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Review

Isolated left ventricular non-compaction cardiomyopathy in adults

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ABSTRACT

Left ventricular non-compaction (LVNC) is a heart-muscle disorder characterized by prominent myocardial trabeculations and deep intertrabecular recesses in the LV cavity. LVNC is often diagnosed by echocardiography and cardiac magnetic resonance imaging, but a universally accepted definition of LVNC is lacking. Although the prevalence of LVNC in adults remains unclear, improvements in diagnostic techniques account for the relatively high incidence of LVNC in recent years. The clinical presentation is highly variable from asymptomatic to symptomatic. Meanwhile, the classical triad of heart failure, ventricular arrhythmias, and systemic embolism constitute typical complications of this disease. Unfortunately, there is no specific therapy for LVNC, and management depends on the clinical manifestations. In this review, we discuss what is currently known about LVNC and conclude that multicenter registries are required for a better understanding of this rare disorder.

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Introduction

Left ventricular non-compaction (LVNC) is a rare congenital cardiomyopathy, with or without LV dysfunction, characterized by excessively prominent trabeculations and associated deep recesses that communicate with the ventricular cavity. LVNC affects both children and adults. The diagnosis of LVNC in adults has been reported with increasing frequency because of improved imaging modalities such as echocardiography and cardiac magnetic resonance imaging (MRI), but still little is known among physicians. The purpose of this article is to provide an overview of the current knowledge of this disease.

History

LVNC, also known as spongy myocardium, is a distinct form of cardiomyopathy. The histology of persistent spongy myocardium with embryonic blood supply was first discussed in the literature

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in 1975 [1]. LVNC was initially described in children and was associated with other congenital cardiac anomalies. In 1984, Engberding and Bender [2] were the first to make the antemortem diagnosis of LVNC in an adult using two-dimensional (2D) echocardiography, which demonstrated a spongy myocardium with prominent sinusoids; they attributed these findings to an abnormal lack of sinusoidal regression during cardiac embryogenesis. Subsequently, in 1990, Chin et al. [3] reported 8 cases of LVNC, with ages ranging from 11 months to 22.5 years, without congenital cardiac anomalies and proposed that it be renamed "isolated non-compaction of the LV myocardium."

Currently, LVNC is a rare disorder listed as an unclassified cardiomyopathy by the World Health Organization [4] and European Society of Cardiology (ESC) [5], and classified as a genetic cardiomyopathy by the American Heart Association (AHA) [6].

Pathogenesis

During normal embryological development, the heart consists of a spongy meshwork of muscle fibers and trabeculations that are separated by recesses (Fig. 1). Before the coronary vessels develop, these intertrabecular recesses, or sinusoids, communicate with the cavum of the ventricle to receive blood supply. After the coronary vasculature develops, the ventricular myocardium gradually becomes compacted and the larger intertrabecular recesses are transformed into capillaries. Trabecular compaction occurs between 12 and 18 weeks of gestation, starting at the base of the heart and progressing toward the apex [7,8]. For unknown reasons, in patients with LVNC, this transition does not occur, leading to the development of a thickened, non-compacted endomyocardial layer with prominent trabeculations that are continuous with the LV cavity and lack communication with the epicardial circulation, deep recesses, and a thin compacted epicardial layer (Fig. 2) [9,10].

Histologically, LVNC has neither specific findings nor a difference has been seen between isolated forms that lack other congenital cardiac anomalies and non-isolated forms. However, interstitial fibrosis and endocardial fibroelastosis have been described on endomyocardial biopsy [11]. Furthermore, at autopsy, the absence of well-formed papillary muscles is highly associated with the diagnosis of LVNC [12].

LVNC can be familial. In one study, 6 of 34 patients (18%) had a family history of LVNC [13]. Moreover, although a genetic mutation that consistently results in the LVNC phenotype has not been identified, mutations in several genes, including Z-band alternatively spliced PDZ-motif protein (ZASP), α-dystrobrevin (DTNA), tafazzin (TAZ-G4.5), and genes encoding sarcomeric proteins, have been reported [14]. Recently, mutations in hyperpolarization-activated cyclic nucleotide channel 4 (HCN4) have also been reported in families with sinus node dysfunction and LVNC [15,16]. Therefore, some affected individuals have been detected by tracking the asymptomatic relatives of affected patients.

Epidemiology

In a study of children with primary cardiomyopathy of all types, LVNC was present in 9.2% of the cases, the third most common type of primary cardiomyopathy following dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM) [17]. Pediatric LVNC can frequently co-exist with anatomical abnormalities, including atrial and ventricular septal defects, congenital aortic stenosis, and aortic coarctation, although the relationships and characterized syndromes have not been identified [18]. Moreover, the prevalence of neuromuscular disorders, including Becker's muscular dystrophy, Friedreich's ataxia, myotonic dystrophy, and mitochondriopathy, are also sometimes seen in patients with LVNC [18], although the reason for the relationship is unknown.

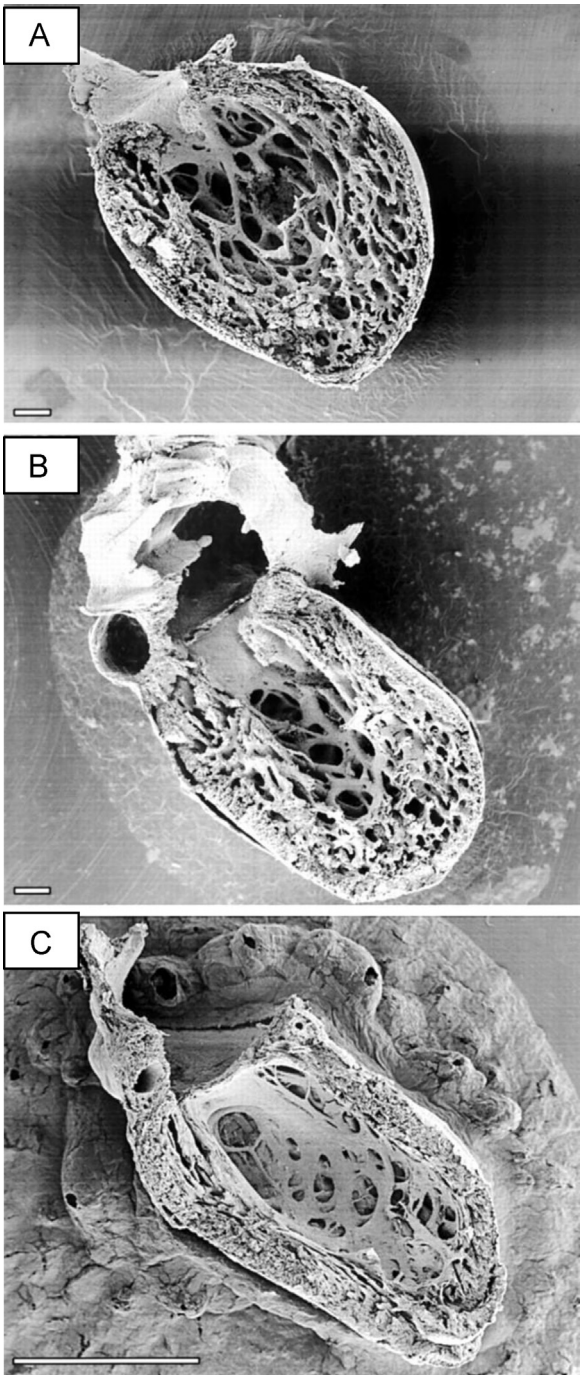

Fig. 1. Parietal views of sagittally dissected human embryonic left ventricles showing the process of normal trabecular compaction. (A) Abundant fine trabeculations are present at 6 weeks. (B) The trabeculations start to solidify at their basal area, contributing to added thickness of the compact layer at 12 weeks. (C) The compact layer forms most of the myocardial mass after completion of compaction in the early fetal period.
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The prevalence of isolated LVNC in adults remains unclear, although in observational studies, LVNC has been found in 0.01–0.26% of all adults referred to an echocardiography laboratory [13,19]. Alternatively, the prevalence of LVNC in the general population has not been published, and the diagnosis is presumably often missed, because the disease is relatively unknown among physicians.