPATIES in ONE FAMILY MEMBERS

father, 64 years
daughter, 35 years
son, 39 years

HCM Risk-SCD Calculator

<table>
<thead>
<tr>
<th>Risk of SCD at 5 years (%)</th>
<th>ESC recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD generally not indicated **</td>
</tr>
</tbody>
</table>

- **”** indicates patients with additional risk factors.
FREQUENCY and MANIFESTATIONS of the MYOCARDITIS in MYOCARDIAL NONCOMPACTION

n=50

CHF degree
NYHA functional class
LV EF, %
systolic PA pressure, Hg mm

p=0.013
p=0.015
p=0.013
p=0.002
### MIOCARDIAL INFARCT in PATIENTS WITH NONCOMPACTATION

**n=8 (16% of patients)**

<table>
<thead>
<tr>
<th>patient</th>
<th>angina</th>
<th>ECG</th>
<th>Tn</th>
<th>coronary stenoses</th>
<th>LV thrombosis</th>
<th>other embolism</th>
<th>myocarditis</th>
<th>outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>M, 39 y.</td>
<td>no</td>
<td>STEMI</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>transplantation</td>
</tr>
<tr>
<td>M, 40 y.</td>
<td>no</td>
<td>STEMI</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ICD</td>
</tr>
<tr>
<td>F, 30 y.</td>
<td>yes</td>
<td>STEMI</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F, 37 y.</td>
<td>no</td>
<td>???</td>
<td>???</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>death</td>
</tr>
<tr>
<td>F, 62 y.</td>
<td>no</td>
<td>QS</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ICD</td>
</tr>
<tr>
<td>M, 72 y.</td>
<td>no</td>
<td>Q</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>angioplasty</td>
</tr>
<tr>
<td>M, 30 y.</td>
<td>no</td>
<td>Q</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>interrupted death, ICD</td>
</tr>
<tr>
<td>M, 42 y.</td>
<td>no</td>
<td>Q</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FREQUENCY of THROMBOSIS and EMBOLISM

all embolic events (with one exception) developed in the absence of anticoagulants in patients with intracardiac thrombosis verified retrospectively

<table>
<thead>
<tr>
<th>thrombosis/embolism (n=13)</th>
<th>risk factors</th>
<th>p</th>
<th>no thrombosis/embolism (n=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 [1.5; 3]</td>
<td>NYHA functional class</td>
<td>0.098</td>
<td>2 [1; 3]</td>
</tr>
<tr>
<td>IIA [I-II; IIB]</td>
<td>CHF degree</td>
<td>&gt; 0.05</td>
<td>IIA [I; IIB]</td>
</tr>
<tr>
<td>30.0%</td>
<td>atrial fibrillation</td>
<td>&gt; 0.05</td>
<td>27.6%</td>
</tr>
<tr>
<td>61.5%</td>
<td>myocarditis</td>
<td>&gt; 0.05</td>
<td>56.8%</td>
</tr>
<tr>
<td>109.2 ± 30.0 ml</td>
<td>LA volume</td>
<td>0.084</td>
<td>88.8 ± 37.0 cm</td>
</tr>
<tr>
<td>6.5 ± 0.9 cm</td>
<td>LV end-diastolic diameter</td>
<td>0.063</td>
<td>6.0 ± 0.0 cm</td>
</tr>
<tr>
<td>29.7 ± 3.8%</td>
<td>LV ejection fraction</td>
<td>0.124</td>
<td>36.5 ± 14.7%</td>
</tr>
<tr>
<td>3.2 ± 0.7 cm</td>
<td>RV diameter</td>
<td>0.088</td>
<td>2.8 ± 0.5 cm</td>
</tr>
<tr>
<td>0 [0; 1.5]</td>
<td>degree of arterial hypertension</td>
<td>&gt; 0.05</td>
<td>0 [0; 2]</td>
</tr>
</tbody>
</table>
INDICATIONS to the ANTICOAGULANTS ADMINISTRATION in MYOCARDIAL NONCOMPACTION

- history or present intracardiac thrombosis
  - embolic history
  - atrial fibrillation
- LV ejection fraction less than 40%
  - microvascular ischemia (angina)?
  - history or present myocardial infarct
    - ICD?
- CHADS\textsubscript{2} risk factors without AF?
- LA volume more than 100 ml?
- definite diagnosis «myocardial noncompaction»?
- association noncompaction with HCM?

anticoagulants in the study group (according to the basic indications)

should to prescribe anticoagulants (LV EF<40%)?

anticoagulants: 42%
no anticoagulants: 38%
PATIENTS 37 y. HYPERTROPHIC CARDIOMYOPATHY

- since 2012 – paroxisms of atrial fibrillation/flutter, electrical cardioversion, long-time amiodarone therapy without effects
- 2013 – ineffective RFA, ICD due to unsustained VT
OUTCOMES and INTERVENTION in MYOCARDIAL NONCOMPACTATION (n=50)

mean follow-up 12,5 [5,5; 25,5] month

<table>
<thead>
<tr>
<th>Drug Therapy</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-blockers</td>
<td>32</td>
<td>64%</td>
</tr>
<tr>
<td>Sotalol</td>
<td>5</td>
<td>10%</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>33</td>
<td>66%</td>
</tr>
<tr>
<td>Digoxin</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>29</td>
<td>58%</td>
</tr>
</tbody>
</table>
CLINICAL CLASSIFICATION of MYOCARDIAL NONCOMPACTATION

1. Asymptomatic variant.
2. Isolated arrhythmic variant (with/ without myocarditis):
   - isolated AF
   - isolated PVBs/ unsustained VT
   - sustained VT/ VF/ sudden cardiac death
   - associations of ventricular and supraventricular arrhythmias
   - associations of rhythm and conduction disturbance
3. Ischemic variant:
   - microvascular angina/ ischemia (with/ without myocarditis)
   - myocardial infarct (embolic, due to myocardidtis, coronary atherosclerosis)
   - association of microvascular ischemia and myocardial infarct
4. Thromboembolic variant.
5. Acute myocarditis with myocardial noncompaction.
6. DCM (noncompaction cardiomyopathy):
   - with myocarditis
   - without myocarditis
7. Myocardial noncompaction in association with other cardiomyopaties/ congenital heart diseases:
   - with hypertrophic cardiomyopathy
   - with restrictive cardiomyopathy
   - with ARVD
   - with muscular dystrophy
   - with cannalopathies (?)
   - with congenital heart disease (septal defects, pulmonary artery stenosis etc.)
8. Mixed variants.

Etiological variants:
1. Primary (genetic):
   - genetically verified
   - genetically unverified
2. Secondary (due to severe cardiac dysfunction)?

By severity:
1. Increased trabecularity of the myocardium (ratio of layers 1:1-1:2).
2. Myocardial noncompaction (ratio of layers 1:2 and more).
CONCLUSIONS

- LVNS in adults is very polymorphic and is isolated only in 32% of patients.
- It can be identified following clinical variants of LVNS in adults: asymptomatic, isolated arrhythmic, ischemic, tromboembolic, dilated cardiomyopathy, association with acute myocardidtis, other cardiomyopathies and mixed.
- Myocarditis, including viral, complicates LVNS in the half of the patients and leads to a significant deterioration of the disease.
- The most typical kind of arrhythmia is the unstable VT, which is associated with significant structural changes of the heart (LV EF < 35%, QRS >120 ms); 24% of patients have life-threatening arrhythmias; the frequency of appropriate ICD/ CRTD shocks during follow-up (mean 12.5 months) is 25%.
- Ischemic symptoms are typical in LVNS; the rate of myocardial infarct (necrosis) was 16%, its mechanisms are, in addition to atherosclerosis, embolism and myocarditis.
- Embolic complications developed in 11% of patients in the presence of intracardiac thrombosis and in the absence of anticoagulation therapy; mean risk factors were severe systolic dysfunction and NYHA functional class of CHF.
- The rate of mortality/ transplantation for the year follow-up was 14%; terminal heart failure, and thromboembolic complications prevail in the structure of the causes of death.