

# Isolated left ventricular non-compaction: an unusual indication for heart transplantation

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We report a patient with isolated left ventricular non-compaction diagnosed by echocardiography and cardiac magnetic resonance imaging. She developed refractory congestive heart failure and subsequently underwent successful heart transplantation. This type of cardiomyopathy is thought to be caused by the arrest of normal embryogenesis of the endocardium and myocardium. The spectrum of clinical, radiological, and pathological abnormalities is discussed.

## Case report

In 2003, a 43-year-old woman was referred to our cardiology clinic with a diagnosis of hypertrophic cardiomyopathy after family screening using transthoracic echocardiography (TTE). Her 14-year-old son had been diagnosed with hypertrophic cardiomyopathy 2 years beforehand. The family history revealed that the patient's mother suffered sudden cardiac death at the age of 56 years. A repeat TTE, however, showed the presence of numerous prominent trabeculations and deep sinusoids, especially in the apical and posterior wall. The left ventricle's systolic function was impaired with an ejection fraction estimated at 32%. Cardiac catheterization showed normal coronary arteries. The cardiac output (CO) and cardiac index (CI), measured using thermodilution, were 3.2 L/min and 2.25 L/min/m<sup>2</sup> respectively. She had no other cardiac abnormalities. Cardiac magnetic resonance (CMR) imaging confirmed extensive areas of prominent trabeculation and inter-trabecular recesses of the left ventricle with relative sparing of the basal septum. The delayed contrast images revealed diffuse patchy endocardial, epicardial and mid-wall myocardial enhancement at the non-compacted left ventricular walls, suggestive of extensive myocardial fibrosis (Fig 1). These areas matched the irreversibly hypoperfused sites detected by the myocardial perfusion imaging. Hence, a diagnosis of isolated left ventricular non-compaction cardiomyopathy (LVNC) was made. A CMR imaging subsequently performed on her son also showed features diagnostic of LVNC rather than hypertrophic cardiomyopathy.

As the patient remained asymptomatic with New York Heart Association class I, she declined further intervention until July 2008 when she presented with rapid deterioration of exercise tolerance and shortness of breath on minimal exertion. An echocardiogram showed markedly impaired left ventricular systolic and diastolic function with an ejection fraction of 11%. She had hypotension (blood pressure 75/50 mm Hg) so intravenous inotropic agents were administered. Cardiac catheterization was performed and her CO was markedly reduced (1.03 L/min only, her CI=0.75 L/min/m<sup>2</sup>). In view of her persistently low CO despite intravenous inotropic agents, an intra-aortic balloon counterpulsation pump (IABP) was inserted for haemodynamic support. She was put on the high-priority heart transplantation waiting list and underwent successful heart transplantation after 4 weeks of IABP support. Pathological examination of the explanted heart found anatomical features of LVNC (Fig 2). Her postoperative course was uneventful and she remained well 3 months after the cardiac transplantation, on a standard immunosuppressive regimen.

## Discussion

Left ventricular non-compaction cardiomyopathy has recently been classified as a primary cardiomyopathy.<sup>1</sup> It is characterised by a two-layer structure of thickened myocardial wall presenting with a thin, compacted epicardial layer, and an excessively thickened non-compacted endocardial layer. The non-compacted endocardial layer consists of prominent myocardial trabeculations and deep intertrabecular recesses that lie in continuity with the left ventricular cavity.<sup>2</sup> Failure of the normal compaction process of the ventricular endomyocardium is thought to reflect an arrest of cardiac embryogenesis. Left ventricular non-compaction cardiomyopathy is associated with a broad spectrum of clinical and pathophysiological findings with an unclear natural history.<sup>3</sup> Apart from causing

### Key words

Cardiomyopathies; Heart failure; Heart transplantation; Heart ventricles; Ventricular dysfunction, left

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## 孤立性左心室心肌致密化不全： 心臟移植的一個罕見指標

本文報告一宗用超聲及磁共振心臟成像診斷的孤立性左心室心肌致密化不全的病例。病人出現難治性充血性心力衰竭，她繼而成功接受心臟移植手術。這種心肌症被認為是心內膜及心肌層於早期胚胎發育受阻引致。本文並討論有關此病的臨床、放射學，以及病理學的異常。

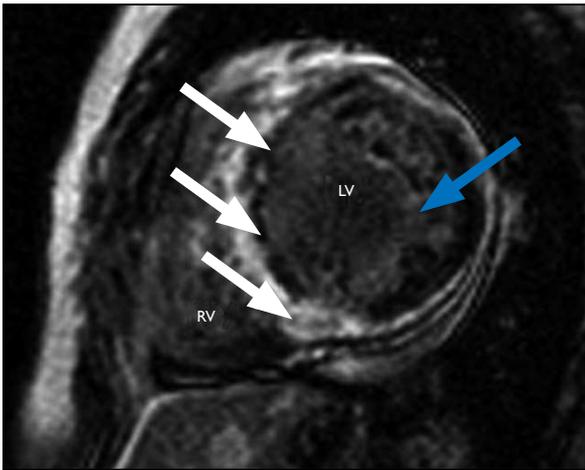


FIG 1. Delayed contrast enhancement image acquired using a 1.5-T magnetic resonance imaging machine at the same location as Figure 2

The trabeculations and deep recesses (blue arrow) are well illustrated. There was diffuse epicardial enhancement suggesting fibrosis at the septum and inferior wall of LV (white arrows) [LV denotes left ventricle, and RV right ventricle]

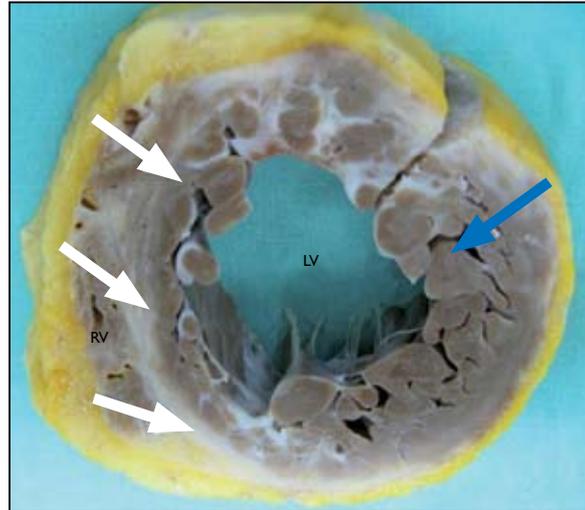


FIG 2. Explanted heart showing left ventricular non-compaction with prominent trabeculations and deep recesses (blue arrow) in the left ventricle

There is diffused fibrosis at the interventricular septum and inferior wall (white arrows) [LV denotes left ventricle, and RV right ventricle]

diastolic and/or systolic left or global ventricular dysfunction with decreased CO and subsequent left ventricular hypertrophy, the prominent aberrant ventricular trabeculae may predispose to abnormal cardiac conduction and potentially fatal ventricular arrhythmias, together with an increased incidence of thrombo-embolism.<sup>4,6</sup> Several studies have recently reported asymptomatic familial disease in some patients and there may be a milder phenotype with a more favourable prognosis than that previously described.<sup>3,7</sup> Improvements in echocardiographic and CMR imaging have also facilitated detection of previously unrecognised asymptomatic cases. Patients with symptoms of heart failure, a history of sustained ventricular tachycardia or an enlarged left atrium have a worse prognosis.<sup>3</sup> Because of the familial association with LVNC, it is recommended that first-degree relatives undergo screening echocardiography.

The pathophysiological mechanisms of the different clinical manifestations in isolated ventricular non-compaction are poorly understood. Heart failure is thought to be secondary to diastolic ventricular dysfunction. Myocardial ischaemia may be the predominant mechanism underlying progressive systolic dysfunction. While the intertrabecular recesses receive blood directly from the left ventricular cavity, the epicardial and endocardial layers of the myocardium, including the trabeculations themselves, rely on the coronary circulation for their blood supply. Epicardial coronary artery anatomy is characteristically normal in LVNC, but magnetic resonance imaging and thallium-201 scintigraphy show subendocardial and transmural

perfusion defects, often corresponding to zones of non-compacted myocardium.<sup>8,9</sup> Both interstitial fibrosis and 'scarring' in the form of focal replacement fibrosis occur, the latter consistent with microscopic ischaemic infarcts in the sub-endocardium.<sup>10</sup>

Clinical studies suggest that LVNC is often familial with a predominantly autosomal dominant inheritance with incomplete penetrance.<sup>11</sup> It has also been linked to mutations in several genes including *ZASP*,  $\alpha$ -dystrobrevin and *G4.5* (encoding tafazzin which is associated with Barth syndrome<sup>11-13</sup>) but these are infrequent causes of the disease. The genetic basis of the disease remains unresolved in most patients with LVNC.

Although LVNC is usually diagnosed using echocardiography and, increasingly, by magnetic resonance imaging, there is no current universally accepted definition of LVNC. Some criteria require a double-layered appearance of the myocardium on two-dimensional echocardiography (maximal end systolic ratio of non-compacted layer to compacted layers of  $>2$  is diagnostic)<sup>2</sup> and CMR imaging<sup>14</sup> while others require only prominent or numerous left ventricular trabeculations.<sup>15</sup> Cardiac magnetic resonance imaging

is unique among non-invasive imaging modalities in that it can identify sub-endocardial scarring and fibrosis, highlight the prominent trabeculations, and provide accurate functional data, making it a critical diagnostic tool. When extensive myocardial fibrosis is seen along with the distinctive features of LVNC on CMR imaging, heart transplantation should be considered early.

We believe symptomatic patients with isolated ventricular non-compaction should be considered for transplant early, as we found this anomaly only minimally responsive to conventional medical therapy. Although the progressive clinical course may be slow, when patients do develop heart failure symptoms they can deteriorate very rapidly, requiring active intervention.

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