

ANTICOAGULATION IN LEFT VENTRICULAR NON COMPACTION: A VERITABLE CONTROVERSY!

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ABSTRACT

Non compaction of left ventricular myocardium (LVNC) is a rare congenital cardiomyopathy resulting from an incomplete myocardial morphogenesis that leads to the persistence of the embryonic myocardium. Non compaction of left ventricular myocardium is recognizable by the presence of prominent trabeculations and deep inter-trabecular recesses of the left ventricle wall. It is not clear whether inter-trabecular recesses can lead to thrombi formation, with possible thromboembolic results. Some authors reported a high incidence of embolic events in patients affected by non-compaction whereas recently, Stollberger, Finesterer, Giovannia and others described the thrombus formation as a rare event in these patients. According to these authors, anticoagulant therapy is the most useful method in treating patients affected by chronic heart failure.

Keywords: Anticoagulation- Non compaction of left ventricular myocardium (LVNC)

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INTRODUCTION

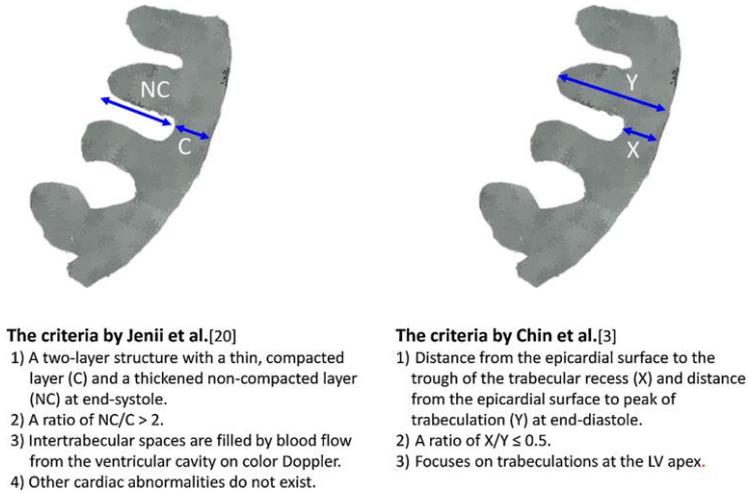
Non compaction of ventricular myocardium (NVM) is an increasingly recognized but apparently uncommon cardiomyopathy, which was characterized by extent hypertrophied left ventricle (LV) wall with multiple trabeculations and deep inter-trabecular recesses communicating with the LV cavity and is considered to be the result of an arrest of the normal process of intrauterine endomyocardial morphogenesis at present. NVM could be a completely isolated finding, or could be associated with other congenital heart anomalies. NVM could become manifest during infancy, usually related to severe clinical course and a poor natural history, however, the clinical course seems to be more variable in adults. In other words, a minority of adult patients with NVM have mild and relatively favorable clinical course and the majority of adult patients with NVM have severe and unfavorable clinical course, which present with LV systolic dysfunction and heart failure, arrhythmias, thromboembolic events, or sudden cardiac death [7, 8]. NVM was included in World Health Organization classification of cardiomyopathies and was classified as a primary cardiomyopathy of genetic origin by the American Heart Association in 2006 [7], however, it remains subject to

controversy because of lack of consensus on its etiopathogenesis, pathogenesis, pathophysiology, diagnosis, management, etc.

Usually, patients with NVM have a relatively severe clinical course and the mortality rate exceeded 35% in adults [9] and 22% in children [10]. One of reasons is the effective therapies have not well been established. In addition, during the past few years, the developments of implantable defibrillators and pacemakers have already provided newer therapeutic elections for patients with NVM [11, 12]. However, the developments have also raised considerable uncertainty and new considerations about the optimal management of NVM.

DIAGNOSIS

The diagnosis of LVNC is mainly attained by echocardiography; other imaging tests such as cardiac MRI can also be used to diagnose the disease or confirm clinical suspicion. The higher incidence of LVNC reported in recent years is primarily due to improvements in echocardiographic techniques and the use of cardiac MRI, although a universally accepted definition of LVNC is lacking



The criteria by Jenni et al.[20]

- 1) A two-layer structure with a thin, compacted layer (C) and a thickened non-compacted layer (NC) at end-systole.
- 2) A ratio of NC/C > 2.
- 3) Intertrabecular spaces are filled by blood flow from the ventricular cavity on color Doppler.
- 4) Other cardiac abnormalities do not exist.

The criteria by Chin et al.[3]

- 1) Distance from the epicardial surface to the trough of the trabecular recess (X) and distance from the epicardial surface to peak of trabeculation (Y) at end-diastole.
- 2) A ratio of X/Y ≤ 0.5.
- 3) Focuses on trabeculations at the LV apex.

Fig1: Echocardiographic criteria of the diagnosis of left ventricular non-compaction by Jenni et al. [13,14] and Chin et al. (LV : left ventricle)

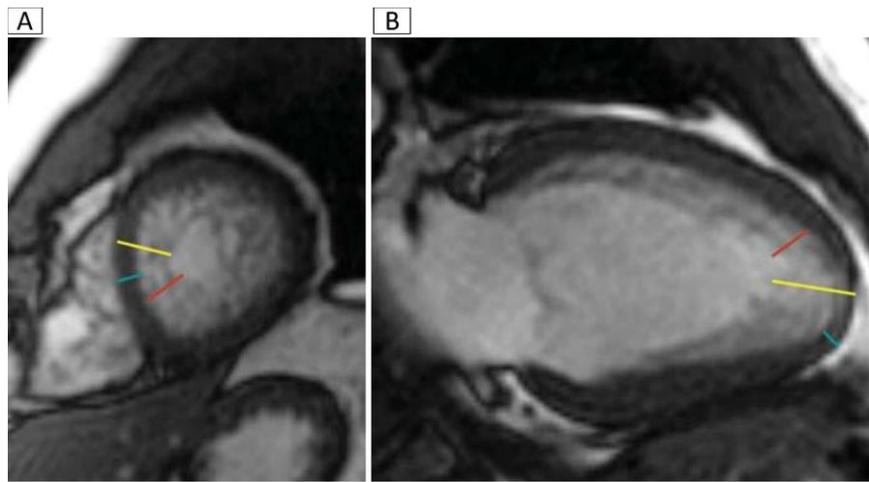


Fig2: Cardiac magnetic resonance images at end-diastole in apical short-axis (A) and left ventricular (LV) long-axis planes (B). Note the whole wall thickness (yellow tracing), the increase in subendocardial LV trabeculation in medial apical, anterior, and inferior segments. The maximum ratio of non-compacted layer (red tracing) to compacted layer (green tracing) is 4 (mean ratio = 2.4) [15]

Individuals with LVNC have variable phenotypic expressions of their cardiomyopathies, and clinical features can range from asymptomatic to symptomatic. The classical triad of heart failure, ventricular arrhythmias, and systemic embolic events constitute the typical complications found in patients with LVNC.

PREVENTION OF THROMBOEMBOLIC EVENTS:

Systemic thromboembolic complications are the third major complication in LVNC , Although intertrabecular recesses was deemed, a favorable location for thrombus formation, the real prevalence of thrombi in patients with NVM is unknown [5] .

There was significant controversy ,some studies shows that The prevalence of thromboembolic events was independent of LV size or function [16].The deep recesses may aggravate the risk of thrombus formation and be an additional factor for this serious complication [17] Therefore, prevention of embolic events is also an extremely important treatment issue and some researchers have suggested long-term prophylactic anticoagulation for all patients with NVM whether or not thrombus has been found [3,18].Repeated embolic events in patients with impaired LV function have been reported in spite of sinus rhythm and adequate anticoagulation, and embolic events have been observed in young patients with sinus rhythm and normal LV function [2].

On the other hand, however, other researchers have deemed that thrombus formation is a rare event in patients with NVM, the number of strokes or embolic events was not increased in patients with LVNC when compared with age-, sex- and left ventricular fractional shortening-matched controls. LVNC by itself is not a risk factor for stroke and peripheral embolism (2). Stroke in LVNC patients may have various causes in addition to LVNC, such as atrial fibrillation /atrial flutter (AFIB/AFLU), heart failure, arterial hypertension, or a coagulopathy (19). If LVNC is associated with AFIB thrombi may not only be derived from the inter-trabecular spaces but also from the left atrium or left atrial appendage. The rates of S/E reported by others studies seem to depend on age, cardiovascular co-morbidities, and the duration of follow-up [19]

In 2004, Stollberger and Finsterer (5) published a review, reporting a low prevalence of ventricular thrombi findings and embolic events. These data were confirmed by a retrospective analysis of 62 patients published by the same authors [2] Dr. Giovannina et al. [6] evaluated prevalence of stroke and echocardiographic finding of thrombus in a continuous series of 229 patients (men and women) affected by NVM and excluded patients affected by AFIB. In the study, in 122 of them, the authors found a ventricular dysfunction with a mean ejection fraction of 24.6% and the average follow-up was 7.3 years (1–12 years) for all the patients, however, only four patients had a history of ischemic stroke and a large thrombus into the left ventricular chamber was observed in a 1-year-old child affected by Behcet's disease (high risk of thrombi formation) [6]

Therefore, long-term prophylactic anticoagulation for all patients with NVM whether or not thrombus has been found should not be recommended. It must be kept in mind, however, there is an indication for oral anticoagulation in patients with NVM and AFIB, high risk of thrombi formation such as Behcet's disease, depressed left ventricular systolic dysfunction, evidence of spontaneous echocardiographic contrast, severe left ventricular dilation, dilated atria or a history of thromboembolic events.

If LVNC is associated with systolic dysfunction and sinus rhythm, the available data allow no concise recommendation about antithrombotic therapy. A recently published study in 2305 patients with sinus rhythm but reduced systolic function found no significant overall difference in the primary outcome between treatment with VKA and treatment with 325 mg/d acetylsalicylic acid. A reduced risk of ischemic stroke with warfarin was

balanced by an increased risk of major hemorrhage [20]. Since there are no data about the therapeutic effects of NOAC in Patients with sinus rhythm and systolic dysfunction one has to decide on an individual basis if VKA or acetylsalicylic acid should be given.

If LVNC is associated with a history of previous stroke or embolism S/E, VKA should be considered as a secondary prophylaxis if causes other than embolism were excluded as the cause of S/E .

That NOAC may not be beneficial in the same indications as oral anticoagulation has been substantiated recently by the early termination of the European RE-ALIGN trial in which patients with bileaflet mechanical prosthetic heart valves were randomized either to dose-adjusted VKA or to dabigatran [21]. RE-ALIGN was terminated early because the dabigatran treatment arm had significantly more thromboembolic events and more major bleedings than the warfarin treatment arm.

From these findings we conclude that if an LVNC patient has AF, VKA should be preferred over NOAC. If a LVNC patient has systolic dysfunction, the choice between acetylsalicylic acid or VKA relies on individual preferences and the spectrum of contraindications. If there is a history of previous S/E, VKA should be considered if other causes were excluded.

CONCLUSION:

Non compaction of left ventricular myocardium, by itself, does not seem to be a risk factor for stroke or embolic events, so there is no indication for oral anticoagulant therapy

The highest degree of consensus exists for LVNC and AFIB respectively AFLU Concerning the association of LVNC and systolic dysfunction there are some indications that these patients profit from early OAC

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