

LEFT VENTRICULAR NON-COMPACTION

Definition

Left ventricular noncompaction (LVNC) describes a ventricular wall anatomy characterized by the presence of prominent left ventricular (LV) trabeculae, a thin compacted layer, and deep intertrabecular recesses that are continuous with the LV cavity and separated from the epicardial coronary arteries (Figure 1).¹⁻³ By definition it pertains to the LV but may also involve the right ventricle. Current evidence suggests that LVNC is a morphologic trait that can be seen in the healthy population or shared by different cardiomyopathies, rather than a distinct cardiomyopathy.^{4,5} The extent of trabeculated vs compact myocardium in the adult is determined by differential (allometric) growth of each myocardial layer. Because trabeculated myocardium does not coalesce to form the compact myocardial wall, the term “left ventricular noncompaction” is rather inaccurate.⁶

In infants and children, caution is warranted because fewer data are available regarding the etiology and prognosis of excessive trabeculation. Clinical evaluation for occult neuromuscular disease or another genetic/metabolic aetiology may be appropriate.⁴

Epidemiology

Its prevalence is estimated to be 0.01-0.05% in adults,^{2,7} but due to uncertainty about assessment of trabeculations that can occur as a response to increased LV loading conditions makes true diagnosis difficult to be established. Myocardial trabeculations even fulfilling the diagnostic criteria for non-compaction cardiomyopathy can be seen in the general population, athletes, patients with sickle cell anemia, and pregnant women in whom they resolve within the next 2 years.^{1,3,8,9}

There is a higher prevalence with the introduction of newer imaging technologies, specifically CMR imaging, which identify LVNC changes more readily. The clinical significance of these findings remains unclear but there is significant potential for overdiagnosis.¹⁰

Aetiology

Left ventricular non-compaction (spongy myocardium or fetal myocardium) was initially described as an arrest in the normal process of myocardial compaction, the final stage of myocardial morphogenesis, resulting in persistence of many prominent ventricular trabeculations and deep intertrabecular recesses. LVNC is genetically heterogeneous, with a predominantly autosomal-dominant inheritance pattern, and has been linked to sarcomere gene mutations, particularly *MYH7*, *MYBPC3*, and *TTN* (Table 1).^{1 11-14} Thus, LVNC can be

observed in healthy subjects with normal LV size and function, and it can be acquired and reversible (Table 2). When associated with LV dilation and dysfunction, hypertrophy, or congenital heart disease, the genetic cause may overlap. There is a shared genetic basis for LVNC and bicuspid aortic valve, with MIB1-NOTCH playing a crucial role.¹⁴

Presentation

The classical clinical presentation is heart failure, arrhythmias and embolic events.¹⁵ However, LVNC may present in several subtypes such as isolated LVNC with or without arrhythmias, dilated LVNC, hypertrophic LVNC, restrictive LVNC and in association with congenital defects such as ASD, VSD, AS, and coarctation. There is a bilayer LV wall consisting of a thick endocardial layer with prominent intertrabecular recesses with a thin, compact epicardial layer. Trabeculations are typically most evident in the apical portion of the LV (Figure 1). Histology is not specific. Clinical features include heart failure, arrhythmias, and thromboembolic events.¹⁶ In infancy, LVNC presents with heart failure with a predominant dilated phenotype. Long-term outcomes are worse than for matched children with dilated cardiomyopathy.¹⁷ Adverse cardiac events occur more often in mutation carriers, and especially with mutations in genes *LMNA*, *RBM20*, with left ventricular systolic dysfunction than in sporadic cases.^{11,12}

Diagnosis

The diagnosis of LVNC requires genetic counseling, DNA diagnostics, and cardiological family screening (Figure 2). LV trabeculations measured in end-diastole in asymptomatic individuals recruited in the MESA study, were not associated with deterioration in LV volumes or function during a 10-year period,⁹ and in patients with LVNC the extent of trabeculation detected by using CMR has less prognostic significance for adverse CEs than LV dilation, systolic dysfunction, or fibrosis.¹⁸

The **ECG** is typically abnormal and may show giant voltages.

Echocardiographic diagnostic criteria are:^{2,19}

1. At least 3 trabeculations, with a ratio of the distance from the epicardial surface to the trough of the trabecular areas divided by the distance from the epicardial surface to the trough of the trabecular areas ≤ 5 .
2. A two layer structure, and a maximal end systolic ratio of non-compacted to compacted layers of > 2 .
3. Colour Doppler evidence of deep perfused intertrabecular recesses.

Such findings, however, can also be found in up to 8% of normal subjects.²⁰

LVEF is the variable most strongly associated with MACE.²¹

Cardiac MRI offers better spatial resolution than echocardiography. Proposed basic criteria for diagnosis of non-compaction include: ^{2 22 23}

1. Noncompacted LV myocardial mass >25%;
2. Total noncompacted LV myocardial mass index >15 g/m²;
3. Noncompacted/compacted myocardium ratio $\geq 3:1$ in at least 1 segment, excluding the apical segment; and
4. Trabeculation in segments 4 to 6 $\geq 2:1$ (noncompacted/compacted).

Late gadolinium enhancement (**LGE**) has been found to confer additional risk in patients without severe systolic dysfunction, and a risk prediction model is developed and validated to guide management.²¹

Recommendations for **genetic testing** are provided in Table 3 and Figure 2.²⁴ The identification of a pathogenic mutation or family history of LVNC are strongly supportive of a definitive diagnosis.

Therapy

Aspirin is administered in all patients, while anticoagulation is indicated in patients with dilated LV and LVEF < 40% or history of thromboembolism. If LV dysfunction is present, the management is that of heart failure. Arrhythmias that occur in up to 20% of patients,² and are managed as in other cardiomyopathies, and ICD may be considered (ACC/AHA 2012 GL on device therapy, IIb-C).

Prognosis depends on the degree of ventricular dysfunction; reported 3- and 6-year survival is 53 to 85%.^{2,7} Carriers of pathogenic TTN, LMNA, and RBM20 variants have unfavourable outcomes.¹¹ Specific recommendations are presented in Figure 3, and Table 4. Exercise and sports recommendations are presented in Table 5.^{25,26}

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