ECOCARDIOGRAFIA 2015
XVII Congresso Nazionale SIEC
Hotel Royal Continental
Napoli, 16-18 Aprile 2015

MIOCARDIO NON COMPATTATO: SOPRA O SOTTOVALUTATO?

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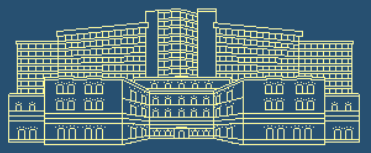

H. Valduce 1879

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CONFLITTI D'INTERESSI: NESSUNO

MIOCARDIO NON COMPATTATO: SOPRA O SOTTOVALUTATO?

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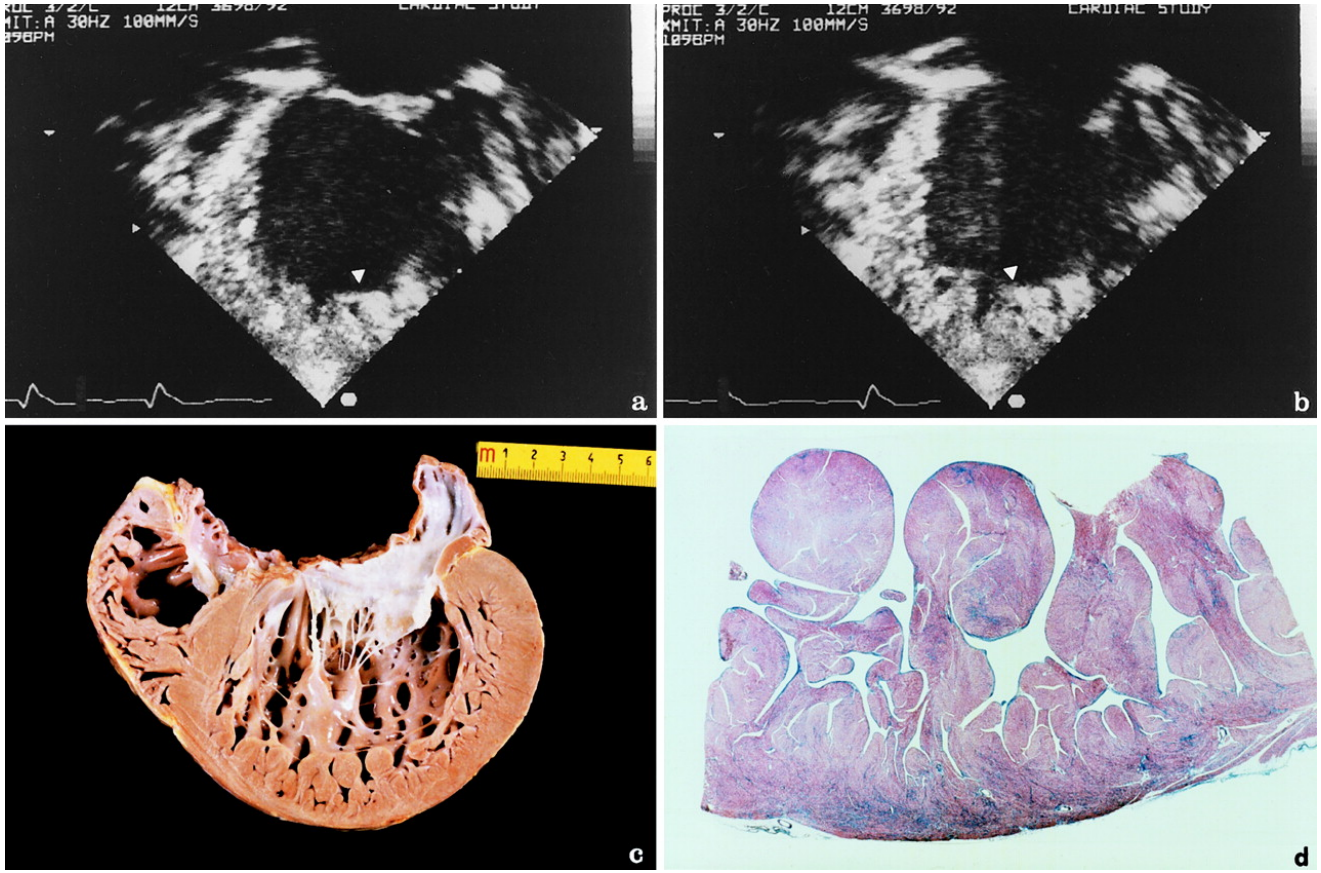
MIOCARDIO NON COMPATTO



A. Angelini, P. Melacini, F. Barbero, G. Thiene. Evolutionary Persistence of Spongy Myocardium in Humans. *Circulation.* 1999;99:2475.

PATOGENESI
E ANATOMIA PATOLOGICA I

- Durante il primo mese di vita fetale, prima dello sviluppo dell'albero coronarico, il miocardio embrionale è costituito da una rete "spugnosa" di fibre intrecciate con profondi recessi intertrabecolari.

- Questi recessi comunicano con le camere ventricolari che vengono irrorate attraverso gli spazi intertrabecolari medesimi (vascolarizzazione degli animali a sangue freddo).

PATOGENESI
E ANATOMIA PATOLOGICA II

Durante la vita fetale (5ª → 8ª settimana di vita fetale) si verificano due processi paralleli:

1. Graduale "compattazione" del miocardio con trasformazione dei recessi intertrabecolari in capillari.
2. Sviluppo della circolazione coronarica.

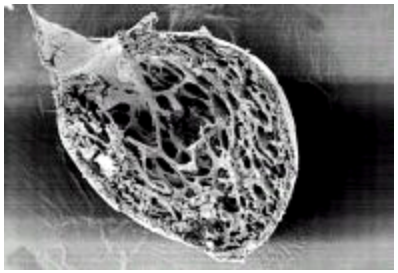
Il processo di compattazione progredisce

epicardio → endocardio

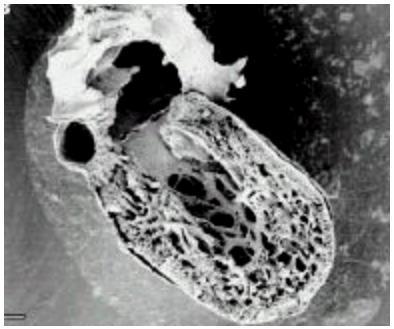
base → punta

setto → parete laterale

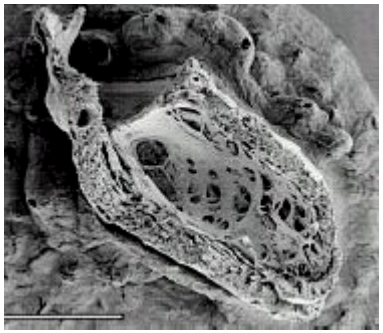
EMBRIOGENESI CARDIACA



Abundant fine trabeculae are present at six weeks.



The trabeculae start to solidify at their basal area, contributing to added thickness of the compact layer, at 12 weeks



The compact layer forms most of the myocardial mass after completion of compaction in the early fetal period.

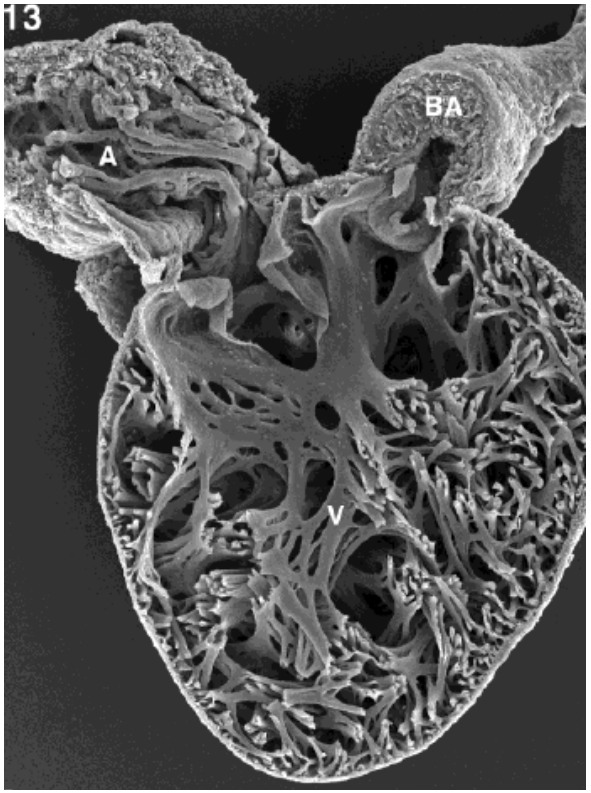
Semdera D et al, Developmental Patterning of the Myocardium Anat Rec 258;2000:319–337.

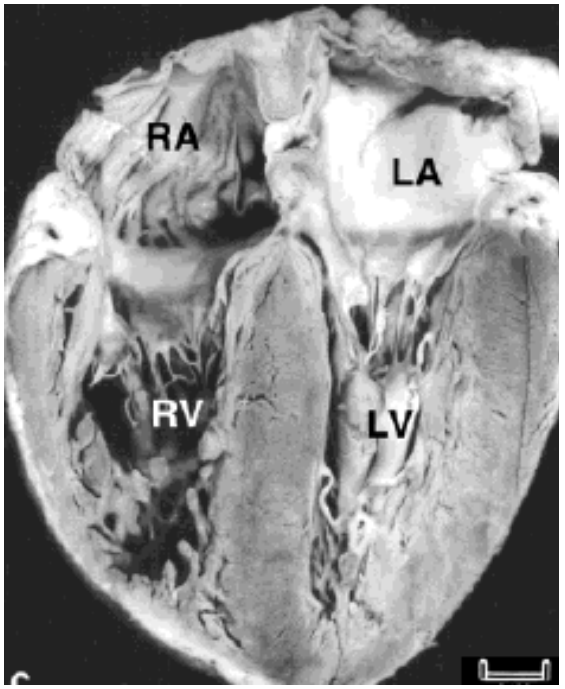
PATOGENESI
E ANATOMIA PATOLOGICA III

- Noncompaction of the ventricular myocardium" si riferisce ad un arresto del normale processo di compattazione delle fibre miocardiche. Ciò dà luogo alla persistenza di trabecolature ventricolari prominenti con ampi recessi intertrabecolari.

- Tale entità (detta anche "miocardio spugnoso") interessa principalmente il VS (il coinvolgimento associato del VD si ha in < 50% dei casi)

FILOGENESI CARDIACA



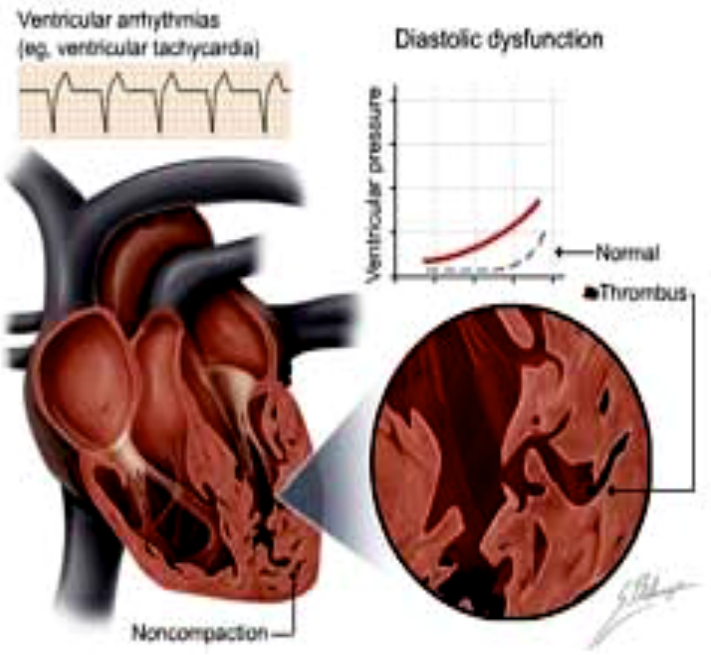


↑ Cuore di uomo adulto

← Cuore di pesce-zebra adulto

NVM: QUADRI CLINICI

- Scompenso cardiocircolatorio secondario a disfunzione sistolica/diastolica VS.
- Tachiaritmie (FA, aritmie ventricolari maligne → morte improvvisa), difetti di conduzione (BB), WPW.
- Eventi cardioembolici (FA,trombosi intratrabecolare).
- Nulla



La diagnosi viene fatta con metodiche di imaging, in primis con ecocardiografia

NVM: IMAGING

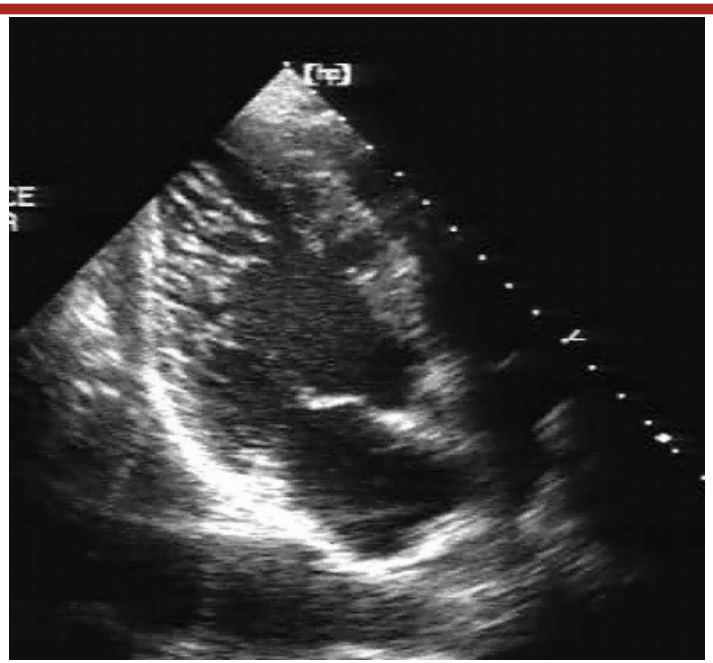
- Trabecolature multiple e prominenti.
- Multipli recessi intertrabecolari comunicanti con la camera ventricolare (Color Doppler - Contrasto).

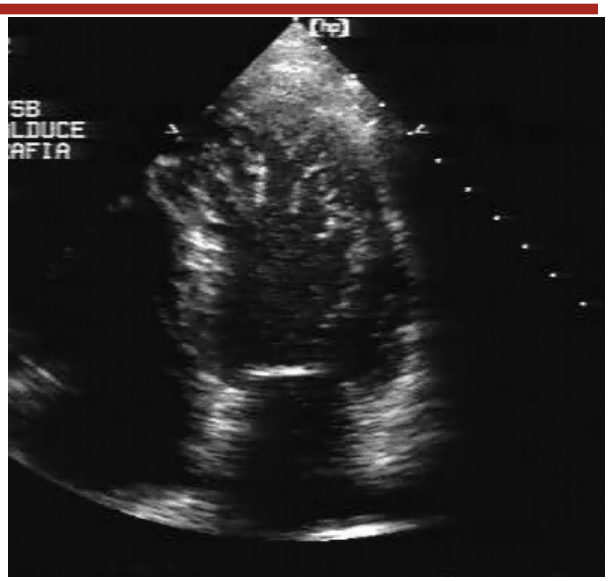
TALI REPERTI SONO MAGGIORMENTE RAPPRESENTATI NELLE PORZIONI MEDIO-APICALI DEI VENTRICOLI.

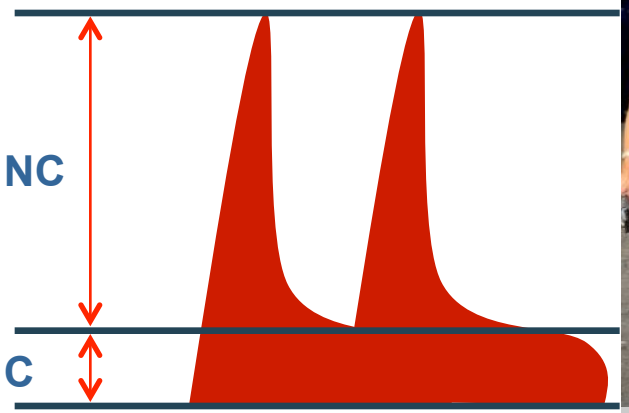
IL VS È SEMPRE INTERESSATO, IL VD PUÒ ESSERLO IN ASSOCIAZIONE

Diagnosi differenziale:
1) Accentuazione della normale trabecolatura (normalmente ≤ 3 trabecole) 2) CMP ipetrofica 3) CMP dilatativa 4) Trombo apicale VS

NVM: ECOCARDIOGRAFIA







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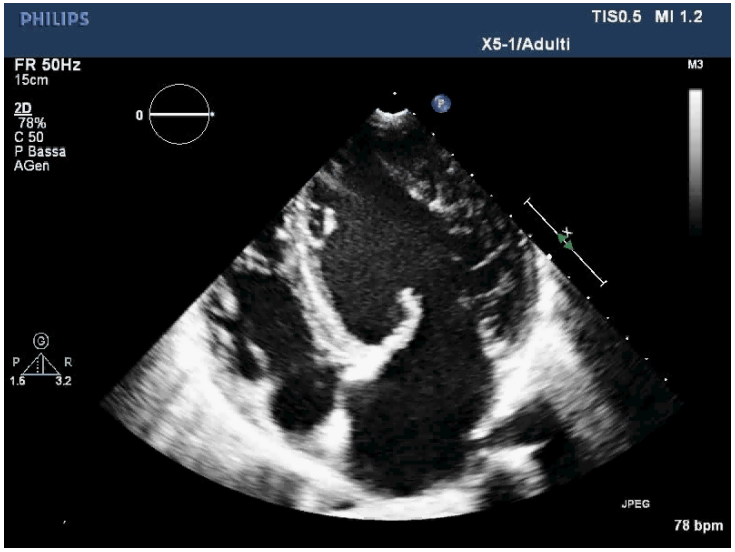

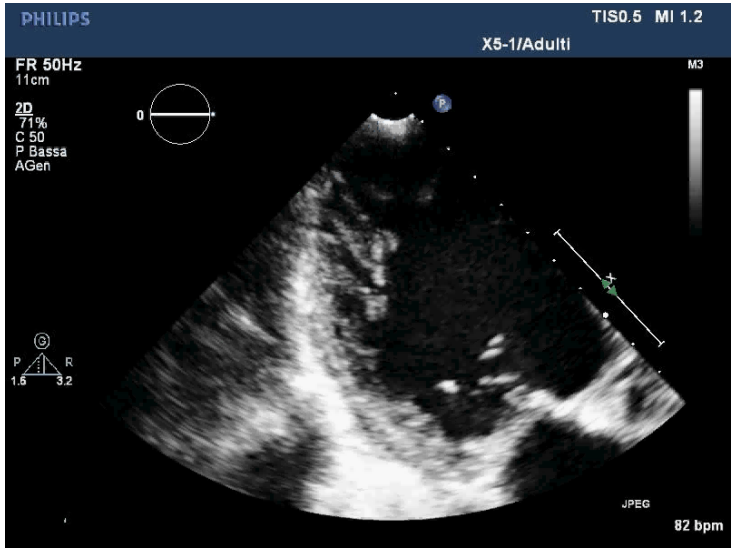

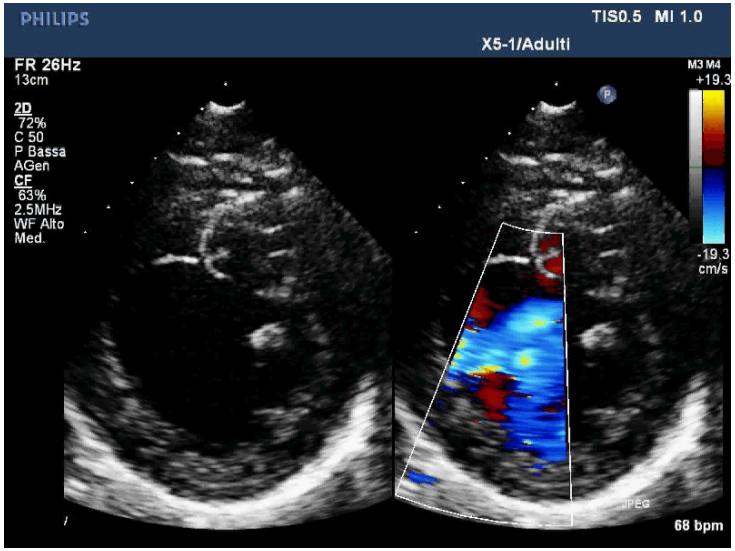

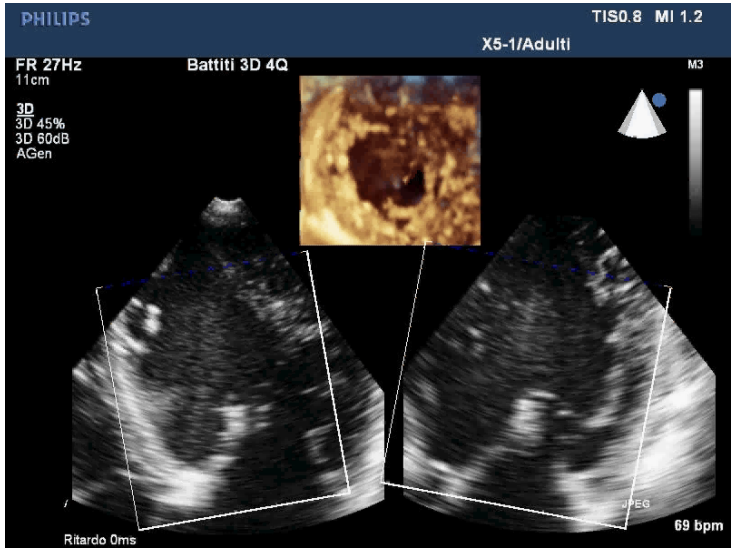

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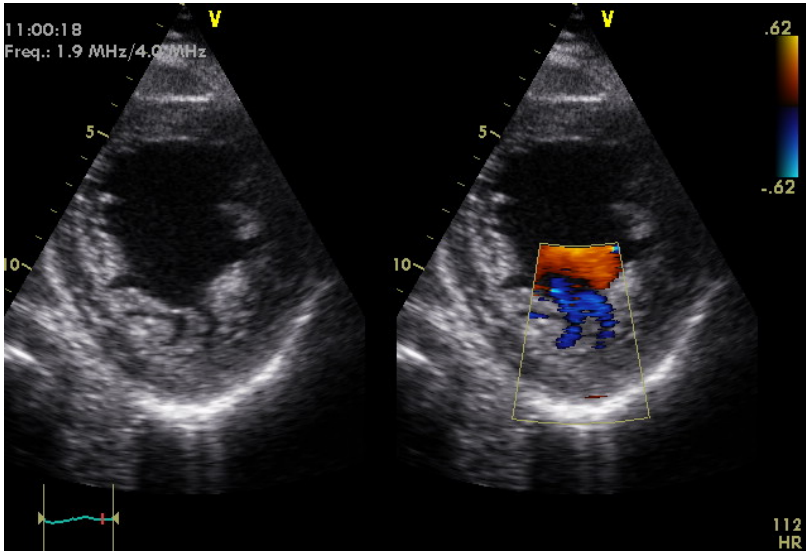
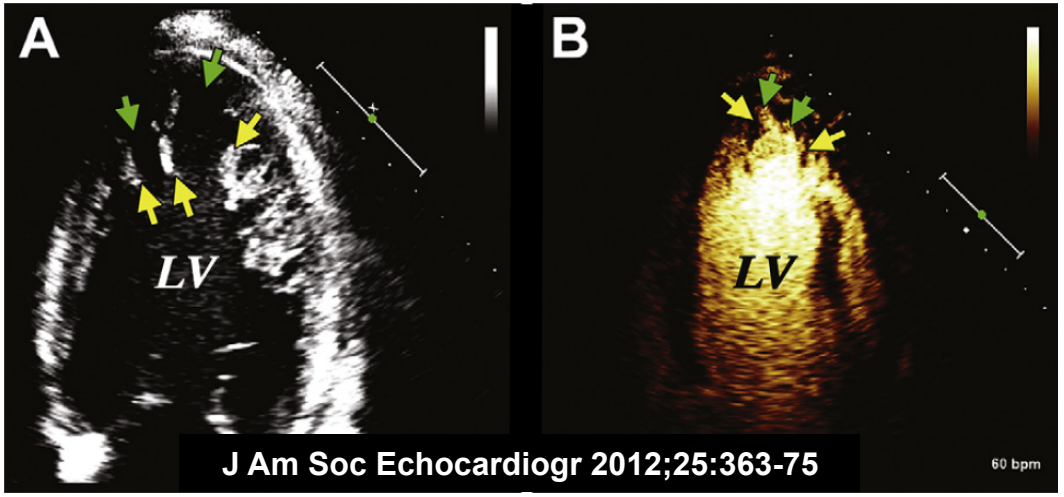
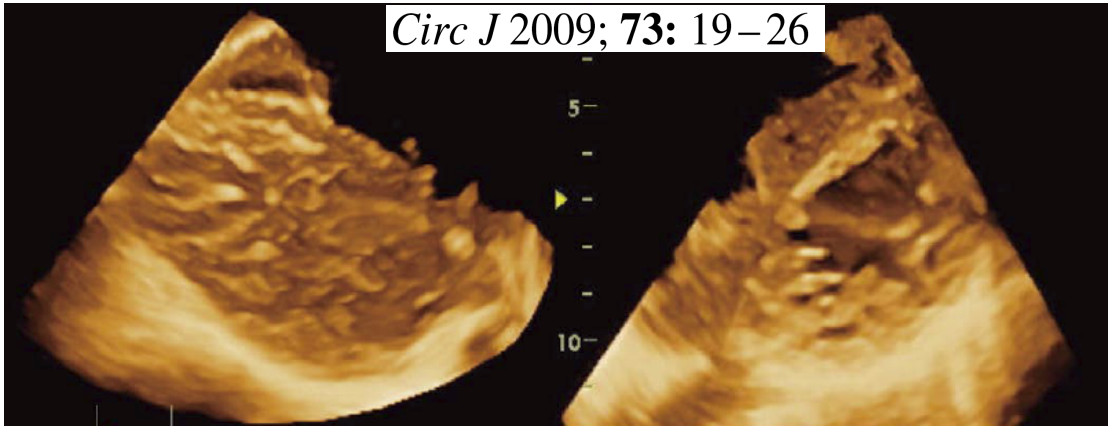
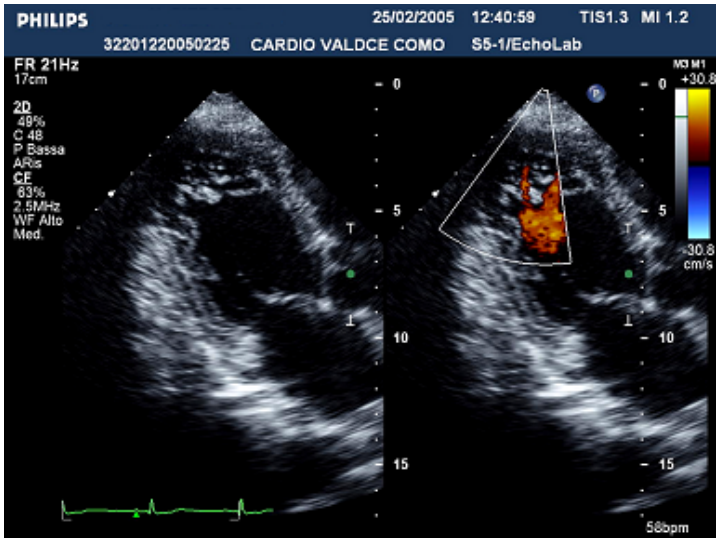








IL CONFINE TRA NORMALE E PATOLOGICO

MT Boyd et al. Frequency and location of prominent left ventricular trabeculations at autopsy in 474 normal human hearts: implications for evaluation of mural thrombi by two-dimensional echocardiography *J Am Coll Cardiol*, 1987; 9:323-326

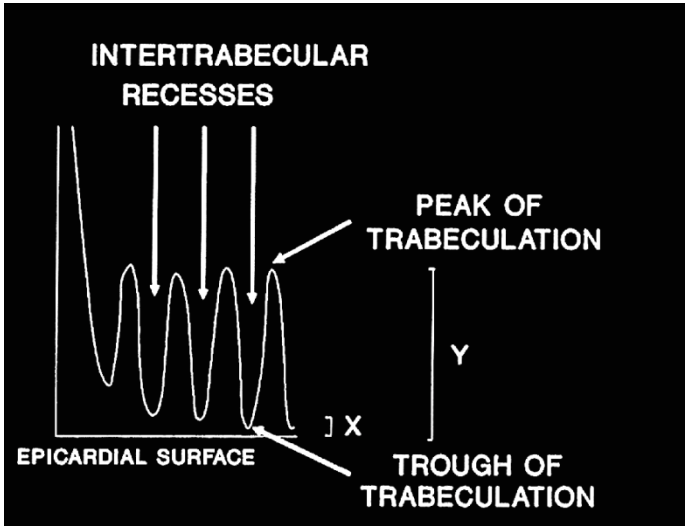
JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

~ 70% of autopsied healthy hearts show some degree of noncompaction

"Accordingly, prominent left ventricular trabeculations are considered to be common variants of the normal human heart. Their size, shape and location may lead to their being misinterpreted, possibly as mural thrombi, by two-dimensional echocardiography."

NVM: CRITERI DIAGNOSTICI ECOCARDIOGRAFICI

- **Criteri di Chin**: stima del rapporto tra X e Y; X = distanza dall'epicardio al fondo del recesso intertrabecolare Y = distanza dall'epicardio al picco delle trabecole.
- Un rapporto **telediastolico** X/Y ≤ 0.5 è considerato diagnostico.
- Questo criterio si focalizza sulle trabecole dell'apice VS (asse corto apicale o apicale 4 camere) e sullo spessore telediastolico della parete libera del ventricolo sinistro



Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. *Circulation* 1990;82:507-13

NVM: CRITERI DIAGNOSTICI ECOCARDIOGRAFICI

- **Criteri di Jenni**: una struttura del miocardio a due strati, una zona esterna sottile e compatta (C) ed una zona interna più spessa, non compatta (NC).
- Il rapporto tra le due zone viene calcolato in **telesistole** nella parasternale asse corto.
- Un rapporto NC/C > 2 è considerato diagnostico.
- Assenza di anomalie strutturali miocardiche associate
- Numerose trabecole e profondi recessi intertrabecolari.
- Recessi intertrabecolari perfusi dal sangue intraventricolare (Color Doppler o ecografia con mezzo di contrasto transpolmonare).

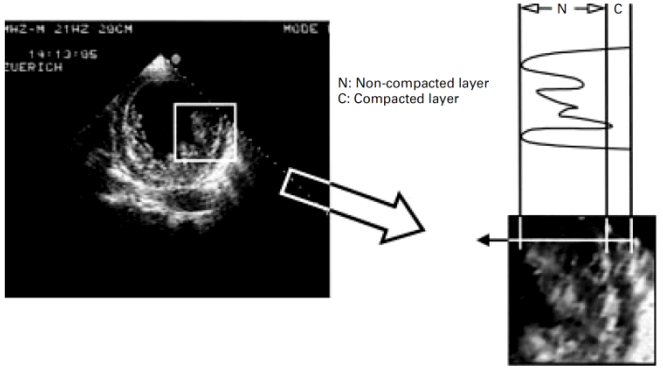
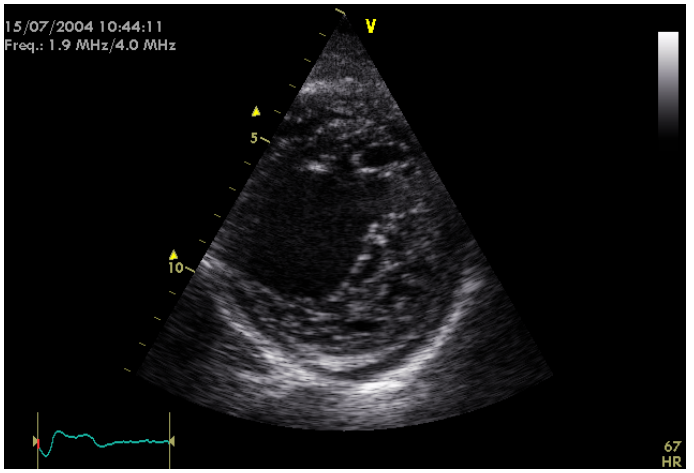


Figure 1 To quantify the extent of non-compaction at the site of maximal wall thickness the end systolic ratio of non-compacted to compacted thickness was determined. The two layers are best visualised at end systole as shown in this short axis view.



Jenni R, Oechslin E, Schneider J, Attenhofer Jost C, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left ventricularnon-compaction: a step towards classification as a distinct cardiomyopathy. *Heart* 2001;86:666-671

NVM: CRITERI DIAGNOSTICI ECOCARDIOGRAFICI

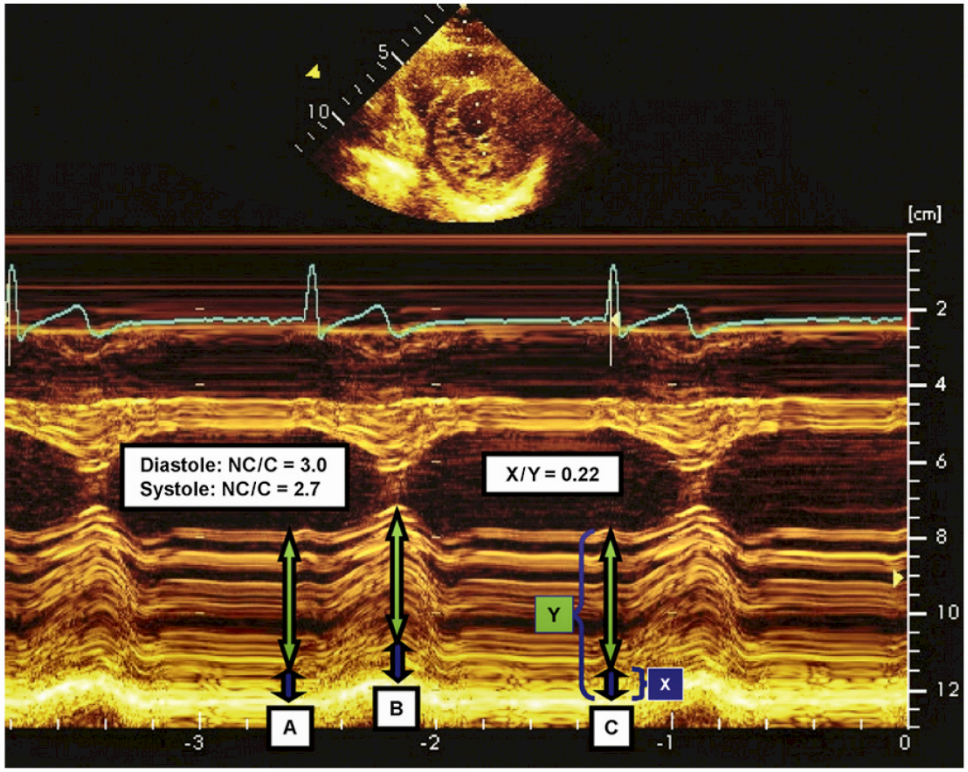


Figure 11 Two-dimensionally guided M-mode images illustrating the different diagnostic criteria of LVNC. (A) Our criteria (not validated): end-diastole: ratio of noncompacted (NC; *green arrows*) to compacted (C; *blue arrows*) myocardium = 3.0. Note that the NC myocardium has near identical thickness at end-systole and end-diastole, indicating an absence of radial thickening of NC myocardium. (B) Jenni criteria: end-systole: NC/C = 2.7. This end-systolic ratio of 2.7 is lower than the end-diastolic ratio because the C layer thickens radially at end-systole, while the NC myocardial thickness remains essentially unchanged, resulting in a reduced calculated ratio. (C) Chin criteria: end-diastole: compacted myocardium (X)/compacted plus noncompacted myocardium (Y) = 0.22.

J Am Soc Echocardiogr 2012;25:363-75

NVM: CRITERI DIAGNOSTICI ECOCARDIOGRAFICI

- **Criteri di Stollberger**: più di tre trabecolazioni che sporgono dalla parete ventricolare, distalmente rispetto al piano dei muscoli papillari, con la medesima ecogenicità della muscolatura ventricolare e visibili in una singola proiezione,.
- Recessi intertrabecolari perfusi dal sangue intraventricolare (Color Doppler o ecografia con mezzo di contrasto transpolmonare).

Stollberger C, Finsterer J, Blazek G. Left ventricular hypertrabeculation,noncompaction and association with additional cardiac abnormalities and neuromuscular disorders. *Am J Cardiol* 2002;90:899–902.

NVM: RIPRODUCIBILITA' DELLA DIAGNOSI ECOCG

LEFT VENTRICULAR NON-COMPACTION

Reproducibility of Echocardiographic Diagnosis of Left Ventricular Noncompaction

Susan F. Saleeb, MD, Renee Margossian, MD, Carolyn T. Spencer, MD, Mark E. Alexander, MD, Leslie B. Smoot, MD, Adam L. Dorfman, MD, Lisa Bergersen, MD, MPH, Kimberlee Gauvreau, ScD, Gerald R. Marx, MD, and Steven D. Colan, MD, *Boston, Massachusetts*

Background: Left ventricular noncompaction (LVNC) cardiomyopathy is variably defined by numerous trabeculations, deep intertrabecular recesses, and noncompacted-to-compacted (NC/C) ratio >2. Limited studies exist on the reproducibility of diagnosing LVNC.

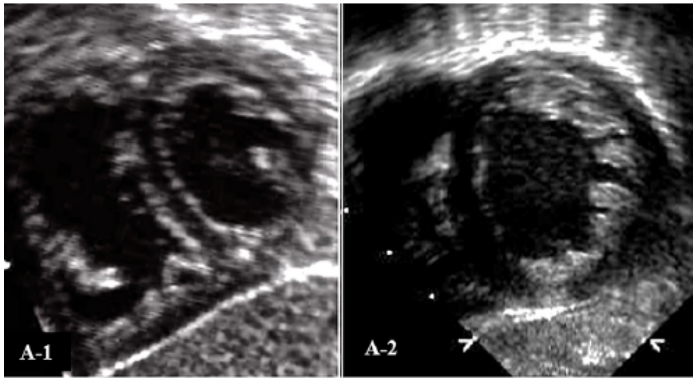
Methods: Clinical records of patients diagnosed with LVNC by echocardiography were reviewed. Blinded review of the index echocardiogram for all patients and a 1:1 match without LVNC was performed independently by two observers, measuring the number of trabeculations and the NC/C ratio.

Results: A total of 104 patients with LVNC were included in the study, 52 with no congenital heart disease (NCongHD) and 52 with congenital heart disease (CongHD). The duration of follow-up was 7.2 years (range, 0.5–23.1 years) for NCongHD and 8.2 years (range, 0–33.3 years) for CongHD. Agreement between observers in determining zero to three versus more than three trabeculations was 59% (NCongHD) and 73% (CongHD). Agreement in measuring an NC/C ratio ≤ 2 versus > 2 was 79% (NCongHD) and 74% (CongHD). Agreement with the original reader in diagnosing LVNC was 67%. There was no association between the number of trabeculations or the NC/C ratio and the likelihood of a major event. Patients with moderate or severe left ventricular dysfunction at the time of diagnosis were more likely to undergo cardiac transplantation or die compared with those with normal or mild dysfunction (NCongHD, 22% vs 0%, $P = .01$; CongHD, 39% vs 3%, $P = .001$).

Conclusions: The reproducibility of making measurements to diagnose LVNC by accepted criteria is poor. Heart transplantation and death are associated with significant ventricular dysfunction and not with increased trabeculations or NC/C ratios. (J Am Soc Echocardiogr 2012;25:194-202.)

Table 3 Change in phenotype over time

Phenotypic Change	NCongHD (n = 52)	CongHD (n = 52)
LV dilation developed	8	8
LV dilation resolved	8	2
LV hypertrophy developed	0	5
LV hypertrophy resolved	2	1
Number of trabeculations increased	2	3
Height of trabeculations increased	3	2
Height of trabeculations decreased	0	4
New segments of hypertrabeculation developed	2	1
Hypertrabeculation developed	0	3
Hypertrabeculation resolved	0	1



(A-1) A newborn with coarctation of the aorta and a ventricular septal defect before repair without evidence for LVNC. Three months after ventricular septal defect closure and arch repair, his myocardium changed in appearance (A-2), consistent with hypertrabeculation.

NVM: CONCORDANZA CRITERI DIAGNOSTICI ECOCG

- **La concordanza tra i tre metodi diagnostici è bassa**.
- In una popolazione di 199 pazienti con disfunzione sistolica VS afferenti ad un ambulatorio dello scompenso cardiaco il 23% soddisfacevano i criteri diagnostici di NVM
- Di questi, 79% soddisfacevano i criteri di Chin, 64% quelli di Jenni, 53% quelli della Stollberger.
- La sovrapposizione di tutti e tre i criteri si aveva nel 30% dei casi.

Table I Diagnostic criteria for left-ventricular non-compaction

1. Chin *et al.*[9]

LVNC is defined by a ratio of $X/Y \leq 0.5$

X = distance from the epicardial surface to the trough of the trabecular recess

Y = distance from the epicardial surface to peak of trabeculation

These criteria focus on trabeculae at the LV apex on the parasternal short axis and apical views, and on left-ventricular free-wall thickness at end-diastole

2. Jenni *et al.*[10]

(i) A two-layer structure, with a thin compacted layer and a thick non-compacted layer measured in end systole at the parasternal short-axis views

LVNC is defined by a ratio of $N/C>2$ where

N = non-compacted layer of myocardium

C = compacted layer of myocardium

(ii) Absence of co-existing cardiac structural abnormalities

(iii) Numerous, excessively prominent trabeculations and deep intratrabecular recesses

(iv) Recesses supplied by intraventricular blood on colour Doppler

3. Stollberger *et al.*[4]

(i) More than three trabeculations protruding from the left-ventricular wall, apically to the papillary muscles, visible in a single image plane

(ii) Intertrabecular spaces perfused from the ventricular cavity, visualized on colour Doppler imaging

Kohli SK, Pantazis AA, Shah JS, Adeyemi B, Jackson G, McKenna WJ, Sharma S, Elliott PM. Diagnosis of left-ventricular non-compaction in patients with left-ventricular systolic dysfunction: time for a reappraisal of diagnostic criteria? *Eur Heart J.* 2008;29:89-95.

NVM: NUOVI CRITERI ECOCG

ELSEVIER

European Journal of Heart Failure 10 (2008) 1088–1093

The European Journal of Heart Failure

www.elsevier.com/locate/ejheart

Left ventricular solid body rotation in non-compaction cardiomyopathy: A potential new objective and quantitative functional diagnostic criterion?

Bas M. van Dalen, Kadir Caliskan, Osama I.I. Soliman, Attila Nemes, Wim B. Vletter, Folkert J. ten Cate, Marcel L. Geleijnse *

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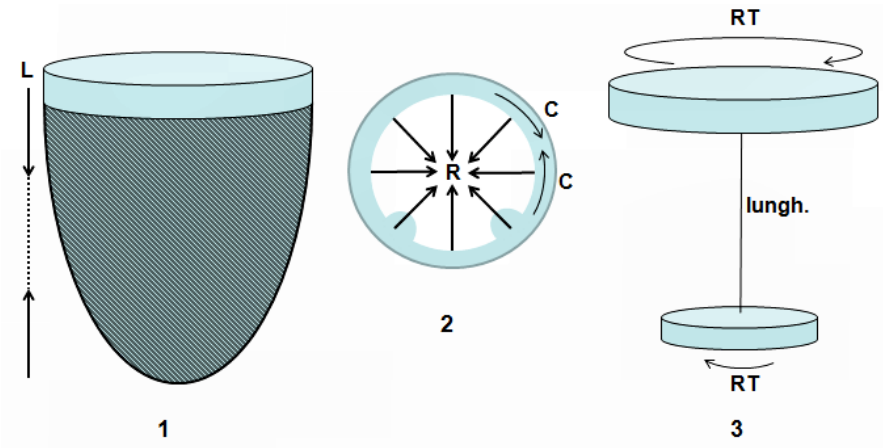
Received 2 May 2008; received in revised form 4 July 2008; accepted 20 August 2008
Available online 24 September 2008



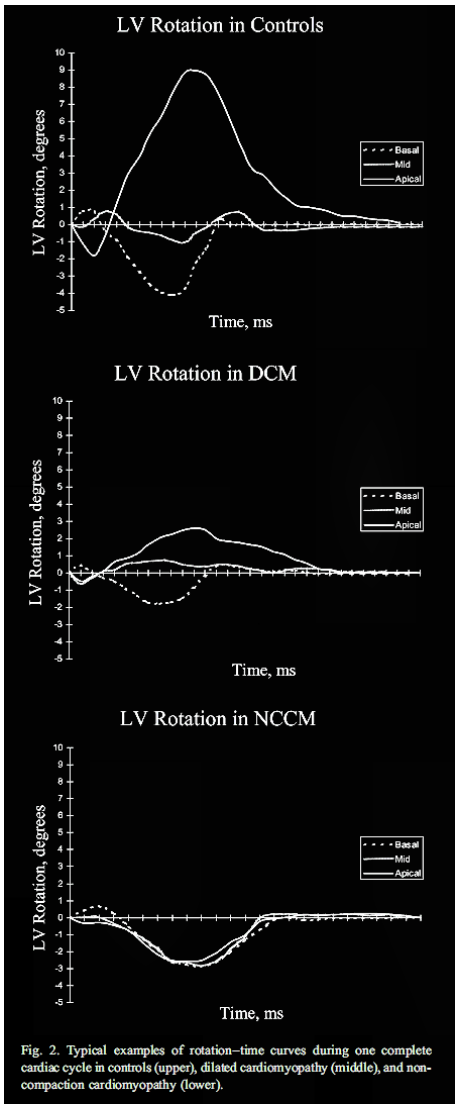


Fig. 2. Typical examples of rotation–time curves during one complete cardiac cycle in controls (upper), dilated cardiomyopathy (middle), and non-compaction cardiomyopathy (lower).

NVM: NUOVI CRITERI ECOCG

Reduced Left Ventricular Compacta Thickness: A Novel Echocardiographic Criterion for Non-Compaction Cardiomyopathy

Catherine Gebhard, MD, Barbara E. Stähli, MD, Matthias Greutmann, MD, Patric Biaggi, MD, Rolf Jenni, MD, MSEE, and Felix C. Tanner, MD, *Zurich, Switzerland*

Conclusions: Maximal systolic compacta thickness <8 mm is specific for LVNC and allows the differentiation of LVNC from normal hearts as well as those with myocardial thickening due to AVS. This observation may be particularly useful as an additional diagnostic criterion for preventing the overdiagnosis of LVNC.
(J Am Soc Echocardiogr 2012;25:1050-7.)

Three-Dimensional Echocardiographic Characterization of Patients with Left Ventricular Noncompaction

Stefano Caselli, MD, PhD, Camillo Autore, MD, Andrea Serdoz, MD, Daria Santini, MD, Maria Beatrice Musumeci, MD, Antonio Pelliccia, MD, and Luciano Agati, MD, *Rome, Italy*

Conclusions: Because of high spatial resolution and accuracy in volumetric quantification, three-dimensional echocardiography allows accurate measurement of the extent of noncompacted myocardium and identification of patients with LVNC.
(J Am Soc Echocardiogr 2012;25:203-9.)

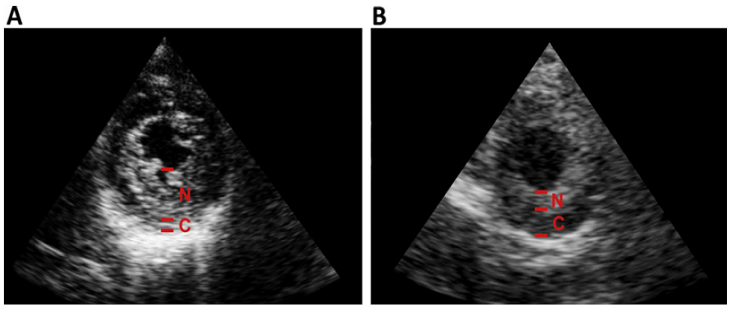


Figure 1 Representative example of echocardiographic measurements in the parasternal short-axis view in a patient with LVNC **(A)** compared with one with AVS **(B)**. *C*, compacted myocardial layer; *N*, noncompacted myocardial layer.

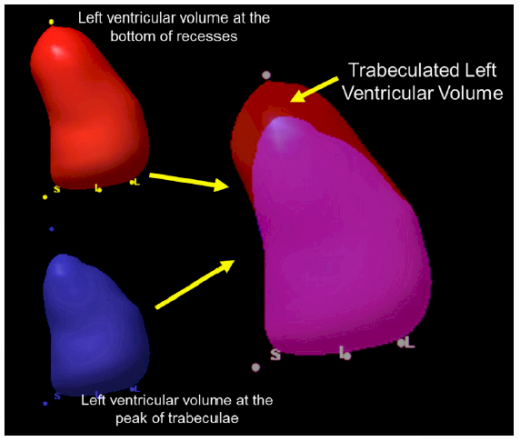


Figure 2 After tracing the endocardial border at the bottom of the trabeculae and at the peak of the recesses, we obtained the end-diastolic volume including trabeculae (*red*) and excluding trabeculae (*blue*). The difference between the two volumes corresponded to the TLV. TLV was also normalized by LV end-diastolic volume including trabeculae as the expression of the proportion of LV cavity occupied by trabeculae (TLV%).

NVM: CRITERI DIAGNOSTICI MNR

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Clinical Insights From Cardiac Imaging

Left Ventricular Non-Compaction

Insights From Cardiovascular Magnetic Resonance Imaging

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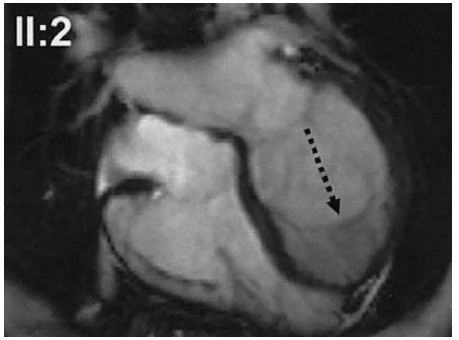

We analyzed magnetic resonance cine images, using the 17-segment model in 45 healthy volunteers, 25 athletes, 39 patients with hypertrophic cardiomyopathy and 14 with dilated cardiomyopathy, 17 with hypertensive heart disease, and 30 with aortic stenosis, as well as images from 7 patients previously diagnosed with LVNC whose diagnoses were supported by additional features. Areas of non-compaction were common and occurred more frequently in all groups studied in apical and lateral, rather than in basal or septal, segments. **A NC/C ratio of 2.3 in diastole** distinguished pathological non-compaction, with values for sensitivity, specificity, and positive and negative predictions of 86%, 99%, 75%, and 99%, respectively.

NVM: CRITERI DIAGNOSTICI MNR

Trabeculated (Noncompacted) and Compact Myocardium in Adults

The Multi-Ethnic Study of Atherosclerosis

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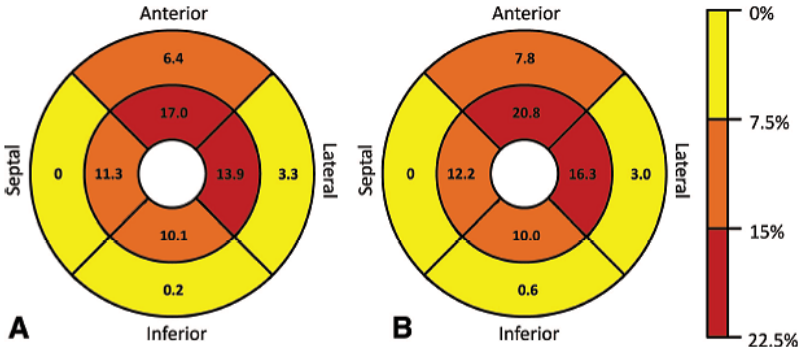
Background—A high degree of noncompacted (trabeculated) myocardium in relationship to compact myocardium (trabeculated to compact myocardium [T/M] ratio >2.3) has been associated with a diagnosis of left ventricular noncompaction (LVNC). The purpose of this study was to determine the normal range of the T/M ratio in a large population-based study and to examine the relationship to demographic and clinical parameters.

Methods and Results—The thickness of trabeculation and the compact myocardium were measured in 8 left ventricular regions on long axis cardiac MR steady-state free precession cine images in 1000 participants (551 women; 68.1±8.9 years) of the Multi-Ethnic Study of Atherosclerosis cohort. Of 323 participants without cardiac disease or hypertension and with all regions evaluable, 140 (43%) had a T/M ratio >2.3 in at least 1 region; in 20 of 323 (6%), T/M >2.3 was present in >2 regions. A multivariable linear regression model revealed no association of age, sex, ethnicity, height, and weight with maximum T/M ratio in participants without cardiac disease or hypertension (P>0.05). In the entire cohort (n=1000), left ventricular ejection fraction (β=−0.02/%; P=0.015), left ventricular end-diastolic volume (β=0.01/mL; P<0.0001), and left ventricular end-systolic volume (β=0.01/mL; P<0.001) were associated with maximum T/M ratio in adjusted models, whereas there was no association with hypertension or myocardial infarction (P>0.05). At the apical level, T/M ratios were significantly lower when obtained on short- compared with long-axis images (P=0.017).

Conclusions—A ratio of T/M of >2.3 is common in a large population-based cohort. These results suggest re-evaluation of the current cardiac MR criteria for left ventricular noncompaction may be necessary. (***Circ Cardiovasc Imaging*. 2012;5:357-366.**)



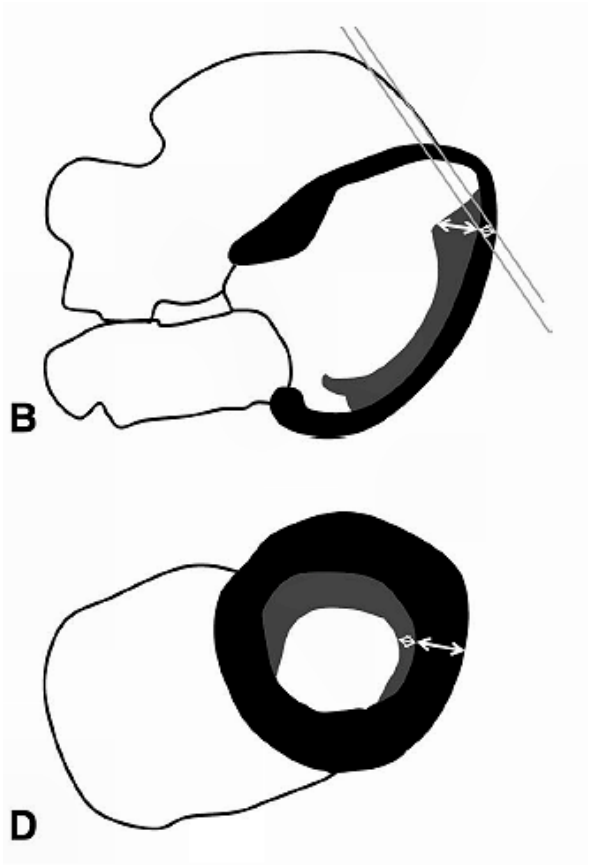


Figure 6. Percent participants with a T/M ratio >2.3 per region at the midcavity level (outer circle) and the apical level (inner circle) of the entire cohort (**A**) and the subset of participants without cardiac disease or hypertension (**B**). T/M ratio indicates thickness of trabeculation/thickness of compact myocardium.

NVM: CRITERI DIAGNOSTICI MNR

European Heart Journal (2010) **31**, 1098–1104
doi:10.1093/eurheartj/ehp595

CLINICAL RESEARCH
Myocardial disease

Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction†

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Aims To describe a method for measuring trabeculated left ventricular (LV) mass using cardiac magnetic resonance imaging and to assess its value in the diagnosis of left ventricular non-compaction (LVNC).

Methods and results Between January 2003 and 2008, we prospectively included 16 patients with LVNC. During the mean period, we included 16 patients with dilated cardiomyopathy (DCM), 16 patients with hypertrophic cardiomyopathy (HCM), and 16 control subjects. Left ventricular volumes, LV ejection fraction, and trabeculated LV mass were measured in the four different populations. The percentage of trabeculated LV mass was almost three times higher in the patients with LVNC ($32 \pm 10\%$), compared with those with DCM ($11 \pm 4\%$, $P < 0.0001$), HCM ($12 \pm 4\%$, $P < 0.0001$), and controls ($12 \pm 5\%$, $P < 0.0001$). A value of trabeculated LV mass above 20% of the global mass of the LV predicted the diagnosis of LVNC with a sensitivity of 93.7% [95% confidence interval (CI), 71.6–98.8%] and a specificity of 93.7% (95% CI, 83.1–97.8%; $\kappa = 0.84$).

Conclusion The method described is reproducible and provides an assessment of the global amount of LV trabeculation. A trabeculated LV mass above 20% of the global LV mass is highly sensitive and specific for the diagnosis of LVNC.

Keywords Left ventricular non-compaction • Magnetic resonance imaging • Cardiomyopathy • Trabeculae

LV volumes, LV ejection fraction, and trabeculated LV mass were measured in the four different populations. The percentage of trabeculated LV mass was almost three times higher in the patients with LVNC (32 +/- 10%), compared with those with DCM (11 +/- 4%, P < 0.0001), HCM (12 +/- 4%, P < 0.0001), and controls (12 +/- 5%, P < 0.0001). A value of trabeculated LV mass above 20% of the global mass of the LV predicted the diagnosis of LVNC with a sensitivity of 93.7% [95% confidence interval (CI), 71.6-98.8%] and a specificity of 93.7% (95% CI, 83.1-97.8%; kappa = 0.84).

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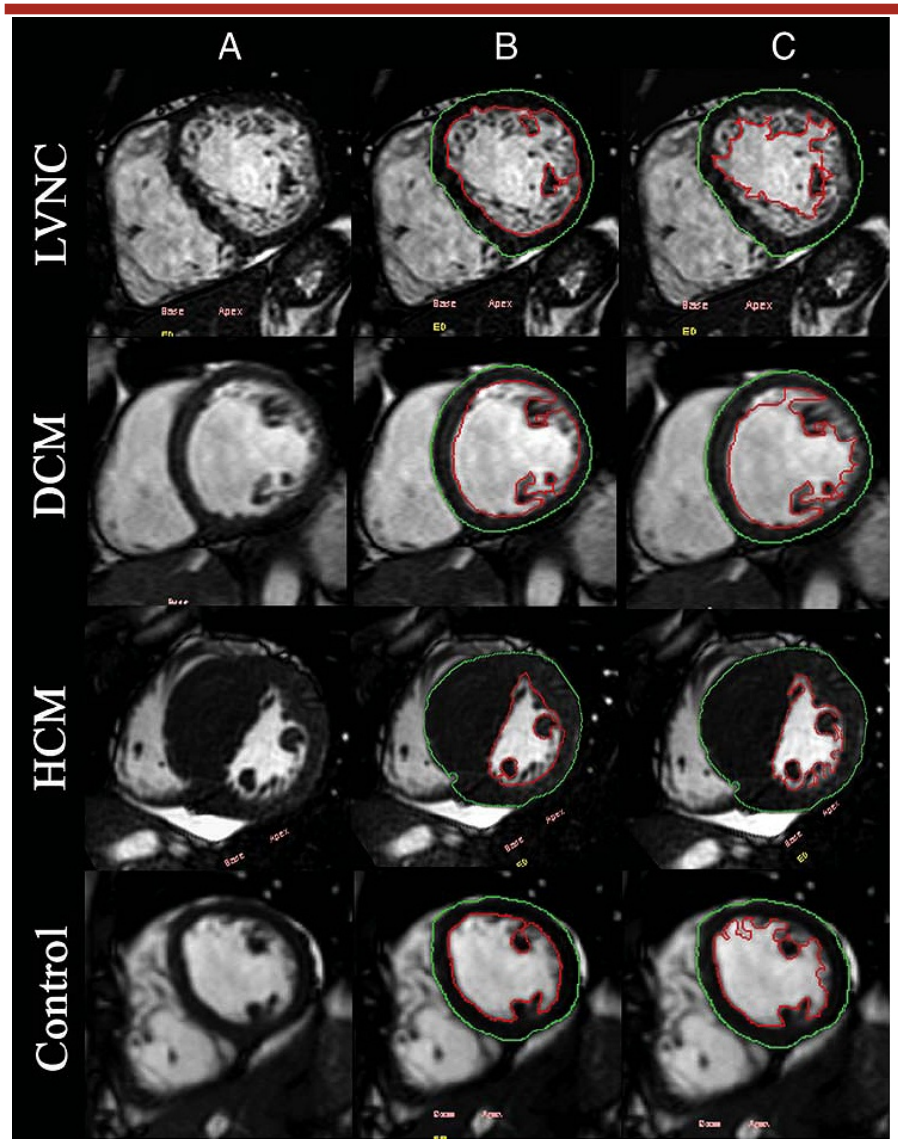

Illustration of the described method for measuring the global and trabeculated left ventricular masses in patients with left ventricular non-compaction, dilated cardiomyopathy, hypertrophic cardiomyopathy, and controls:

- **Column A shows the short-axis end-diastolic cine images used for measurement without contouring.**
- **Column B shows the inclusion of papillary muscles and the exclusion of left ventricular trabeculation for the measurements of the compacted left ventricular mass.**
- **Column C shows inclusion of papillary muscles and trabeculation for the measurements of global left ventricular mass**

Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction†

Alexis Jacquier[1]*, Franck Thuny[2], Bertrand Jop[2], Roch Giorgi[3,4], Frederic Cohen[1], Jean-Yves Gaubert[1], Vincent Vidal[1], Jean Michel Bartoli[1], Gilbert Habib[2], and Guy Moulin[1]

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Captur et al. Journal of Cardiovascular Magnetic Resonance 2013, 15:36
http://jcmr-online.com/content/15/1/36

Journal of Cardiovascular Magnetic Resonance

RESEARCH Open Access

Quantification of left ventricular trabeculae using fractal analysis

Gabriella Captur[1,2], Vivek Muthurangu[2,3], Christopher Cook[1], Andrew S Flett[1,2], Robert Wilson[4], Andrea Barison[1,5], Daniel M Sado[1,2], Sarah Anderson[1], William J McKenna[1,2], Timothy J Mohun[4], Perry M Elliott[1,2] and James C Moon[1,2*]

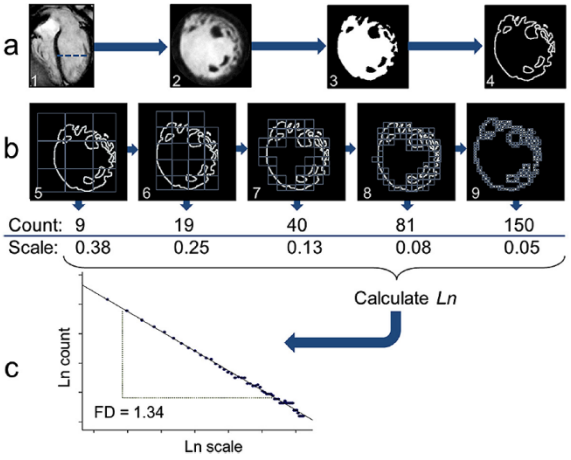

Figure 1 Image processing sequence and fractal analysis of left ventricular cine images. Example analysis of a single slice (**a**-2) out of a cine volumetric left ventricular stack, belonging to an LVNC case. Dashed line across the 4-chamber view marks the slice location (**a**-1). Automatic thresholding, binarization (**a**-3) and edge-detection (**a**-4) are followed by fractal analysis (**b**). In the box-counting method a series of grids of boxes of progressively smaller size are laid over the ROI and boxes containing detail are counted (**b**-5 to 9). The same set of grid calibres is applied to the ROI in four different orientations. In this pictorial representation, only 5 box sizes are shown but the complete analysis for this slice actually involves 55 box sizes. Each orientation generates a separate natural logarithmic plot of box-count (*y* axis) against scale (*x* axis, calculated from box/image size) (**c**). The slope of the line-of-best-fit across the points represents a FD. The mean value from the four plots is the slice FD. In this case, the straight line supports the existence of a fractal pattern. FD for this slice is 1.34. FD = fractal dimension; Ln = natural logarithm; LVNC = left ventricular noncompaction; ROI = region of interest.

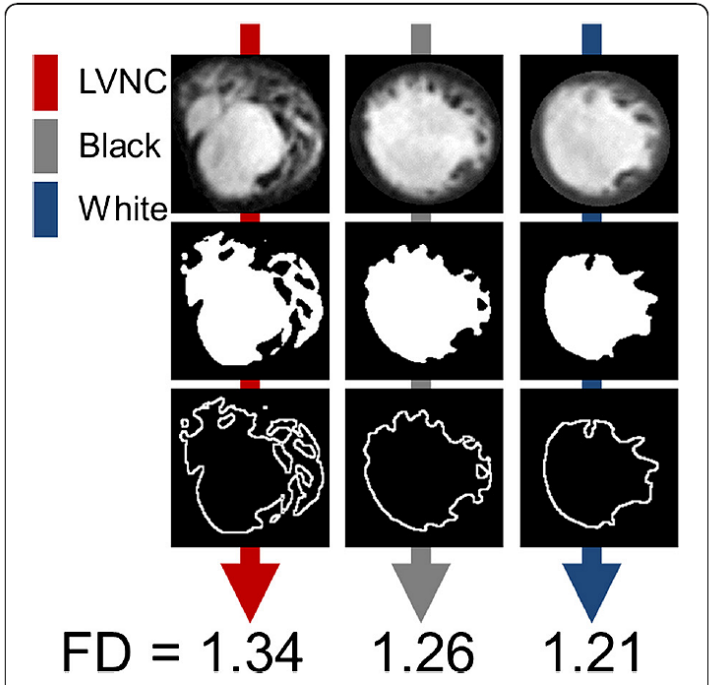

Figure 2 Illustrative left ventricular slices from each of the three study populations with corresponding FDs. Fractal analysis of each slice generates a value for the FD. In this study we demonstrate that FD differs significantly between LVNC, healthy black and white populations. Abbreviations as in Figure 1.

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Myocardial fibrosis in isolated left ventricular non-compaction and its relation to disease severity

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See page 127 for the editorial comment on this article (doi:10.1093/eurjhf/hfq233)

Aims	The aim of the present study was to evaluate the prevalence and extent of myocardial fibrosis in patients with isolated left ventricular non-compaction (LVNC) and to determine its relation to clinical status and LV systolic function.
Methods and results	The cardiac magnetic resonance imaging (MRI) database of our institution was searched for all patients with a first diagnosis of isolated LVNC. The diagnosis of isolated LVNC was based on the presence of standard cardiac MRI and clinical criteria. For each patient, cine and contrast-enhanced cardiac MR images were analysed to evaluate LV systolic function and the prevalence and extent of late gadolinium enhancement (LGE), a surrogate of myocardial fibrosis. A total of 42 patients (mean age 46 $\pm$ 20 years, 62% male) were identified. Late gadolinium enhancement was observed in 23 (55%) patients with isolated LVNC, occupying 4.8 $\pm$ 6.7% of the LV mass. Both the presence and extent of LGE were significantly related to the number of abnormal clinical features (i.e. symptomatic status, resting electrocardiogram abnormalities, and 24 h Holter monitoring abnormalities; $P < 0.001$ and $P = 0.001$, respectively). Similarly, LGE was more prevalent and extensive in patients with LV ejection fraction (EF) <50% compared with patients with LVEF $\geq$50% (90 vs. 23%; $P < 0.001$ and 8.9 $\pm$ 7.6 vs. 1.1 $\pm$ 2.4%; $P < 0.001$, respectively). At multivariate analysis, both the presence and extent of LV LGE were independently related to LVEF ($\beta = -0.63$; $P < 0.001$ and $\beta = -0.62$; $P < 0.001$, respectively).
Conclusion	Myocardial fibrosis is related to clinical disease severity and LV systolic dysfunction in isolated LVNC.

Keywords	Isolated left ventricular non-compaction • Late gadolinium enhancement • Magnetic resonance imaging • Myocardial fibrosis

OVERLAPPING CMPs

European Heart Journal (2005) 26, 187–192
doi:10.1093/eurheartj/ehi025

Clinical research

Natural history and familial characteristics of isolated left ventricular non-compaction

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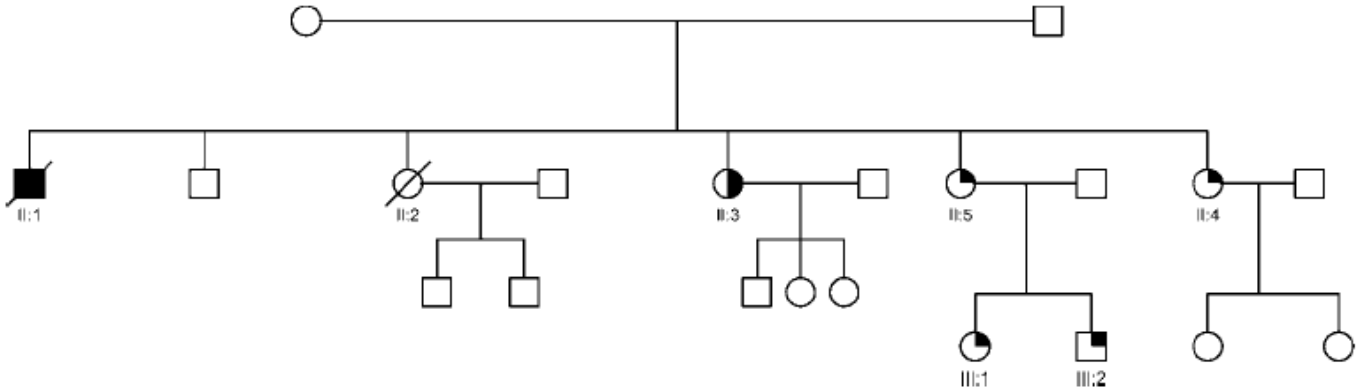

Figure 1 Phenotypic heterogeneity in LVNC. Family pedigree NC3 showing phenotypic heterogeneity, with isolated DCM, isolated LVNC and LVE co-existing within the same family. The family was screened after the death of a proband (II:1) with DCM, who died 3 years after a cardiac transplant for end-stage heart failure. His explanted heart showed DCM and on review had no evidence of LVNC or excessive trabeculations of the left ventricle. A sister (II:2) died of cardiac failure immediately post-partum. Another sister (II:3) had a mildly dilated left ventricle, and systolic function at the lower limit of normal (FS = 26%). A further sister (II:4) had a history of syncope, isolated left ventricular enlargement, a thickened posterior wall, preserved systolic function, frequent runs of non-sustained ventricular tachycardia on cardiac monitoring, and received a prophylactic ICD. Another sister (II:5), her daughter (III:1), and son (III:2), have extensive LVNC and normal systolic function. Solid square and circle symbols indicate affected males and females with DCM, respectively; open symbols, unaffected; half-symbols, left ventricular enlargement; quarter symbols, LVNC; and slashes, death.

OVERLAPPING CMPs

Different Types of Cardiomyopathy Associated With Isolated Ventricular Noncompaction

Elena Biagini, MD[a], Luca Ragni, MD[b], Marinella Ferlito, MD[a], Ferdinando Pasquale, MD[a], Carla Lofiego, MD[a], Ornella Leone, MD[c], Guido Rocchi, MD[a], Enrica Perugini, MD[a], Silvia Zagnoni, MD[c], Angelo Branzi, MD[a], Fernando M. Picchio, MD[b], and Claudio Rapezzi, MD[a,*]

Although mainly described in the context of dilated and hypokinetic left ventricles, it is unclear whether isolated ventricular noncompaction (IVNC) is a distinct cardiomyopathy, a subtype of dilated cardiomyopathy, or a morphogenetic disorder. To investigate the spectrum of cardiomyopathies associated with IVNC, children and adults with stringent echocardiographic diagnoses of IVNC were reviewed. Seventy-three patients (12 children aged <15 years) seen since 1994 satisfied stringent echocardiographic criteria for IVNC. Sixty-five patients (89%; 11 children) had dilated cardiomyopathy, 2 adults had clear-cut hypertrophic cardiomyopathy, 1 adult had restrictive cardiomyopathy (to the investigators' knowledge, the first reported example of this particular association), and 5 patients (1 child) had normal left ventricular morphology and function. In conclusion, knowledge that IVNC can co-exist with restrictive and hypertrophic cardiomyopathy (in addition to the dilated form) supports the concept that IVNC is a morphologic trait rather than a distinct cardiomyopathy. This knowledge should be taken into account during echocardiographic examination and encourage the use of contrast echocardiography (and magnetic resonance) and could also orient molecular biology studies. (Am J Cardiol 2006;98:821–824)

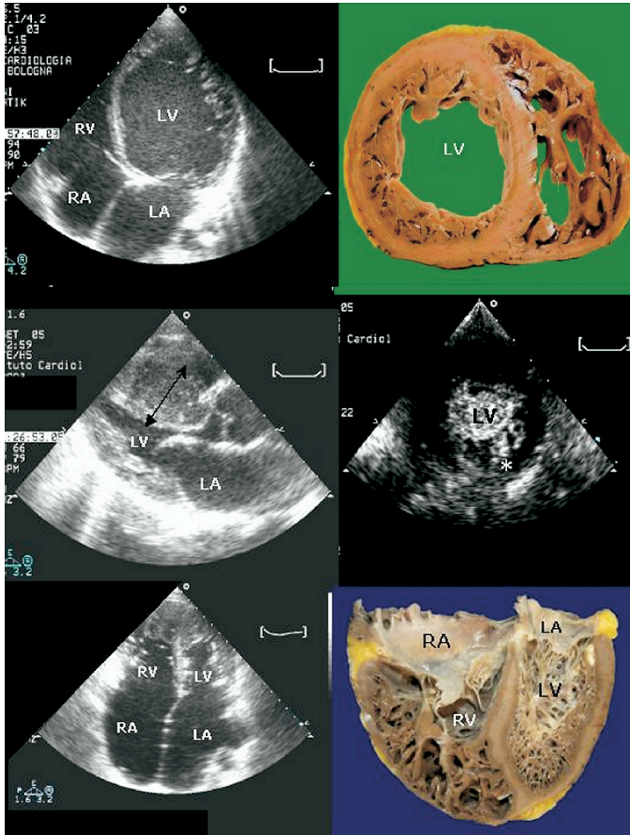

Figure 2. Spectrum of associated cardiomyopathies: *(top)* dilated cardiomyopathy (in a patient who underwent transplantation), *(middle)* 2-dimensional and contrast echocardiographic images in a patient with hypertrophic cardiomyopathy (*arrow*, maximal diastolic thickness of the interventricular posterior septum; *asterisk*, the noncompacted posterior wall at end-systole), and *(bottom)* restrictive cardiomyopathy (the patient underwent transplantation). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

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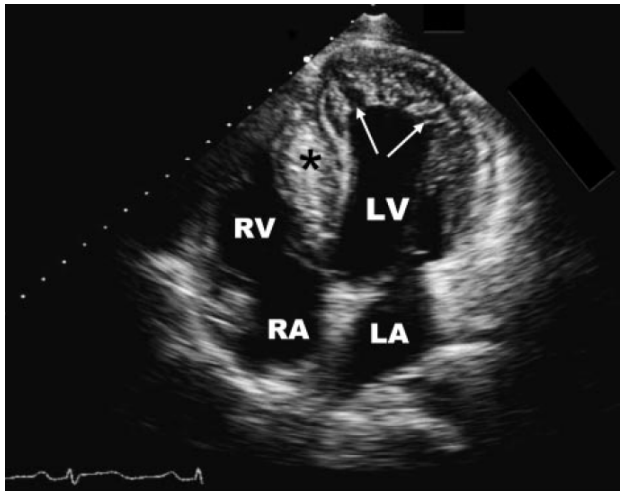
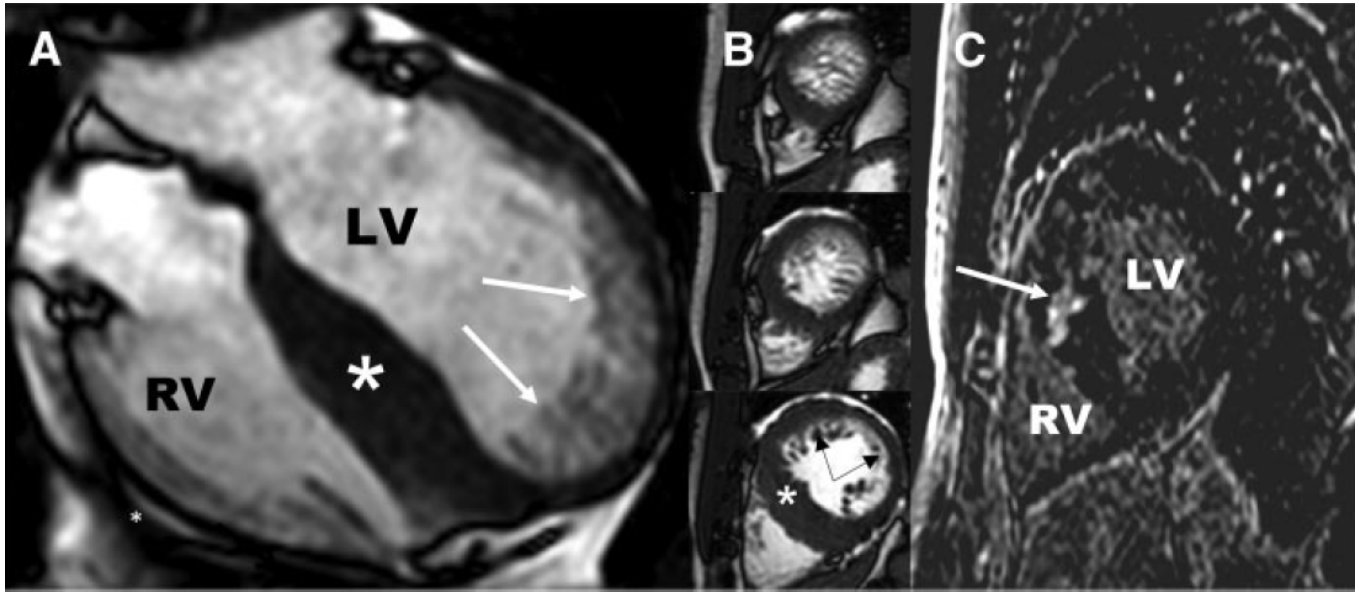


Overlapping Phenotypes

Left Ventricular Noncompaction and Hypertrophic Cardiomyopathy

Alyson Kelley-Hedgepeth, MD; Jeffery A. Towbin, MD; Martin S. Maron, MD

(*Circulation.* 2009;119:e588-e589.)



OVERLAPPING GENE MUTATIONS

Table 2 Gene Mutations Reported in Human LVNC

Gene	*Disease*	*Location*	*References*	*Child/adult*
α-Dystrobrevin (DTNA)	*LVNC with CHD, muscular dystrophy in human*	*18q12*	*12*	*Child*
G4.5 (TAZ)	*Barth syndrome, LVNC, DCM, EFE*	*Xq28*	*12, 14, 15*	*Child*
LIM domain binding protein (LDB3, Cypher/ZASP)	*LVNC, DCM*	*10q22-q23.2*	*13, 16*	*Child/adult*
Lamin A/C	*LVNC, DCM, muscular dystrophy in human*	*1q22*	*17*	*Child/adult*
Sarcomere proteins				
β-myosin heavy chain (MYH7)	*HCM, DCM, LVNC*	*14q11.2-q13*	*18*	*Adult*
α-cardiac actin (ACTC)	*HCM, DCM, LVNC*	*15q11-q14*	*18*	*Adult*
Cardiac troponin T (TNNT2)	*HCM, DCM, LVNC*	*1q32*	*18*	*Adult*

LVNC, left ventricular noncompaction; CHD, congenital heart disease; DCM, dilated cardiomyopathy; EFE, endocardial fibroelastosis; HCM, hypertrophic cardiomyopathy.

REVIEW

Circ J 2009; **73:** 19–26

Left Ventricular Noncompaction

Fukiko Ichida, MD

Circulation Journal
Japanese Circulation Society

OVERLAPPING GENE MUTATIONS

Heart Failure

Mutations in Sarcomere Protein Genes in Left Ventricular Noncompaction

Sabine Klaassen, MD*; Susanne Probst, MSc*; Erwin Oechslin, MD; Brenda Gerull, MD; Gregor Krings, MD; Pia Schuler, MD; Matthias Greutmann, MD; David Hürlimann, MD; Mustafa Yegitbasi, MD; Lucia Pons, MD; Michael Gramlich, MD; Jörg-Detlef Drenckhahn, MD; Arnd Heuser, MD; Felix Berger, MD; Rolf Jenni, MD; Ludwig Thierfelder, MD

Background—Left ventricular noncompaction constitutes a primary cardiomyopathy characterized by a severely thickened, 2-layered myocardium, numerous prominent trabeculations, and deep intertrabecular recesses. The genetic basis of this cardiomyopathy is still largely unresolved. We speculated that mutations in sarcomere protein genes known to cause hypertrophic cardiomyopathy and dilated cardiomyopathy may be associated with left ventricular noncompaction.

Methods and Results—Mutational analysis in a cohort of 63 unrelated adult probands with left ventricular noncompaction and no other congenital heart anomalies was performed by denaturing high-performance liquid chromatography analysis and direct DNA sequencing of 6 genes encoding sarcomere proteins. Heterozygous mutations were identified in 11 of 63 samples in genes encoding β-myosin heavy chain (*MYH7*), α-cardiac actin (*ACTC*), and cardiac troponin T (*TNNT2*). Nine distinct mutations, 7 of them in *MYH7*, 1 in *ACTC*, and 1 in *TNNT2*, were found. Clinical evaluations demonstrated familial disease in 6 of 11 probands with sarcomere gene mutations. *MYH7* mutations segregated with the disease in 4 autosomal dominant LVNC kindreds. Six of the *MYH7* mutations were novel, and 1 encodes a splice-site mutation, a relatively unique finding for *MYH7* mutations. Modified residues in β-myosin heavy chain were located mainly within the ATP binding site.

Conclusions—We conclude that left ventricular noncompaction is within the diverse spectrum of cardiac morphologies triggered by sarcomere protein gene defects. Our findings support the hypothesis that there is a shared molecular etiology of different cardiomyopathic phenotypes. **(*Circulation*. 2008;117:2893-2901.)**

Key Words: cardiomyopathy ■ genetics ■ heart failure ■ remodeling ■ myocardium

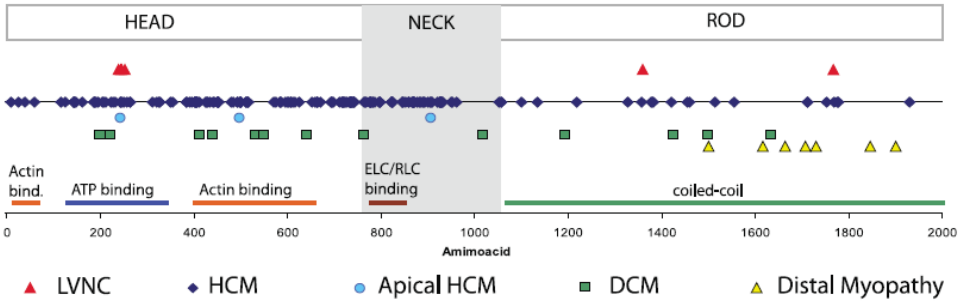


Figure 4. Distribution of *MYH7* mutations in cardiomyopathies. The mutations were selected from the CardioGenomics database (http://www.cardiogenomics.org), last updated April 24, 2006. Disease-causing mutations for HCM, apical HCM, DCM, distal myopathy, and LVNC (present study) are shown.

Our findings support the hypothesis that there is a shared molecular etiology of different CMP phenotypes.
It is increasingly realized that the current nomenclature fails to adequately describe the substantial overlap between the classic CMP syndromes.
Indeed, this discordance between the etiology and the "clinical syndrome" is one of the main messages of our study.

GENETIC EVALUATION OF CMPs

Guideline

Genetic Evaluation of Cardiomyopathy—A Heart Failure Society of America Practice Guideline

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Miami, Florida; Denver, Colorado; Boston, Massachusetts; Houston, Texas

Substantial progress has been made recently in understanding the genetic basis of cardiomyopathy. Cardiomyopathies with known genetic cause include hypertrophic (HCM), dilated (DCM), restrictive (RCM), arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) and left ventricular noncompaction (LVNC). HCM, DCM, and RCM have been recognized as distinct clinical entities for decades, whereas ARVD/C and LVNC are relative newcomers to the field. Hence the clinical and genetic knowledge for each cardiomyopathy varies, as do the recommendations and strength of evidence. (*J Cardiac Fail 2009;15:83–97*)

Therapy Based on Genetic Testing

As discussed previously (Section 17.4), the finding of any specific mutation as the cause of the cardiomyopathy does not in itself guide therapy. However, the clinical characteristics associated with some disease genes (Table 5), when integrated with the clinical and family data, may influence the overall case assessment, and may appropriately impact all aspects of the clinical recommendations.

Therapy Based on Cardiac Phenotype

17.6. Medical therapy based on cardiac phenotype is recommended as outlined in the general guidelines. (Level of Evidence = A)

NVM: PROGNOSI

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

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Zurich, Switzerland

OBJECTIVES We sought to describe characteristics and outcome in adults with isolated ventricular noncompaction (IVNC).

BACKGROUND Isolated ventricular noncompaction is an unclassified cardiomyopathy due to intrauterine arrest of compaction of the loose interwoven meshwork. Knowledge regarding diagnosis, morbidity and prognosis is limited.

METHODS Echocardiographic criteria for IVNC include—in the absence of significant heart lesions—segmental thickening of the left ventricular myocardial wall consisting of two layers: a thin, compacted epicardial and an extremely thickened endocardial layer with prominent trabeculations and deep recesses. Thirty-four adults (age ≥16 years, 25 men) fulfilled the diagnostic criteria and were followed prospectively.

RESULTS At diagnosis, mean age was 42 ± 17 years, and 12 patients (35%) were in New York Heart Association class III/IV. Left ventricular end-diastolic diameter was 65 ± 12 mm and ejection fraction 33 ± 13%. Apex and/or midventricular segments of both the inferior and lateral wall were involved in >80% of patients. Follow-up was 44 ± 40 months. Major complications were heart failure in 18 patients (53%), thromboembolic events in 8 patients (24%) and ventricular tachycardias in 14 patients (41%). There were 12 deaths: sudden in six, end-stage heart failure in four and other causes in two patients. Four patients underwent heart transplantation. Automated cardioverter/defibrillators were implanted in four patients.

CONCLUSIONS Diagnosis of IVNC by echocardiography using strict criteria is feasible. Its mortality and morbidity are high, including heart failure, thrombo-embolic events and ventricular arrhythmias. Risk stratification includes heart failure therapy, oral anticoagulation, heart transplantation and implantation of an automated defibrillator/cardioverter. As IVNC is a distinct entity, its classification as a specific cardiomyopathy seems to be more appropriate. (J Am Coll Cardiol 2000;36:493–500) © 2000 by the American College of Cardiology

NVM: PROGNOSI

AHA Scientific Statement

Contemporary Definitions and Classification of the Cardiomyopathies

An American Heart Association Scientific Statement From the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention

Barry J. Maron, MD, Chair; Jeffrey A. Towbin, MD, FAHA; Gaetano Thiene, MD; Charles Antzelevitch, PhD, FAHA; Domenico Corrado, MD, PhD; Donna Arnett, PhD, FAHA; Arthur J. Moss, MD, FAHA; Christine E. Seidman, MD, FAHA; James B. Young, MD, FAHA

Abstract—Classifications of heart muscle diseases have proved to be exceedingly complex and in many respects contradictory. Indeed, the precise language used to describe these diseases is profoundly important. A new contemporary and rigorous classification of cardiomyopathies (with definitions) is proposed here. This reference document affords an important framework and measure of clarity to this heterogeneous group of diseases. Of particular note, the present classification scheme recognizes the rapid evolution of molecular genetics in cardiology, as well as the introduction of several recently described diseases, and is unique in that it incorporates ion channelopathies as a primary cardiomyopathy. (***Circulation***. 2006;113:1807-1816.)

The natural history of LVNC is largely unresolved

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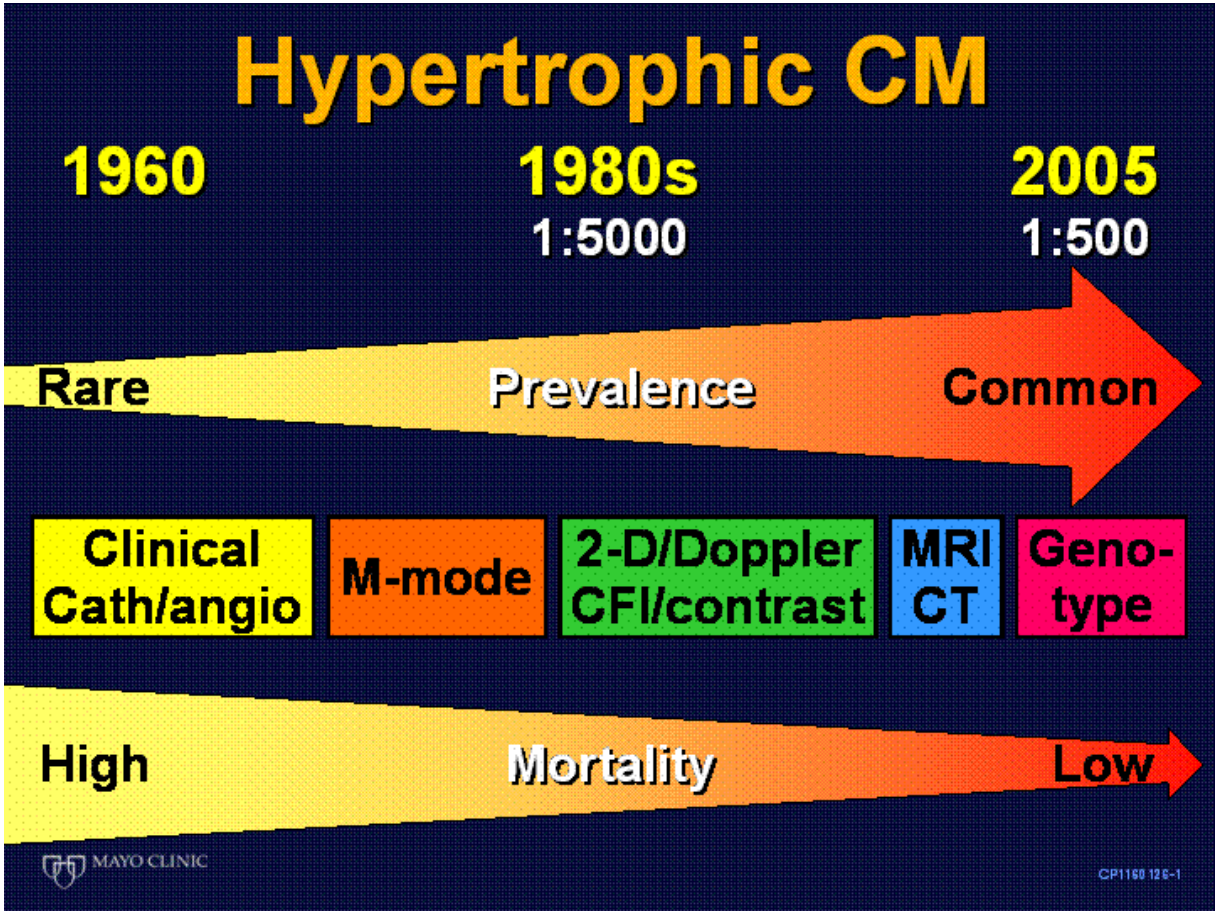
PROGNOSI INFAUSTA…….



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European Heart Journal (2005) 26, 187–192
doi:10.1093/eurheartj/ehi025

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Clinical research

Natural history and familial characteristics of isolated left ventricular non-compaction

Ross T. Murphy, Rajesh Thaman, Juan Gimeno Blanes, Deirdre Ward, Elias Sevdalis, Efi Papra, Anatoli Kiotsekolglou, Maria T. Tome, Denis Pellerin, William J. McKenna, and Perry M. Elliott*

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Received 25 March 2004; revised 18 August 2004; accepted 29 September 2004; online publish-ahead-of-print 30 November 2004

Conclusion This study demonstrates that LVNC is associated with a better prognosis than previously reported. In patients with familial disease, relatives may have features consistent with dilated cardiomyopathy rather than LVNC.

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HEART FAILURE AND CARDIOMYOPATHY

Wide spectrum of presentation and variable outcomes of isolated left ventricular non-compaction

C Lofiego, E Biagini, F Pasquale, M Ferlito, G Rocchi, E Perugini, L Bacchi-Reggiani, G Boriani, O Leone, K Caliskan, F J ten Cate, F M Picchio, A Branzi, C Rapezzi

Heart 2007;**93**:65–71. doi: 10.1136/hrt.2006.088229

- 65 eligible patients were followed up for 6–193 months (mean 46 SD 44).
- In 53 (82%), IVNC was associated LV dilatation and hypokinesia, and in the remaining 12 (18%) LV volumes were normal
- Diagnosis was symptom based in 48 (74%) and non-symptom based in 17 (26%) (familial referral in 10).
- No major cardiovascular events occurred in the non-symptom based group, whereas 15 of 48 (31%) symptomatically diagnosed patients experienced cardiovascular death or heart transplantation ($p = 0.01$, Kaplan–Meier analysis)
- Independent predictors of cardiovascular death or heart transplantation were NYHA class III–IV, sustained ventricular arrhythmias

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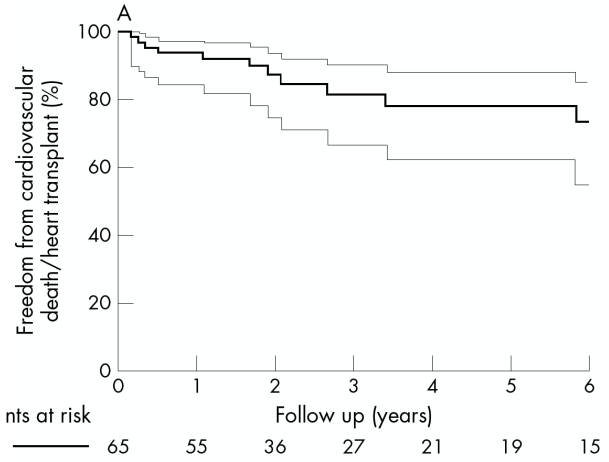


Table 3 Analysis of candidate predictors of death or heart transplantation in the study population

	Univariate analysis		Multivariate analysis	
Variables at presentation	**HR (95% CI)**	**p Value**	**HR (95% CI)**	**p Value**
NYHA class III–IV	5.8 (2.0 to 17.0)	0.001	10.9 (2.8 to 41.6)	0.0001
Sustained ventricular arrhythmias	6.1 (1.6 to 23.1)	0.008	10.1 (2.1 to 47.4)	0.004
Left atrial size (cm)	2.5 (1.5 to 4.4)	0.001	3.7 (1.8 to 7.6)	0.0001
Non-symptom-based diagnosis	0.1 (0.01 to 2.4)	0.04		
Restrictive pattern	2.7 (0.9 to 7.9)	0.06		
LV ejection fraction	0.9 (0.8 to 1.0)	0.08		
Permanent atrial fibrillation	3.3 (0.7 to 15.2)	0.12		
Left bundle branch block	0.50 (0.1 to 1.6)	0.24		
Syncope	1.9 (0.5 to 7.2)	0.30		
Age at first evaluation	1.06 (0.98 to 1.05)	0.34		
Age at initial diagnosis of myocardial disease	1.007 (0.98 to 1.04)	0.60		
Male sex	1.5 (0.5 to 4.9)	0.44		
Number of non-compacted segments >5	0.4 (0.2 to 1.9)	0.60		

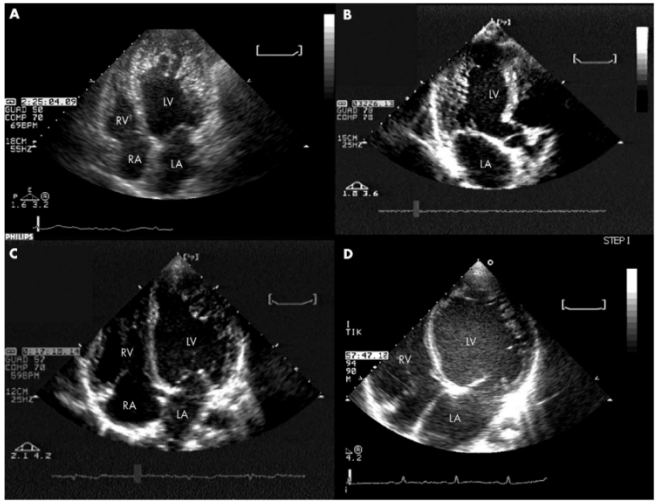
HR, hazard ratio; LV, left ventricular; NYHA, New York Heart Association.

HEART FAILURE AND CARDIOMYOPATHY

Wide spectrum of presentation and variable outcomes of isolated left ventricular non-compaction

C Lofiego, E Biagini, F Pasquale, M Ferlito, G Rocchi, E Perugini, L Bacchi-Reggiani, G Boriani, O Leone, K Caliskan, F J ten Cate, F M Picchio, A Branzi, C Rapezzi

Heart 2007;**93**:65–71. doi: 10.1136/hrt.2006.088229



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Isolated Left Ventricular Noncompaction Syndrome

Christopher Stanton, MD, Charles Bruce, MD, Heidi Connolly, MD, Peter Brady, MBChB, MD, Imran Syed, MD, David Hodge, MSc, Samuel Asirvatham, MD, and Paul Friedman, MD*

Isolated left ventricular noncompaction (ILVNC) is a rare congenital cardiomyopathy characterized by prominent trabeculae, deep intertrabecular recesses, and thickened myocardium with 2 distinct layers (compacted and noncompacted). Clinical characteristics, outcomes, and appropriate therapies remain poorly defined. Data were collected on patients diagnosed with ILVNC by echocardiographic criteria at the Mayo Clinic from 2001 through 2006. These data were entered prospectively into a clinical database and retrospectively analyzed. All-cause mortality, stroke, and development of atrial fibrillation (AF) were compared to community and nonischemic dilated cardiomyopathic (DC) controls. Implantable cardioverter-defibrillator (ICD) therapies were examined. Thirty patients with confirmed ILVNC were included in analyses (mean age at diagnosis 39 ± 19.5 years, 60% men). Three patients with ILVNC died during follow-up (mean 2.5 ± 1.2 years) compared to 5 DC and 1 community controls. No mortality difference was observed among these groups ($p = 0.42$ and 0.054, respectively). No ILVNC deaths were observed in patients with normal LV ejection fraction. New-onset AF was diagnosed in 2 patients with ILVNC, and none was observed in DC controls. Stroke occurred in 2 DC controls and none was observed in patients with ILVNC. ICDs were implanted in 11 patients with ILVNC. No appropriate therapies were identified during follow-up, but 2 patients underwent inappropriate therapies related to AF. In conclusion, mortality in patients with ILVNC is similar to that in DC patients. Deaths were observed only in patients with decreased LV ejection fraction, suggesting that ICD therapy may be reserved for this subgroup. New-onset AF may lead to inappropriate ICD discharges. (Am J Cardiol 2009;104:1135–1138)

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- 181 adults; 108 ♂, 73♀
- Mean age at inclusion: 49.6 ± 17.6 (18 - 90) yrs.
- Pts divided into two diagnostic subgroups:

  - symptom-based (i.e., symptomatic at enrollment; 90 pts, 50%)

  - nonsymptom-based (familial screening or occasional finfing)

Corrado G, Fazio G, Zachara E, Rapezzi C, Sormani L, Carerj S, Beretta S. Natural history of isolated noncompaction of the ventricular myocardium in adults. Data from the Società Italiana di Ecografia Cardiovascolare (SIEC) registry.
Circulation (Abs) 2008;118:S_948

REGISTRO ITALIANO NVM

Baseline clinical, ECG and echocardiographic characteristics according to modality of diagnosis

	Overall (n = 177)	Symptom-based diagnosis (n = 90)	Non-symptom-based diagnosis (n = 73)	p Value*
Age at first evaluation (years)	49,6 (17,6)	53,1 (16,2)	44,7 (18,7)	0.0024
Familial occurrence	65 (40%)	15 (17%)	50 (66%)	NA
Left bundle branch block	39 (24%)	33 (20%)	6 (4%)	<0.0001
Normal ECG	44 (27%)	8 (5%)	36 (22%)	0.04
LV end diastolic diameter (mm)	60,4 (13,1)	67,2 (12,5)	54,0 (9)	<0.0001
LV ejection fraction (%)	41 (17)	32 (13)	52 (13)	<0.0001
Left atrial size (mm)	42,5 (11,5)	46,5 (10,6)	34,9 (10,5)	<0.0001
Moderate or severe mitral regurgitation	17 (19%)	14 (16%)	3 (3%)	0.4
Number of non-compacted segments	5 (2)	5 (2)	5 (2)	0.4
Transmitral restrictive pattern	24 (29%)	18 (44%)	6 (14%)	0.002

Data are mean (SD) or number (%).
*Comparison between subgroups with symptom-based and non-symptom-based diagnosis. LV, left ventricular.

REGISTRO ITALIANO NVM

- Mean follow-up 64.2 ± 74.7 (2 - 360) months.
- Major events (death, heart failure, thromboembolism, malignant ventricular arrhythmia): 69 pts (38%).
- Most events occurred in the symptom-based

Analysis of candidate predictors of events in the study population

	Univariate analysis		Multivariate analysis	
Variables at presentation	**OR (95%CI)**	**p**	**OR (95%CI)**	**p**
Age at first evaluation	1,0265 (1,0061 to 1,0473)	0,0108		
Age at initial diagnosis of myocardial disease	1,0033 (0,9787 to 1,0284)	0.7971		
Male gender	1,3422 (0,7061 to 2,5515)	0,3691		
NYHA class III-IV	15,9860 (6,4498 to 39,6216)	0,0000	4,1395 (1,5213 to 11,2638)	0,00541
Sustained ventricular arrhythmias	8,5263 (1,8373 to 39,5674)	0,0062		
Symptom-based diagnosis	25,3636 (10,1081 to 63,6433)	0,0000	4,0427 (1,1962 to 13,6636)	0,02456
Previous heart failure	24,4898 (9,6725 to 62,0058)	0,0000		
Previous thromboembolism	2,5574 (0,7355 to 8,8916)	0,1397		
LV ejection fraction	0,8528 (0,8122 to 0,8954)	0,0000	0,9061 (0,8545 to 0,9607)	0,0009692
LV end diastolic dimension	1,1144 (1,0586 to 1,1731)	0,0000		
Left atrial size (cm)	1,1532 (1,1000 to 1,2090)	0,0000		
Number of NC segments	0,9230 (0,7846 to 1,0859)	0,3341		
Restrictive pattern	2,6911 (1,6940 to 4,2752)	0,0000		
2-3 degree mitral regurgitation	2,7521 (0,7140 to 10,6082)	0,1414		
Permanent atrial fibrillation/flutter	2,5522 (1,1455 to 5,6866)	0,0219		
Left bundle branch block	5,2083 (2,2618 to 11,9937)	0,0001		

NYHA: New York Heart Association; NC: non-compacted segments

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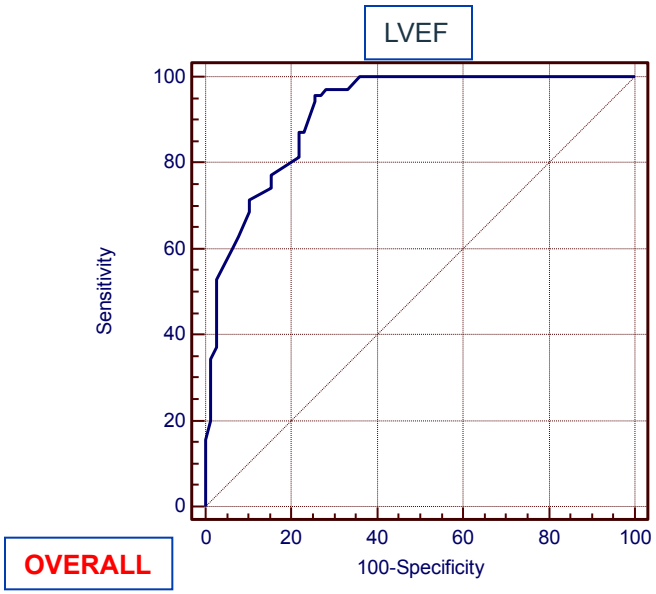
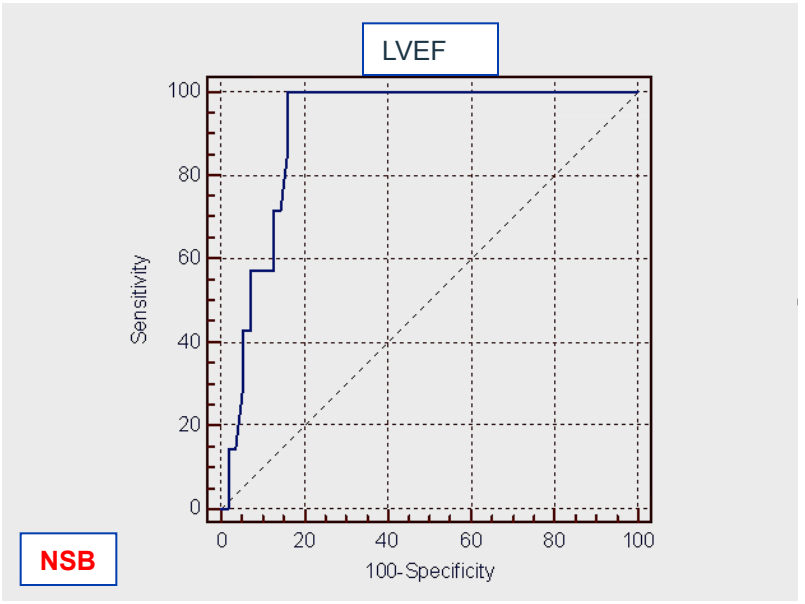
Criterion values and coordinates of the ROC curve

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
<=41	95,71	88,0 - 99,1	74,36	63,2 - 83,6	3,73	0,058

+LR : Positive likelihood ratio

-LR : Negative likelihood ratio





Criterion values and coordinates of the ROC curve

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
<=43	100,00	58,9 - 100,0	83,93	71,7 - 92,4	6,22	0,00

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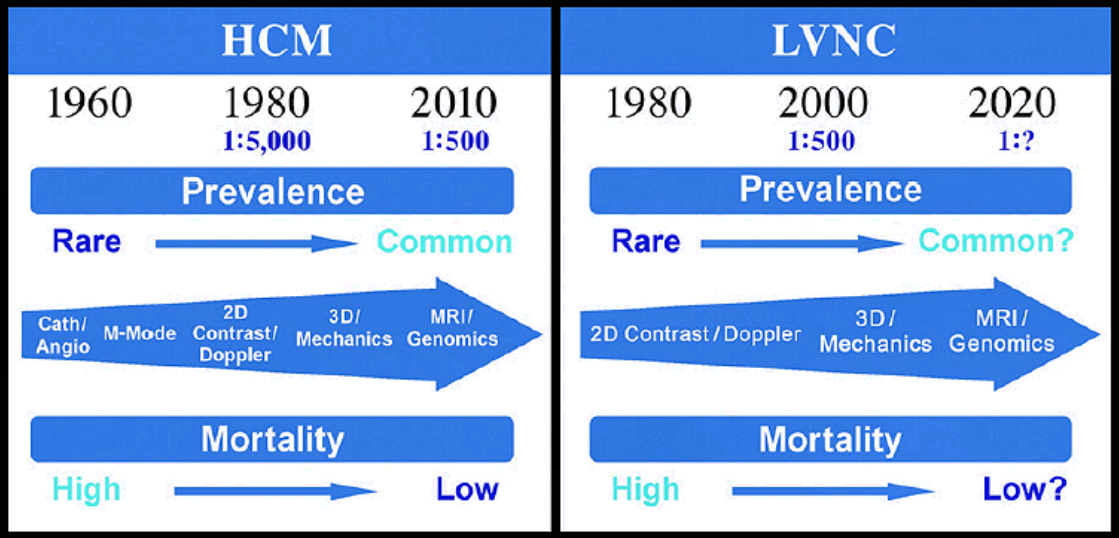


Figure 1 Future of LVNC. Diagram demonstrating how hypertrophic cardiomyopathy (HCM) is akin to LVNC. Research on HCM over the past 50 years has improved understanding of the prevalence and mortality of this heterogeneous disease entity. The same paradigm can be applied to LVNC to better understand this entity. *Angio*, Angiography; *Cath*, catheterization; *MRI*, magnetic resonance imaging.

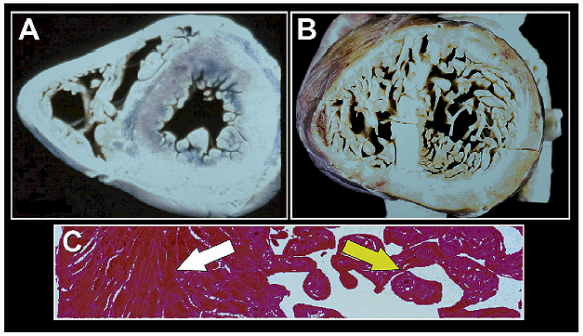
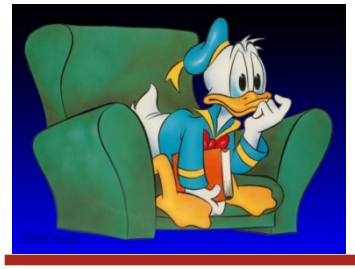


Figure 2 Postmortem gross pathologic specimen examination (both right and left ventricles) of a normal heart **(A)** compared to a heart with noncompacted myocardium **(B)**. **(C)** Microscopic examination of the compacted (*white arrow*) and noncompacted (*yellow arrow*) myocardium from the heart in **(B)**. Image courtesy of Bill Edwards, MD, Cardiac Pathology Department, Mayo Clinic (Rochester, MN).

J Am Soc Echocardiogr 2012;25:363-75



NVM: COS'E?

European Heart Journal (2008) **29**, 270–276
doi:10.1093/eurheartj/ehm342

ESC REPORT

Classification of the cardiomyopathies: a position statement from the european society of cardiology working group on myocardial and pericardial diseases

Perry Elliott, Bert Andersson, Eloisa Arbustini, Zofia Bilinska, Franco Cecchi, Philippe Charron, Olivier Dubourg, Uwe Kühl, Bernhard Maisch, William J. McKenna, Lorenzo Monserrat, Sabine Pankuweit, Claudio Rapezzi, Petar Seferovic, Luigi Tavazzi, and Andre Keren*

It is not clear whether LVNC is a separate cardiomyopathy, or merely a congenital or acquired morphological trait shared by many phenotypically distinct cardiomyopathies.

NVM: COME DIAGNOSTICARLA?

Table 1 Diagnostic criteria used to define LVNC

Echocardiographic criteria	
Chin *et al.*[14]	Jenni *et al.*[7]
• LVNC is defined by a ratio of X/Y ≤ 0.5	• Bilayered myocardium consisting of a thin C layer and a much thicker NC layer with deep endomyocardial recesses: NC/C > 2
• These criteria evaluate trabeculae at the LV apex using the parasternal short-axis and apical views and on the LV free wall thickness at end-diastole	• Predominant location of the pathology is midlateral, midinferior, and apex
	• Evidence of intertrabecular recesses filled with blood from the LV cavity
	• Acquisition of images views: short-axis with measurement of NC/C ratio performed at end-systole
Stöllberger and Finsterer[19]	Authors' proposal (criteria not validated)
• Four or more trabeculations protruding from the LV wall, located apically to the papillary muscles and visible in one imaging plane	• An evaluation of the trabeculations' sizes (NC myocardium) in relation to C wall thicknesses in multiple imaging windows and at different ventricular levels throughout the cardiac cycle
• Trabeculations with the same echogenicity as the myocardium and synchronous movement with ventricular contractions	• Identification of the bilayered myocardium (C and NC) in the short-axis views at the mid and apical levels and in the apical two- and four-chamber and apical long-axis views
• Perfusion of the intertrabecular recesses from the LV cavity	• Thicknesses of the C and NC sections of the myocardium are best measured in the short-axis views at end-diastole, with an NC/C ratio > 2 being diagnostic of LVNC
• Acquisition of the images in the apical four-chamber view, atypical views to obtain the best quality image to differentiate between false chords, aberrant bands and trabeculations	
MRI criteria	
Petersen *et al.*[23]	Jacquier *et al.*[22]
• Ratio between NC and C layers > 2.3 at end-diastole	• Trabeculated LV mass > 20% of global LV mass (measurements made at end-diastole)

C, Compacted; *MRI*, magnetic resonance imaging; *NC*, noncompacted; *X*, distance from the epicardial surface to the trough of the trabecular recess; *Y*, distance from the epicardial surface to the peak of the trabeculation.

J Am Soc Echocardiogr 2012;25:363-75

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European Heart Journal – Cardiovascular Imaging (2013) **14**, 930–931
doi:10.1093/ehjci/jet090

INVITED EDITORIAL

Left ventricular non-compaction: troubles and traps of current imaging techniques

Giovanni Corrado*

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Table 2 Diagnostic assessment and therapeutic strategies

Diagnostic assessment	
Doppler echocardiography	Validated echocardiographic criteria (*Table 1*) Speckle tracking (LV solid body rotation/twist)
Cardiac MRI	Ratio between non-compacted and compacted layer >2.3 Trabeculated LV mass >20% of the global LV mass
Genetic testing	
Neurological assessment	If suspicion of skeletal/mitochondrial myopathy
Family screening (fist-degree relatives)	Doppler echocardiography, (genetic assessment as appropriate)
Electrophysiology study	Symptomatic arrhythmias, syncope
Therapeutic strategies	
Normal LV size/systolic function	Regular follow-up (every 2 years)
Heart failure therapy	As per guidelines for heart failure
Anticoagulation	LVEF <40%
ICD	Secondary prevention/(primary prevention?)
Biventricular pacing	Advanced heart failure/LVEF <35%/ dyssynchrony (as per guidelines)

ICD, implantable cardioverter/defibrillator; EF, ejection fraction; LV, left ventricular; MRI, magnetic resonance imaging.

European Heart Journal (2011) **32**, 1446–1456
doi:10.1093/eurheartj/ehq508

REVIEW

Frontiers in cardiovascular medicine

Left ventricular non-compaction revisited: a distinct phenotype with genetic heterogeneity?

Erwin Oechslin [1,2]* and Rolf Jenni [3]

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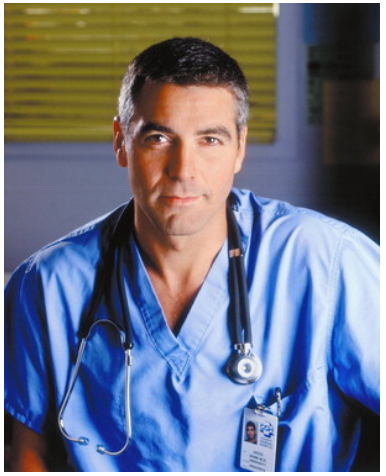

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Research

Case Report/Case Series

Hypertrabeculation vs Left Ventricular Noncompaction on Echocardiogram

A Reason to Restrict Athletic Participation?

David C. Peritz, MD; Aaron Vaughn, MD; Mario Ciocca, MD; Eugene H. Chung, MD

IMPORTANCE Left ventricular noncompaction (LVNC) is a rare cause of progressive cardiomyopathy thought to result from incomplete myocardial development. It has been associated with an increased risk of sudden death, especially in those with a depressed left ventricular ejection fraction. Thus, the current recommendation for patients with this diagnosis is restriction from participation in competitive sports.

OBSERVATIONS An asymptomatic 18-year-old African American collegiate football player had a murmur on his preparticipation physical examination. Subsequent cardiology workup revealed hypertrabeculation vs LVNC. Second and third opinions were sought from national experts in the field: one gave the diagnosis of LVNC and recommended restriction; the other gave the diagnosis of hypertrabeculation. After a family meeting including the player, mother, team physician, and consulting cardiologist, the player was permitted to participate in football.

CONCLUSIONS AND RELEVANCE Distinguishing between pathologic LVNC and physiologic hypertrabeculation is a diagnostic challenge and is becoming increasingly commonplace with enhanced echocardiography and magnetic resonance imaging modalities. Given the limited data on such patients, careful workup and discussion between patient and providers is required.

JAMA Intern Med. 2014;174(8):1379-1382. doi:10.1001/jamainternmed.2014.1066
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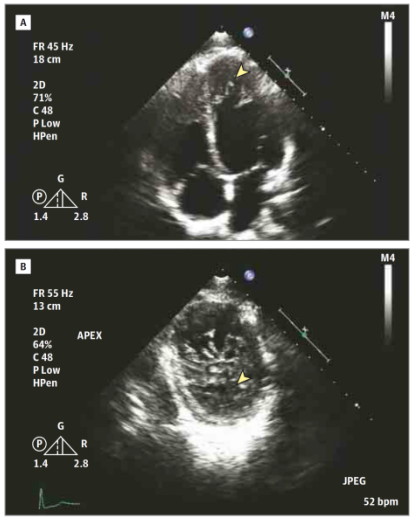
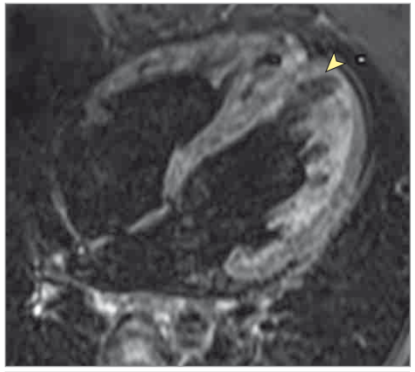
Figure 2. Echocardiogram Revealing Hypertrabeculation but Normal Systolic Function



A, Increased ventricular wall thickness. The left ventricular ejection fraction is more than 55%. B, Prominent trabeculation of the apical portion of the left ventricle with deep intertrabecular recesses. Arrowhead in each view indicates area of hypertrabeculation.

Figure 3. Magnetic Resonance Imaging: Apical Hypertrabeculation Without Segmental Myocardial Thinning



Magnetic resonance image showing no apical thrombi and no evidence of systolic dysfunction. Arrowhead indicates area of hypertrabeculation.

Conclusions

To our knowledge, no reported cases of sudden death in athletes have been attributed to LVNC. We expect as imaging modalities continue to improve and as preparticipation screening becomes more prevalent, scenarios such as ours will become increasingly common. Patients with hypertrabeculation but preserved left ventricular function may represent a low-risk group. Close follow-up along with longitudinal registry studies will continue to be important to establishing risk in patients such as ours.

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NVM ACQUISITA (e talora reversibile..)

- High trained athletes
- Sickle cell anemia patients.
- Pregnancy

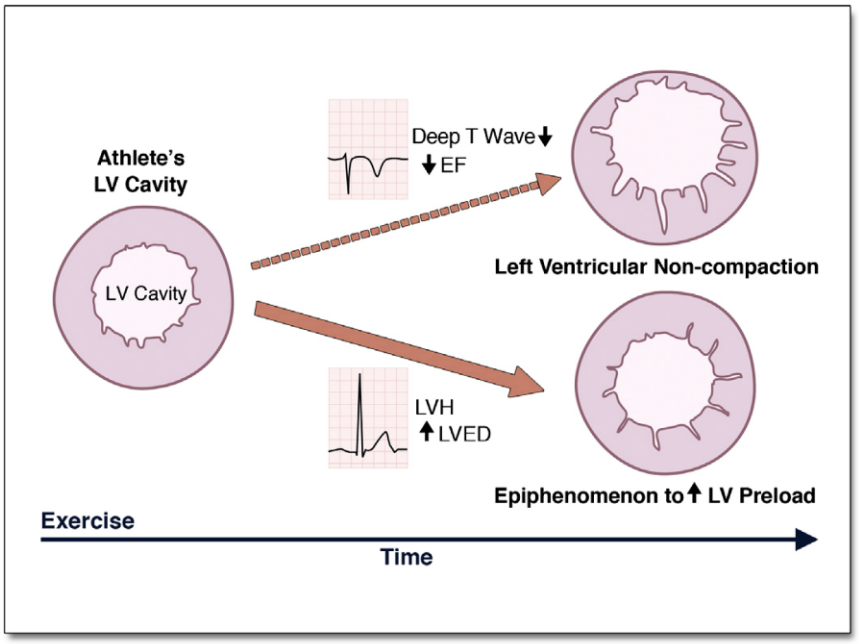

FIGURE 2 Potential Significance of Increased LV Trabeculation in Young Individuals Engaging in Intensive Physical Training

In the majority of athletes, increased LV trabeculation is likely to represent expressions of physiological cardiac remodeling. However, a small minority may express a triad of reduced LV systolic function, repolarization changes raising suspicion of left ventricular noncompaction (LVNC). EF = ejection fraction; LV = left ventricle/ventricular; LVED = left ventricular end-diastolic diameter; LVH = left ventricular hypertrophy. Adapted with permission from Gati et al. (15).

Gati S, Chandra N, Bennett RL, et al. Increased left ventricular trabeculation in highly trained athletes: do we need more stringent criteria for the diagnosis of left ventricular non-compaction in athletes? Heart 2013;99:401–8

Gati S, Papadakis M, Van Niekerk N, et al. Increased left ventricular trabeculation in individuals with sickle cell anaemia: physiology or pathology? Int J Cardiol 2013;168:1658–60.

Gati S, Papadakis M, Papamichael ND, et al. Reversible de novo left ventricular trabeculations in pregnant women: implications for the diagnosis of left ventricular noncompaction in low-risk populations. Circulation 2014;130:475–83

ECOCARDIOGRAFIA 2015
XVII Congresso Nazionale SIEC
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Napoli, 16-18 Aprile 2015

PROBABILMENTE ENTRAMBI

MIOCARDIO NON COMPATTATO: SOPRA O SOTTOVALUTATO?

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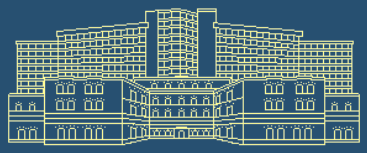

H. Valduce 1879

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GRAZIE PER L'ATTENZIONE

MIOCARDIO NON COMPATTATO: SOPRA O SOTTOVALUTATO?

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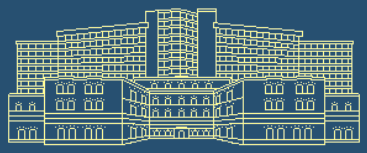

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