Left Ventricular Non-Compaction (LVNC)

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- Pamela Youde Nethersole Eastern Hospital

- Hong Kong Core Cardiology Certificate Course (Module 4)
- 14 July 2019

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A Mystery of Spongy Myocardium

Heart 1926

An unusual anomaly of the coronary vessels in the malformed heart of a child

Grant T. Heart 13, 273-283, 1926

Arch Pathol 1975

Arch Pathol. 1975 Jun;99(6):312-7.

Postnatal persistence of spongy myocardium with embryonic blood supply.

Dusek J, Ostádal B, Duskova M.

Abstract

Focal presence of the embryonic pattern of myoarchitecture and of a lacunary blood supply was found in the left ventricular wall of five infant hearts. Four of these hearts showed various malformations; one was a case of cardiac fibroma. The persisting intertrabecular spaces and sinusoids communicated with the ventricular lumen; there appeared to be some communication with the coronary branches. The intertrabecular spaces of the spongy myocardium were lined with a continuous layer of endothelial cells, thus resembling the microscopical appearance of myocardium of adult cold-blooded vertebrates rather than the embryonic phase of myocardial development of warm-blooded animals.

PMID: 1147832

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A Mystery of Spongy Myocardium

Z Kardiol. 1984 Dec;73(12):786-8.

[Echocardiographic detection of persistent myocardial sinusoids].

[Article in German]
Engberding R, Bender F.

Abstract

In a 33-year-old woman the diagnosis of isolated persistent myocardial sinusoids could be e
ventriculography. This anomaly has been reported in infants with atresia of semilunar valves
with anomalies of the coronary vessels. In adults myocardial sinusoids have only been obs
arteries. To our knowledge, no other case of severe cardiac disease due to isolated myoca

PMID: 6441365

Identification of a Rare Congenital Anomaly of the Myocardium by Two-Dimensional Echocardiography: Persistence of Isolated Myocardial Sinusoids

ROLF ENGBERDING, MD
FRANZ BENDER, MD

Engberding R, Bender F. Am J Cardiol. 1984;53:1733–4.

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A Mystery of Spongy Myocardium

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

Circulation **1990;82:507–513**

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PII S0735-1097(00)00755-5

Long-Term Follow-up of 34 Adults With Isolated Left Ventricular Noncompaction: A Distinct Cardiomyopathy With Poor Prognosis

Erwin N. Oechslin, MD, Christine H. Attenhofer Jost, MD, Jerry R. Rojas, MD, Philipp A. Kaufmann, MD, Rolf Jenni, MD, MSEE

Zurich, Switzerland

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A Mystery of Spongy Myocardium

CASE REPORT

KL Tsui 徐健霖
KK Chan 陳國強
TC Leung 梁達智
KH Lam 林家慶
SK Li 李樹堅

Isolated ventricular non-compaction presenting with ventricular tachycardia

出現心室過速的單純性心肌致密化不全

Isolated ventricular non-compaction is a rare congenital cardiomyopathy, manifested morphologically as prominent myocardial trabeculations and deep inter-trabecular recesses that communicate with the ventricular cavity. Heart failure is the most common presenting condition. Other manifestations include arrhythmia and cardioembolic events. This report is illustrative of isolated ventricular non-compaction in a 78-year-old woman. The diagnosis was made when she presented with ventricular tachycardia many years after a stroke. She subsequently underwent implantation of a cardioverter-defibrillator. This report documents an uncommon presentation of this disease entity in the oldest patient at presentation as yet reported in the literature.

單純性心肌致密化不全是一種罕見的先天性心肌症，形態學上顯示心室內粗亂未致密化的肌小梁及深陷的小梁隱窩。心臟衰竭是最常見的徵狀。其他病徵包括心律失常和心臟栓塞。本報告報導了一名78歲婦女的單純性心肌致密化不全。患者中風多年後出現心動過速，由此診斷為患上此病。她隨後植入心臟復律及纖顫器。本報告記錄現有文獻中患上此病的最年老患者及其罕有病徵。

Hong Kong Med J 2003;9:137-40

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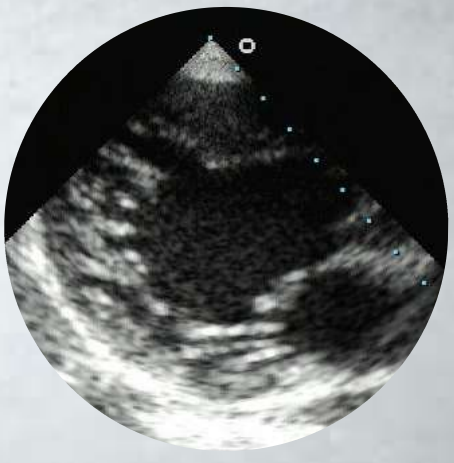
A Mystery of Spongy Myocardium

Prominent trabeculations & deep intertrabecular recesses



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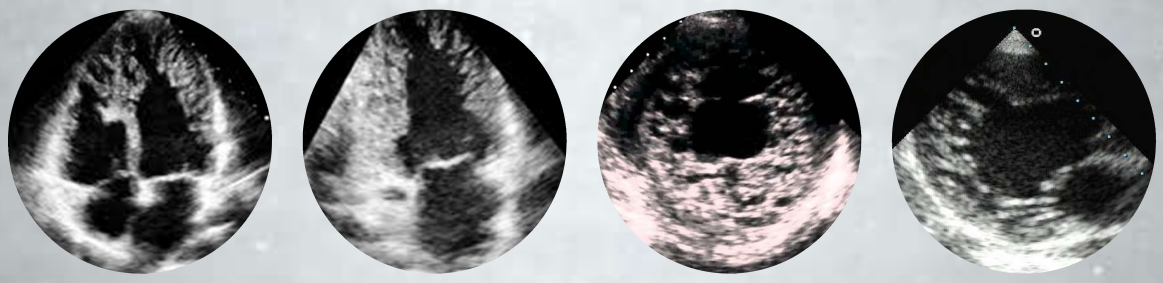
A Mystery of Spongy Myocardium

Left Ventricular Non-Compaction (LVNC)



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Is it Spongy?

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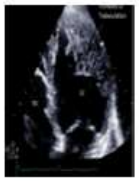
LVNC: Diagnosis - Echo

	Chin et al. (17)	Jenni et al. (1,18)	Stöllberger et al. (20)
Patients (n)	8	34	62
Description of criteria	2-layered structure with an epicardial compacted and endocardial noncompacted layer (Later revised to include a ratio)	2-layered structure with a compacted epicardial and noncompacted endocardial layer Color Doppler evidence of intertrabecular recesses supplied by intraventricular blood Absence of coexisting cardiac structural abnormalities	>3 trabeculations protruding from LV wall apically to papillary muscle in 1 imaging plane (Later revised to include ratio and a 2-layered myocardium)
Cardiac phase	End-diastole	End-systole	End-diastole
Ratio*	X/Y ≤ 0.5	NC/C ≥ 2	NC/C ≥ 2
			

Gati S. J Am Coll Cardiol Img 2014;7:1266–75

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LVNC: Diagnosis - Echo

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			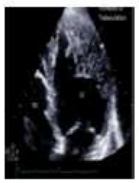

Gati S. J Am Coll Cardiol Img 2014;7:1266–75

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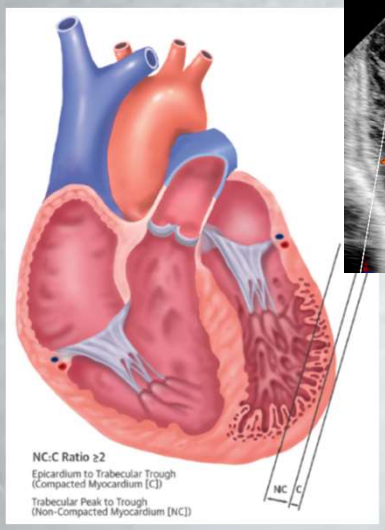
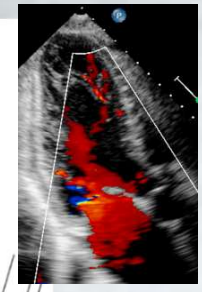
LVNC: Diagnosis - Echo

Jenni criteria





- Prominent trabeculations and deep recesses
- Involving mid-lateral, apical & mid-inferior regions of LV
- NC/C >/= 2 at end-systole
- Perfused inter-trabecular recesses on color Doppler

Jenni R, et al. Heart 2001;86:666-71
Figure from Hussein A, et al. J Am Coll Cardiol 2015;66:578-85

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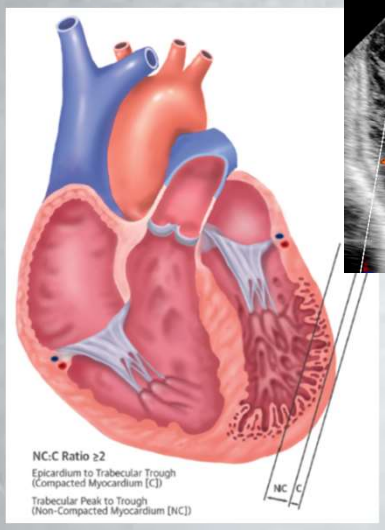
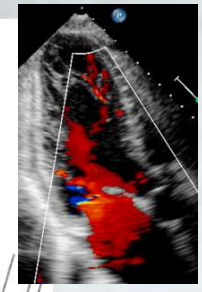
LVNC: Diagnosis - Echo

Jenni criteria





- Prominent trabeculations and deep recesses
- Involving mid-lateral, apical & mid-inferior regions of LV
- NC/C >/= 2 at end-systole
- Perfused inter-trabecular recesses on color Doppler

Proposed extra criteria:

- Max C-thickness at systole < 8mm

Gebhard, et al. J Am Soc Echocardiogr 2012

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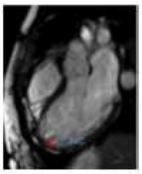
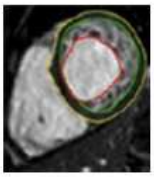
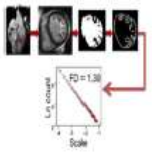
LVNC: Diagnosis - CMR

	Petersen et al. (33)	Jacquier et al. (34)	Captur et al. (38)
Patients (n)	7	16	30
Description of criteria	2-layered structure with a compacted epicardial and noncompacted endocardial layer Images from horizontal and long-axis views at points of prominent trabeculations	Calculated total LV trabeculated mass from SSFP short axis; papillary muscles excluded from trabeculated mass Myocardial mass	Global LV trabecular complexity as a continuous variable termed fractal dimension 2D space is divided into a grid of boxes and skeletonized data within are calculated for 4 different-sized grids The exponent of line of best fit across the points on log-log plot of box counts represents fractal dimension
Cardiac phase	End-diastole	End-diastole	–
Ratio*	NC/C >2.3	LV trabecular mass >20%	FD ≥1.30
			

Gati S. J Am Coll Cardiol Img 2014;7:1266–75

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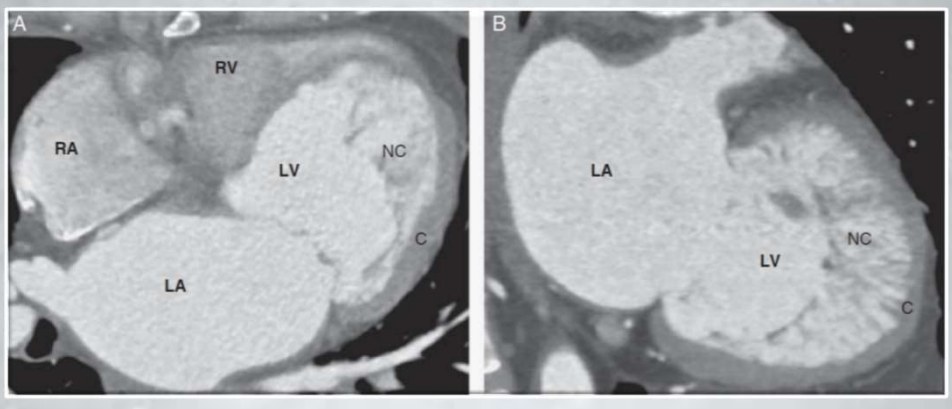
LVNC: Diagnosis - CT



J Thorac Imaging 2014;29:60–66

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LVNC: Diagnosis

Limitations

No universally accepted diagnostic criteria

- Criteria derived from small cohorts
- Trabeculations present commonly in normal individuals and in heart failure patients (8.3% & 23.6% in one study, *Kohli SK, EHJ 2008*)

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LVNC: Diagnosis

Other Non-Diagnostic Findings on Echo / Imaging

- Reduced global LV systolic function
- Diastolic dysfunction
- LV thrombi
- Abnormal or absence of well-defined papillary muscles
- RV involvement / RV dysfunction
- Evidence of fibrosis by late gadolinium enhancement (LGE) on CMR

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LVNC: Diagnosis

Associated with Other Congenital Abnormalites

- Congenital RVOT/LVOT abnormalities
  e.g. pulm atresia, TOF, coarctation of aorta
- Ebstein anomaly
- ASD, VSD, PDA
- Congenitally corrected transposition
- Congenital neuromuscular disease

Isolated LVNC = absence of other cardiac and non-cardiac congenital abnormalites

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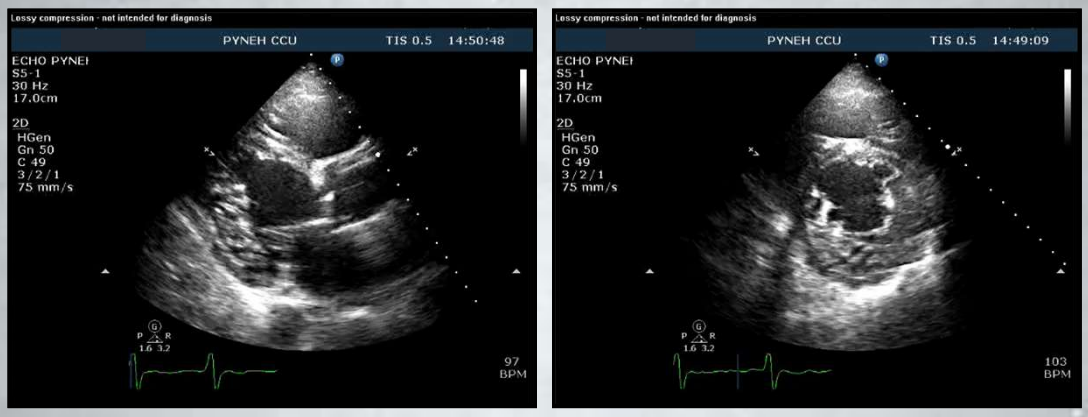
M/65 c/o AF, APO



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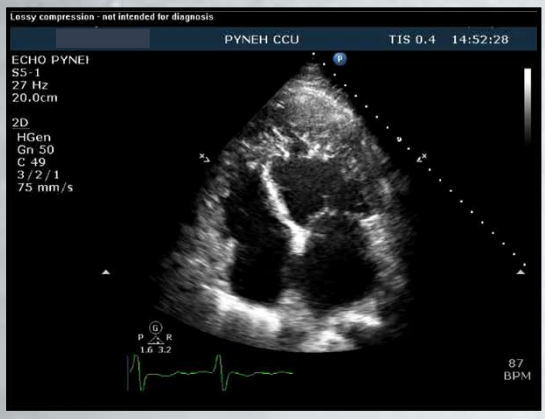
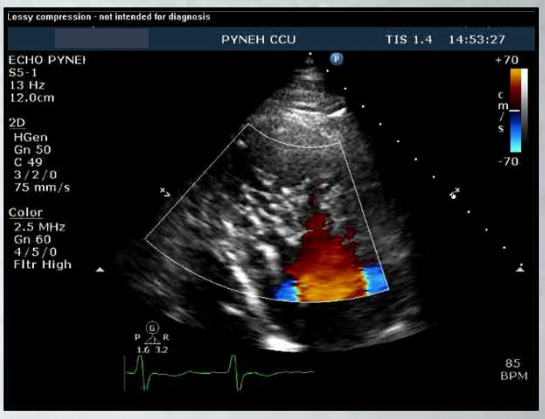
M/65 c/o AF, APO





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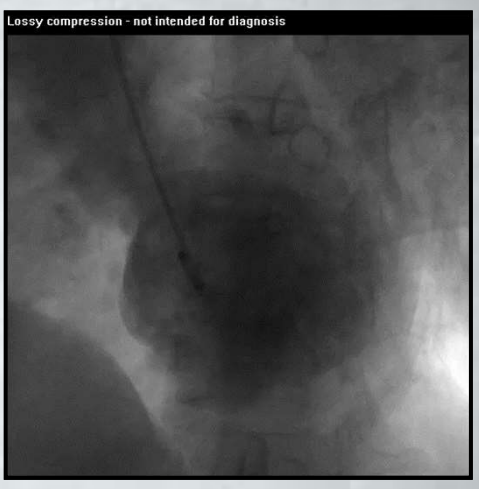
M/65 c/o AF, APO



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Why Is It Spongy ?

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LV Trabeculation to Compaction in Fetal Heart Development

The myocardium becomes compacted between 5th & 8th week
From basal segments to the apex
From epicardium to endocardium

Sedmera D, et al. Anat Rec 2000;258:319-337

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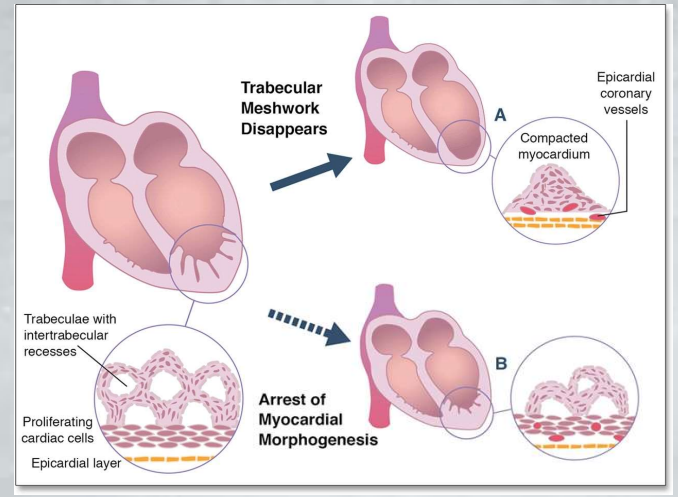
Pathogenesis: LVNC as Congenital Disease



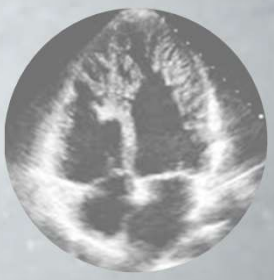


Diagram adapted from: Gati S. JACC Cardiovascular Imaging 2014.

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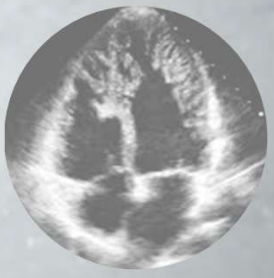
Pathogenesis: LVNC as Acquired Phenotype



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Pathogenesis: LVNC as **Acquired** Phenotype

Increased left ventricular trabeculation in highly trained athletes: do we need more stringent criteria for the diagnosis of left ventricular non-compaction in athletes?

Sabiha Gati,[1,2] Navin Ch
Vasileios F Panoulas,[4] S
Michael Papadakis,[1] Fra

Heart 2013;**99**:401–408.

- 1146 athletes Vs 415 healthy controls
- Increased trabeculations: 18.3% Vs 7.0% (p</= 0.0001)
- Fulfill LVNC criteria: 8.1% Vs 0%
- No adverse event on FU ~ 4 years

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Pathogenesis: LVNC as **Acquired** Phenotype

Left ventricular noncompaction in patients with β-thalassemia: Uncovering a previously unrecognized abnormality

Antonio Piga,[1]* Filomena Longo,[1] Khaled M. Musallam,[2] Andrea Veltri,[3] Francesca Ferroni,[4] Amedeo Chiribiri,[3,5] and Rodolfo Bonamini[4]

Am. J. Hematol. 87:1079–1083, 2012.

- transfusion-dependent patients with b-thalassemia
- 18/135 patients (13.3%) fulfilled CMR criteria for LVNC

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Pathogenesis: LVNC as **Acquired** Phenotype

Reversible De Novo Left Ventricular Trabeculations in Pregnant Women

Implications for the Diagnosis of Left Ventricular Noncompaction in Low-Risk Populations

Sabiha Gati, BSc (Hons), MRCP; Michael Papadakis, MRCP, MD; Nikolaos D. Papamichael, MD; Abbas Zaidi, MRCP, MD; Nabeel Sheikh, BSc (Hons), MRCP; Matthew Reed, BSc; Rajan Sharma, MD, FRCP; Baskaran Thilaganathan, BSc (Hons), PhD, FRCOG; Sanjay Sharma, BSc (Hons), MD, FRCP, FESC

Circulation 2014;130;475-483

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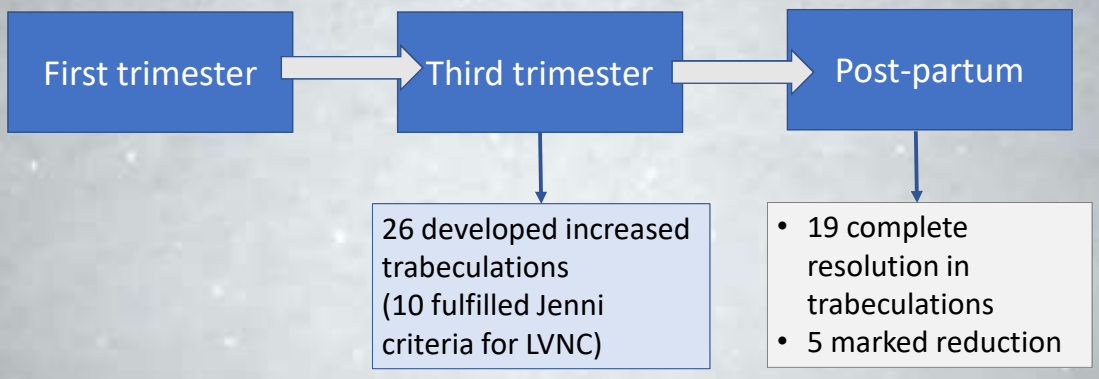
Pathogenesis: LVNC as **Acquired** Phenotype

102 pregnant women; longitudinal echo study



Circulation 2014;130;475-483

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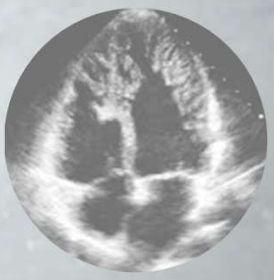
Pathogenesis: LVNC as Acquired Phenotype

Postulation…

A phenotypic response to high preload & afterload



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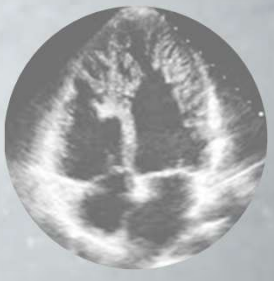
Pathogenesis: LVNC as Genetic Disease



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Pathogenesis: LVNC as Genetic Disease

Major Gene Mutations Associated with LVNC and Their Overlap With Other Cardiac Disorders

Disorder	TAZ-G4.5 Mutation	DTNA Mutation	Z-Band Mutation	FKBP12 Mutation	LMNA Mutations	NKX2.5, TBX5, CSX Mutations	ACTC, TNNT2, MYH7 Mutation	SCN5A Mutation	HCN4 Mutation
LVNC	×	×	×	×	×	×	×	×	×
Ventricular/atrial septal defect		×		×		×			
Arrhythmogenic right ventricular cardiomyopathy				×					
Dilated cardiomyopathy	×		×	×	×		×		
Hypertrophic cardiomyopathy							×		
Other cardiomyopathies*	×		×			×		×	
Other conduction abnormalities†					×	×	×	×	×
Tetralogy of Fallot						×			
Ebstein anomaly						×			
Brugada syndrome								×	
Romano-Ward syndrome								×	

*X-linked infantile cardiomyopathy, X-linked endocardial fibroelastosis, hypoplastic left heart syndrome. †Bundle blocks, atrioventricular nodal blocks, tachyarrhythmias, bradyarrhythmias.

ACTC = alpha-cardiac actin (24); CSX = cardiac specific gene located on 5q (65,66); DTNA = alpha-dystrobrevin gene, transition C to T mutation, located on 18q12 (19); FKBP12 = responsible for release of calcium from sarcoplasmic reticulum via ryanodine receptor (67); HCN4 = hyperpolarization-activated cyclic nucleotide channel 4 (68); LMNA = lamin A/C related sequence located on 1q22 (69); LVNC = left ventricular noncompaction; MYH7 = B-myosin heavy chain (23-25); NKX2.5 = homeobox protein located on chromosome 5 (65,66); SCN5A = human cardiac sodium channel alpha-subunit gene (70); TAZ-G4.5 = encodes tafazzin located on Xq28, (18,19,71); TBX5 = T-box transcription factor located on chromosome 12 (65,66); TNNT2 = cardiac troponin T (24); ZASP = Z-band alternatively spliced PDZ motif-containing protein on 10q22.2-q23.3 (72).

Hussein A, et al. JACC 2015.

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Pathogenesis: LVNC as Genetic Disease

- Positive genetic testing in 40-50%
- Family Hx of LVNC in 12-50%
- Autosomal dominant (more common), X-linked or autosomal recessive

Hussein A, et al. JACC 2015.

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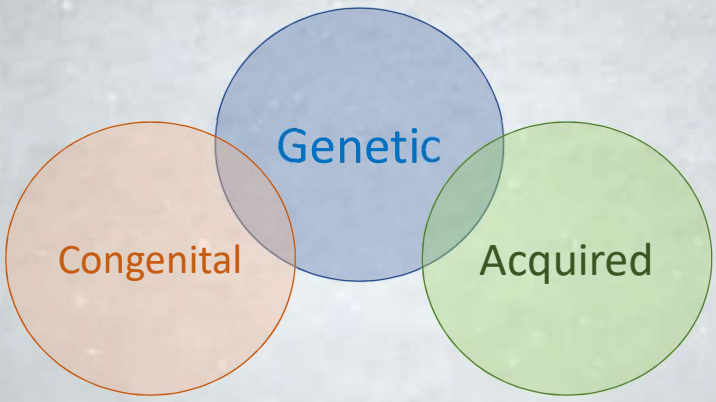
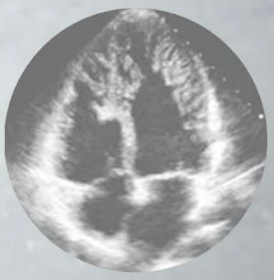
Pathogenesis

LVNC: A Phenotype





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How Often Is Spongy

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Prevalence

- Difficult to determine, due to:
  - Lack of standard diagnostic criteria
  - Depending on the population studied
- 0.014% - 1.3% in echo series
- 3-4% in heart failure series

JACC 2015;66:578-85.
Lancet 2015; 386: 813–25

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Clinical Features

Asymptomatic

- On screening
- ECG abnormalities
- Echo for any reason

ECG abnormality	Prevalence
Atrial enlargement	19%
Atrioventricular block I degree	15%
Right Bundle Branch Block	3-4%
Left Bundle Branch Block	15-44%
Left ventricular hypertrophy	18-41%
T wave inversion	16-41%
ST segment abnormalities	9-51%
WPW (only pediatric)	8-17%
Q waves	9%
Left axis deviation	9%
Prolonged QT interval	9-52%
Poor R wave progression	7%

Caselli, et al. Am J Cardiol 2015;116:801-808

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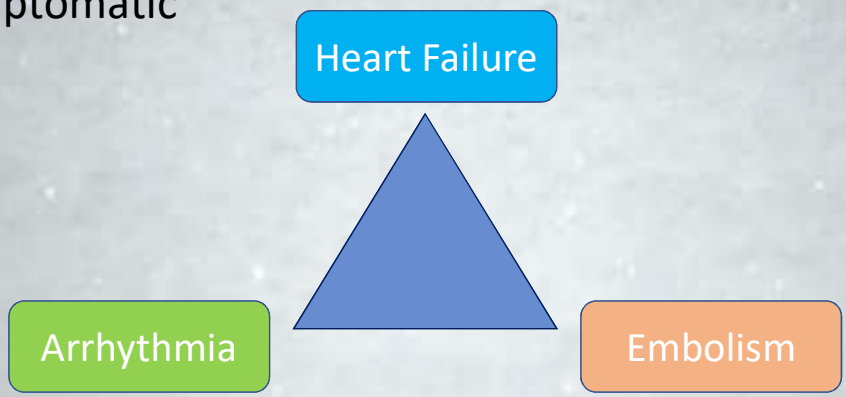
Clinical Features

Symptomatic



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Clinical Features

Symptomatic

Heart Failure

- Most common presentation
- 30-53% on FU x 2.3-3.8 years
- HFrEF more common
- May be HFpEF or HRmrEF

Thavendiranathan, et al. Heart 2013.

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Clinical Features

Symptomatic

Arrhythmia

- Sustained VT: 0-9%
- NSVT: 20-33% over 2.3-3.8 yrs
- AF 6-26%
- SCD 1-9%
- Heart block

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Clinical Features

Symptomatic

- Predisposed by thrombus in intertrabecular recesses (?)
- Risk factors: LV systolic dysfunction, AF & Hx of thromboembolism
- ~5% over 2.3-3.8 years in most series

Embolism

Thavendiranathan, et al. Heart 2013.

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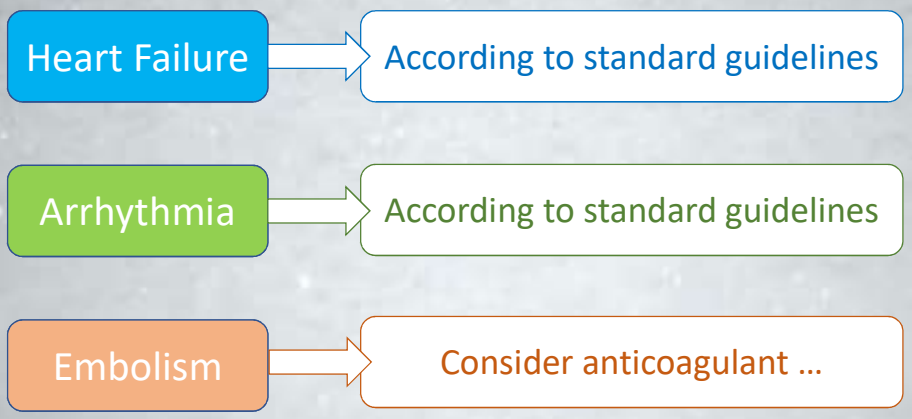
Management



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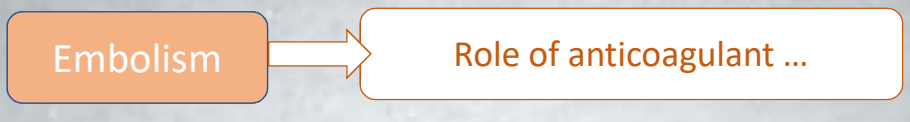
Management



- AF fulfilling standard criteria
- Hx of cardioembolic event
- Evidence of intracardiac thrombus

To consider:

- AF not fulfilling standard criteria
- Impaired LVEF < 40%

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Management:
Family Screening & Genetic Studies

- Screening of first-degree relatives: History, P/E, ECG, Echo, CK
- Family history for 3 generations
- Role of routine genetic testing not established

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Left Ventricular Non-Compaction in Athletes: To Play or Not to Play

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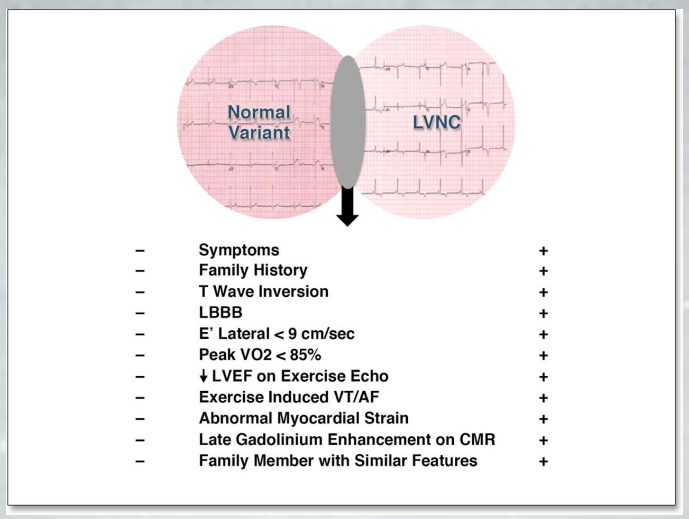

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Recommendation on Competitive Athletes

AHA/ACC Scientific Statement 2015

Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 3: Hypertrophic Cardiomyopathy, Arrhythmogenic Right Ventricular Cardiomyopathy and Other Cardiomyopathies, and Myocarditis

A Scientific Statement From the American Heart Association and American College of Cardiology

Barry J. Maron, MD, FACC, Chair; James E. Udelson, MD, FAHA, FACC; Robert O. Bonow, MD, MS, FAHA, MACC; Rick A. Nishimura, MD, FAHA, MACC; Michael J. Ackerman, MD, PhD; N.A. Mark Estes III, MD, FACC; Leslie T. Cooper, Jr, MD, FAHA, FACC; Mark S. Link, MD, FACC; Martin S. Maron, MD, FACC; on behalf of the American Heart Association Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology, Council on Cardiovascular Disease in the Young, Council on Cardiovascular and Stroke Nursing, Council on Functional Genomics and Translational Biology, and the American College of Cardiology

ESC European Society of Cardiology — European Heart Journal (2019) 40, 19–33 doi:10.1093/eurheartj/ehy730 — 2018 — SPECIAL ARTICLE Sports cardiology

Recommendations for participation in competitive and leisure time sport in athletes with cardiomyopathies, myocarditis, and pericarditis: position statement of the Sport Cardiology Section of the European Association of Preventive Cardiology (EAPC)

Antonio Pelliccia[1]*, Erik Ekker Solberg[2], Michael Papadakis[3], Paolo Emilio Adami[1,4], Alessandro Biffi[1], Stefano Caselli[5], Andrè La Gerche[6], Josef Niebauer[7], Axel Pressler[8,9], Christian M. Schmied[10], Luis Serratosa[11,12], Martin Halle[8,9], Frank Van Buuren[13], Mats Borjesson[14,15], Francois Carrè[16], Nicole M. Panhuyzen-Goedkoop[17,18], Hein Heidbuchel[19,20], Iacopo Olivotto[21], Domenico Corrado[22], Gianfranco Sinagra[23], and Sanjay Sharma[24]

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Recommendation on Competitive Athletes

- Impaired LV systolic function
- Significant atrial or ventricular arrhythmias
- Hx of syncope

No

Only restrict sports in which occurrence of syncope may cause serious harm or death (such as rock climbing, scuba diving, or car/motor racing)

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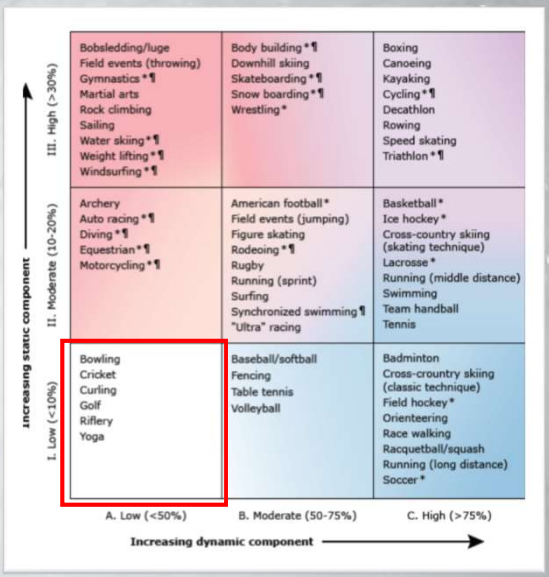
Recommendation on Competitive Athletes

- Impaired LV systolic function
- Significant atrial or ventricular arrhythmias
- Hx of syncope

Yes

Restricted to low intensity (class IA) sports



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Spongy

How Will It Be?

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Prognosis

- High mortality in early series e.g. 35% on mean FU 3.7 years
  (Oechslin EN, et al. J Am Coll Cardiol 2000)
- Lower mortality in more recent series 2-15%
  (Thavendiranathan, et al. Heart 2013)
- In a pooled series, mortality 14% during 39 months; ~one half SCD
  (Bhatia NL, et al. J Cardiac Fail 2011)
- Asymptomatic patients have overall good prognosis

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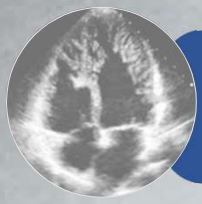
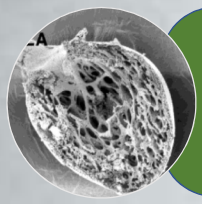
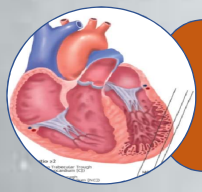


Non-compacted myocardium with prominent trabeculations & deep intertrabecular recesses



Incomplete intrauterine compaction of myocardium
Acquired causes
Genetic causes



Echo & MRI criteria proposed yet no standard criteria
Common: NC/C end-systole >/= 2

Left Ventricular Non-Compaction (LVNC)

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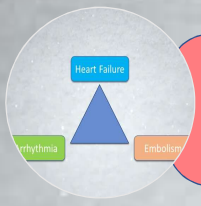
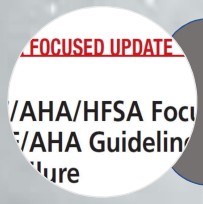


Asymptomatic, or triad of heart failure, arrhythmias, and embolic events



Rx as for other cardiomyopathy
Anticoagulant
Family screening

Left Ventricular Non-Compaction (LVNC)

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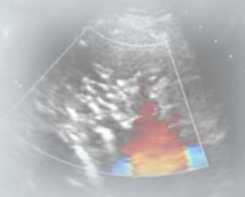
Thank You!



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