Left ventricular non-compaction: the New Cardiomyopathy on the Block

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Disclosures

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Left ventricular non-compaction (LVNC)

- First described in 1920s
- Most recently recognized as a distinct form of cardiomyopathy
- Can be associated with LV dilation, hypertrophy, systolic or diastolic dysfunction, and/or congenital heart disease
- Prominent trabeculae and deep intertrabecular recesses, resulting in thickened myocardium with two layers consisting of non-compacted myocardium and a thin compacted layer of myocardium
- Numerous genes have been implicated in addition to X-linked/chromosomal and familial disorders

Miyake and Kim, Card Electro Clin 2015
From: Left ventricular non-compaction revisited: a distinct phenotype with genetic heterogeneity?
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Pathogenesis

- The developing embryological heart is a loose mesh of muscle fibres.
- During gestation, this mesh coalesces or condenses to compact myocardium and usually this process is more complete in the LV than the RV.
- Failure in the compaction pathway is thought to occur in LVNC.
- The “crypts” or recesses usually do not communicate with the coronary circulation although the trabeculations are theoretically at risk for sub-endocardial ischemia.
Trabeculations

NC:C Ratio ≥2
Epicardium to Trabecular Trough
(Compacted Myocardium [C])
Trabecular Peak to Trough
(Non-Compacted Myocardium [NC])

Genetics of LVNC

• Genetically heterogeneous
• Can be associated with chromosomal abnormalities
  • Tri 21, 18, 13, 1p36 del etc
• Reported in multiple syndromes:
  • Barth
  • Mitochondrial
  • Myotonic dystrophy
Genetics of LVNC

- Reported mutations in:
  - LMNA
  - ZASP (LBD3)
    - Associated with myofibrillar myopathy: progressive muscle weakness
  - DTNA
    - Cytoskeleton of dystrophin complex
  - Sarcomere genes (i.e. MYH7, MYBPC3, TTN, TNNT2 etc)
  - If LVNC + Ebstein’s anomaly (MYH7)
LVNC and CHD
Presentation

- Clinical manifestation is highly variable from asymptomatic to progressive heart failure to life-threatening arrhythmias
- A rare form of cardiomyopathy but true incidence is not well known, ranging from 0.05% to 0.14% of adults referred for echocardiograms
- LVNC may account for approximately 9% of newly diagnosed cardiomyopathies in children
- An entirely normal ECG seen in 13% of those diagnosed with LVNC and these individuals were often younger and less likely to present with heart failure

Hussein et al JACC 2015
Oechslin et al JACC 2000
Diagnostic criteria? That depends on which one…

- Jenni – most widely accepted. Non-compact to compact ratio > 2:1 in end-systole in the parasternal short axis view. Colour flow within the recesses. Prominent trabeculations in the LV apex or mid segments.
- Chin – ratio between the distance to the epicardial surface and trabecular recess and the epicardial surface to the trabecular peak (<0.5).
- Stollberger – more than 3 trabeculations seen in a single image plane and distanced from the papillary muscle. Colour flow within the recesses as well.
- Petersen (MRI) – NC to C ratio > 2.3 in end-diastole.
- However, no gold standard exists (including MRI) and the above criteria lack specificity, especially in children.
Diagnostics

• A number of large population studies have shown that individuals who meet imaging criteria for LVNC don’t develop heart failure or adverse events on long term follow up
• Definitive diagnosis of LVNC should include short-axis view by echocardiogram or CMR criterion plus one of the following features:
  • LVNC diagnosed in another family member
  • Regional wall motion abnormalities
  • LVNC-related complications (arrhythmia, heart failure, or thromboembolism)
  • Being a carrier of a pathogenic mutation in a gene previously associated with LVNC in various families
LVNC and restrictive physiology
LVNC and dilated cardiomyopathy
Clinical Characterization of Left Ventricular Noncompaction in Children

Ricardo H. Pignatelli, MD*; Colin J. McMahon, MB, MRCPI*; William J. Dreyer, MD; Susan W. Denfield, MD; Jack Price, MD; John W. Belmont, MD; William J. Craig, MD; Jen Wu, MD; Howaida El Said, MD; Louis I. Bezold, MD; Sarah Chunie, RN; Susan Fernbach, RN; Neil E. Bowles, PhD; Jeffrey A. Towbin, MD

- 36 children with LVNC evaluated at single center 1997 -2002
- 27 had ECG abnormalities and 83% had decreased LV function
- 25% recovered function and 14% died during the study period
- The same cohort was reviewed again 17 years later
  - 28% died with 6% lost to follow up. 11% had gone on to transplant
  - All patients with an EF < 55% were on cardiac medications
  - Of the 23 survivors only 40% were involved in non-competitive sports and no pregnancies were reported
22 children met criteria for a NC to C ratio > 2:1
Chromosomal abnormalities or syndromes were detected in 32%
20/22 children required heart failure medications
Extremely poor outcomes were noted in children with a NC to C ratio > 3 or with a dilated left ventricle (> 5cm)
Angiographic diagnosis, prevalence and outcomes for left ventricular noncompaction in children with congenital cardiac disease

Marina L. Hughes,1,2 Bendix Carstensen,3 James L. Wilkinson,1 Robert G. Weintraub1

• 1994-2000 study ~1500 children who underwent angiography of their LVs
• 31 with LVNC and 15 in single ventricle physiology pts
• Mortality was doubled in the LVNC/SV group
• Interestingly, no pt with Ebstein’s was found to have LVNC in this study
• Diagnosis by angiography?

Hughes et al, Cardiol Young 2007
242 children identified between 1990 and 2009 with LVNC
13% died and 5.4% received a heart transplant
62% presented with LV dysfunction which was associated with mortality (HR 11, P< 0.001)
33% had an arrhythmia with most common being VT
No patient with normal cardiac function or preceding arrhythmia died
Sudden death and LVNC

• Out of the 242 children with LVNC - 15 patients died suddenly
• 14/15 had LV dilation, hypertrophy or both
• 13/15 had decreased LV function
• 9/15 had documented arrhythmia before having cardiac arrest

• Adult cohorts have also shown high rates of SCD, ranging from 35-71%

Hussein et al JACC 2015
Oechslin et al JACC 2000
Sudden death and LVNC

• One adult study showed VT is found in 38-47% of affected individuals with SCD accounting for a significant portion of the mortality

• Risk factors for SCD
  • increased LV dimension
  • decreased LV systolic function
  • heart failure (NYHA class III/IV)
  • ventricular arrhythmias
  • atrial fibrillation
  • Inability to induce VT with programmed ventricular stimulation has limited negative predictive value
<table>
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<tr>
<th>Table 4</th>
<th>Predictors of death or heart transplantation</th>
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<td><strong>Clinical predictors</strong>&lt;sup&gt;30,51,59&lt;/sup&gt;</td>
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<td>Age at initial presentation</td>
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<td>Functional capacity, NYHA class III–IV</td>
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<td>Sustained ventricular arrhythmias</td>
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<td><strong>Echocardiographic parameters</strong>&lt;sup&gt;24,30,51,57,63&lt;/sup&gt;</td>
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<tr>
<td>Ratio of non-compacted to compacted layers</td>
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<td>Number of affected segments</td>
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<td>LV end-diastolic diameter</td>
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<td>Abnormal lateral mitral tissue Doppler Ea velocity</td>
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Anticoagulation

• Oral anticoagulation is recommended in patients with atrial fibrillation, after a cardioembolic event, in those with severe systolic dysfunction, or if an atrial or a ventricular clot has been identified (i.e. Vitamin K antagonist or ASA)

• Pediatric pts with LVNC and normal systolic function and no other TE risk factors likely do not need any anticoagulation (but practice patterns are variable)
ICD and LVNC

• There are no specific criteria for ICD implantation in children with LVNC. Standard indications for implant usually apply.
  • Sustained ventricular tachycardia or after sudden cardiac arrest
  • Primary prevention can be considered for reduced EF (<35%) or NYHA class II-IV heart failure

• Study of 12 adults with LVNC and s/p ICD implant for secondary prevention – 50% received appropriate ICD therapy
Exercise restriction and LVNC

- left ventricular ejection fraction of <50%
- ECG abnormalities or arrhythmia
- symptomatic presentation
- Positive family history of cardiomyopathy should be counseled to refrain from competitive endurance sports or weight lifting (similar to patients with hypertrophic cardiomyopathy)
- AHA/ACC guidelines on competitive sports in cardiomyopathies – participation may be considered for asymptomatic pts with normal LV function and no history of syncope or arrhythmia

Caselli et al Am j Car 2015
Maron et al AHA/ACC guidelines 2015
Follow up and outcomes

• More recent studies have reported substantially lower morbidity and mortality. Among 45 patients referred to a cardiomyopathy center, survival free of transplantation was 97% over 4 years of follow-up.

• In another study, 46-month survival tracked closely with the presence of symptoms at presentation (69% vs. 100% when absent).

• For asymptomatic patients with normal function and no arrhythmias – follow up every 2 years.
THANK YOU!