Clinical Presentation and Echocardiographic Characteristics of Patients with Left Ventricular Noncompaction

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ABSTRACT

Background
Left ventricular noncompaction is a primary genetic cardiomyopathy caused by arrest of normal embryogenesis of the endocardium and myocardium. This anomaly is frequently associated with arrhythmias, heart failure and thromboembolic events.

Objectives
The goal of the present study was to describe the clinical presentation and the electrocardiographic and echocardiographic characteristics of patients with this cardiomyopathy.

Methods
Twenty-two patients with left ventricular noncompaction detected by echocardiography between July 2004 and April 2009 were analyzed. Electrocardiogram and transthoracic Doppler echocardiography was performed to all the patients, and 12 patients underwent 24-hour Holter monitoring. Weight, height and body mass index were calculated and compared with 66 patients distributed into three groups of 22 patients each: 1) control group without heart disease, 2) hypertrophic cardiomyopathy; and 3) idiopathic dilated cardiomyopathy.

Results and Conclusions
In the population with left ventricular noncompaction, female gender prevailed, lower weight and body mass index was observed and dyspnea was the most common symptom. The electrocardiogram showed sinus rhythm, conduction disturbances and repetitive ventricular arrhythmia. Transthoracic echocardiography showed different degrees of systolic and diastolic left ventricular dysfunction with areas of non-compaction in the mid and apical inferior, posterior and lateral segments, in some cases complicated with intraventricular thrombi and occasionally associated with coronary artery fistulas.

Key words
Echocardiography - Cardiomyopathies - Body Mass Index

Abbreviations
LBBB Left bundle-branch block
ICD Implantable cardioverter defibrillator
ECG Electrocardiogram
TTE Transthoracic echocardiography
EF Ejection fraction
HF Heart failure
BMI Body mass index
DCM Dilated cardiomyopathy
HCM Hypertrophic cardiomyopathy
LVNC Left ventricular noncompaction
SD Sudden death
HTx Heart transplantation

INTRODUCTION
Left ventricular noncompaction (LVNC) is a primary genetic cardiomyopathy caused by arrest of normal embryogenesis of the endocardium and myocardium. The disease is characterized by the development of excessive deep trabecular intramyocardial recesses. (1, 2) and is frequently associated with arrhythmias, heart failure (HF) and thromboembolic events.

The goal of the present study was to describe the clinical presentation and the electrocardiographic and echocardiographic characteristics of patients with LVNC.

METHODS
Twenty-two consecutive patients with LVNC detected by echocardiography between July 2004 and April 2009 were analyzed. The study population consisted of 22 patients undergoing transthoracic Doppler echocardiography (TTE) us-
ing SONOS5500 (Philips Medical Systems, Bothell, Washington) and Vivid 7 (GE Medical Systems) ultrasound scanners. Electrocardiogram (ECG) was performed to all the patients, and 12 patients also underwent 24-hour Holter monitoring.

The diagnosis of LVNC was made by TTE in the presence of:
1. Marked endocardial thickening with prominent trabeculations and deep intertrabecular recesses over a thin adjacent epicardial layer with an end-systolic endocardial to epicardial thickness ratio ≥ 2:1.
2. Color Doppler evidence of deep perfused intertrabecular recesses.
3. Absence of coexisting valvular heart diseases, congenital heart diseases or other cardiac anomalies.

Weight, height and body mass index (BMI) were calculated and compared with three groups of 22 patients matched by sex and age: 1) control group of patients without heart disease (CG), 2) patients with hypertrophic cardiomyopathy (HCM); and 3) patients with diagnosis of idiopathic dilated cardiomyopathy (DCM).

Statistical analysis
Quantitative variables with normal distribution were expressed as mean ± standard deviation and those with non-gaussian distribution as median (interquartile range). Analysis of variance was used for intergroup comparison of quantitative variables. A p value < 0.05 was considered statistically significant.

RESULTS
Twenty two patients with LVNC were studied from July 2004 to April 2009. Mean age was 40.59 ± 17 years and 63.6% (14/22) were women.

The characteristics of patients with LVNC are described in Table 1.

Symptoms were present in 81.8% of patients (18/22); the mean time from onset of symptoms to diagnosis was 48.16 ± 72 months, with a median of 24 (225-48) months.

Fifteen patients (83.3%) complained of dyspnea, 5 (27.7%) presented ventricular arrhythmias, 3 (16.7%) had syncope and 2 (11.1%) angina. Functional class I-II dyspnea was present in 53.3% (8/15) of patients and class III-IV in 46.7% (7/15).

Two patients (9.1%) presented embolic stroke. Three patients (13.6%) developed major events: a 58 year-old man presented sudden death (SD), a 18 year-old woman required implantable cardioverter-defibrillator (ICD) therapy due to syncope caused by ventricular tachycardia and a 26 year-old woman underwent heart transplantation (HTx) due to refractory HF.

The ECG showed sinus rhythm in 100% of the cases (22/22), first degree atrioventricular block in 4.5% (1/22), left bundle branch block (LBBB) in 22.7% (5/22) and right bundle branch block in 4.5% (1/22). The 24-hour Holter monitoring identified ventricular premature beats with couplets in 66.6% of patients (8/12) and non-sustained ventricular tachycardia in 50% (6/12).

Transthoracic Doppler echocardiography (TTE) showed left ventricular enlargement (diastolic dimension of 60.68 ± 12 mm) and left atrial area of 20 ± 5 cm2. It also revealed left ventricular dysfunction with an ejection fraction (EF) < 50% calculated by Simpson’s rule (average 35 ± 16%) in 86.4% (19/22) of the cases. Left ventricular systolic dimension. SV: Shortening fraction. EF: Ejection fraction. IVS: Interventricular septum. PW: Posterior wall. LA: Left atrium.

Table 1. Characteristics of patients with left ventricular non-compaction (n = 22)

<table>
<thead>
<tr>
<th>Clinical</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>40.59 ± 17</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>14/22 (63.6)</td>
</tr>
<tr>
<td>Symptoms, n (%)</td>
<td>18/22 (81.8)</td>
</tr>
<tr>
<td>Dyspnea, n (%)</td>
<td>15/18 (83.3)</td>
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<tr>
<td>Syncope, n (%)</td>
<td>3/18 (16.7)</td>
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<tr>
<td>Angina, n (%)</td>
<td>2/18 (11.1)</td>
</tr>
<tr>
<td>Ventricular arrhythmia, n (%)</td>
<td>5/18 (27.7)</td>
</tr>
<tr>
<td>Embolic stroke, n (%)</td>
<td>2/22 (9.1)</td>
</tr>
<tr>
<td>Major events, n (%)</td>
<td>3/22 (13.6)</td>
</tr>
<tr>
<td>SD, n (%)</td>
<td>1/22 (4.5)</td>
</tr>
<tr>
<td>ICD, n (%)</td>
<td>1/22 (4.5)</td>
</tr>
<tr>
<td>HTx, n (%)</td>
<td>1/22 (4.5)</td>
</tr>
<tr>
<td>Time from symptoms - diagnosis, months</td>
<td>24 (2.25-48)</td>
</tr>
<tr>
<td>ECG</td>
<td></td>
</tr>
<tr>
<td>Sinus rhythm, n (%)</td>
<td>22/22 (100)</td>
</tr>
<tr>
<td>Left bundle-branch block, n (%)</td>
<td>5/22 (22.7)</td>
</tr>
<tr>
<td>First-degree AV block</td>
<td>1/22 (4.5)</td>
</tr>
<tr>
<td>Right bundle-branch block, n (%)</td>
<td>1/22 (4.5)</td>
</tr>
<tr>
<td>24-hour Holter monitoring (12/22)</td>
<td></td>
</tr>
<tr>
<td>Ventricular couplets, n (%)</td>
<td>8/12 (66.6)</td>
</tr>
<tr>
<td>NSVT, n (%)</td>
<td>6/12 (50)</td>
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<tr>
<td>Echocardigraphy</td>
<td></td>
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<tr>
<td>LVDD, mm</td>
<td>60.7 ± 12</td>
</tr>
<tr>
<td>LVSD, mm</td>
<td>48.3 ± 15</td>
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<tr>
<td>SF, %</td>
<td>22.2 ± 11</td>
</tr>
<tr>
<td>EF, %</td>
<td>35 ± 16</td>
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<tr>
<td>IVS thickness, mm</td>
<td>10.3 ± 1.9</td>
</tr>
<tr>
<td>PW thickness, mm</td>
<td>8 ± 1.3</td>
</tr>
<tr>
<td>LA dimension, mm</td>
<td>36 ± 7</td>
</tr>
<tr>
<td>LA area, cm2</td>
<td>20.1 ± 5</td>
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<tr>
<td>Diastolic filling pattern</td>
<td></td>
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<tr>
<td>Normal, n (%)</td>
<td>6/22 (27.3)</td>
</tr>
<tr>
<td>Prolonged relaxation, n (%)</td>
<td>2/22 (9.1)</td>
</tr>
<tr>
<td>Pseudonormalization, n (%)</td>
<td>3/22 (13.6)</td>
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<tr>
<td>Restrictive, n (%)</td>
<td>11/22 (50)</td>
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10% (2/19) (EF 39-30%) and severe in 58% (11/19) (EF ≤ 29%). The diastolic filling pattern was normal in 27.3% (6/22) of patients and was impaired in 72.7% of the cases: prolonged in 9.1% (2/22), pseudonormal in 13.6% (3/22) and restrictive in 50% (11/22) (see Table 1).

The LVNC areas were located in the mid inferior segment in 50% of the cases (11/22), in the mid posterior segment in 81.8% (18/22), in the mid lateral segment in 63.6% (14/22), in the apical lateral segment in 77.2% (17/22) and in the apical inferior segment in 81.8% (18/22). The basal segments were not compromised (Figure 1).

The morphometric characteristics are detailed in Table 2. In the LVNC group, body weight was 60.91 ± 12 kg, height 1.61 ± 0.10 m and BMI 23.4 ± 3.2. In the groups matched by sex and age these characteristics were: 1) CG: weight 73.90 ± 13 kg, height 1.63 ± 0.09 m and BMI 27.63 ± 4.54; 2) HCM: weight 73.55 ± 16 kg, height 1.65 ± 0.14 m and BMI 26.88 ± 4.46; and 3) idiopathic DCM: weight 75.18 ± 25.89 kg, height 1.64 ± 0.09 m and BMI 27.81 ± 8.41. The statistical analysis showed that the patients in the LVNC group had lower weight and BMI (see Table 2).

Two patients (9.01%) developed left ventricular thrombus in the mid lateral and apical lateral segments.

**DISCUSSION**

Left ventricular noncompaction is characterized by the presence of trabeculations and deep recesses communicating with the left ventricular cavity and producing a spongy-like appearance. Initially described in 1984 by Engberding, this condition was recognized and included as a primary genetic cardiomyopathy in 2006. (3, 4)

An association between LVNC and facial dysmorphism, including strabismus, low-set ears, a prominent forehead and micrognathia has been described in children. (5) In our LVNC series in an adult population, patients had lower weight and BMI compared not only with the general population but also with patients with HCM or idiopathic DCM, a characteristic not mentioned in previous studies (Figure 2).

Different authors analyzing populations with HF have remarked the relationship between low BMI and higher mortality rate even in different subgroups of patients. This finding is not associated with the level of ventricular dysfunction, time of disease progression or comorbidities.

In patients with HF on outpatient follow-up, BMI showed an inverse relationship with mortality that was independent of the etiology. The relationship with mortality was continuous and was higher with lower BMI values and lower with higher BMI levels. This relationship persisted even after considering differences in the clinical characteristics, time from diagnosis, the severity of HF and the comorbidities associated with different levels of BMI. (6, 7)

In the specific case of LVNC, the concept of genetic disease and the physical changes previously described in children become important; thus the lower weight found could be the expression of these changes in adults. Considering that the population with LVNC presents systolic dysfunction, it would be interesting to analyze BMI as an independent marker of adverse outcomes in this group of patients.

**Clinical Presentation**

Different authors have reported that LVNC can affect children and even 94 year-old adults, who can remain asymptomatic for a long time or develop early symp-

![Fig. 1. Percentage distribution of left ventricular noncompaction according to the 16-segment model of the LV. BPS: Basal posteroseptal. BAS: Basal anteroseptal. BA: Basal anterior. BL: Basal lateral. BP: Basal posterior. BI: Basal inferior. MPS: Mid posteroseptal. MAS: Mid anteroseptal. MA: Mid anterior. ML: Mid lateral. MP: Mid posterior. MI: Mid inferior. AS: Apical septal. AA: Apical anterior. AL: Apical lateral. AI: Apical inferior.]

![Fig. 2. Picture of a 26-year old woman with left ventricular noncompaction. Weight: 35 kg, height: 1.35 m and BMI: 19.](image-url)
toms. (8-12) Although the incidence of LVNC is more frequent in men, a variable incidence has been reported in some studies. The incidence is balanced in the publication by Lilje et al (52% men and 48% women), and the study by Galizio et al reporting several publications about adult and pediatric patients in which 63% and 60%, respectively, were females. (12, 13)

The diagnosis can be made in asymptomatic persons undergoing echocardiographic evaluation for other conditions or by screening the relatives of a patient with confirmed LVNC.

When the patient has clinical expression, symptoms are particularly associated with the development of ventricular failure, presence of arrhythmias or thromboembolic complications. In the population studied, the following symptoms occurred, in order of frequency: dyspnea (83.3%), ventricular arrhythmia (27.7%), syncope (16.7%), angina (11.1%) and stroke (9.1%). The mean time interval from the onset of symptoms to diagnosis confirmation was 24 months, with the peculiarity of two patients, father and daughter, with dyspnea and arrhythmias during 22 and 17 years, respectively, before the diagnosis of LVNC was made.

**Electrocardiogram**

Electrocardiographic abnormalities are common in patients with LVNC and include conduction disturbances as LBBB in 20-40% of patients or complete AV block and repetitive supraventricular arrhythmias, as paroxysmal supraventricular tachycardia or atrial fibrillation, in 4% to 26% of the cases. The incidence of ventricular arrhythmias varies from 6% to 60%, and ventricular tachycardia occurs in 4%-30% of patients with LVNC. (14-21)

The incidence of LBBB is 25% in patients with HF and is associated with changes in left ventricular systolic and diastolic function. The presence of a LBBB produces changes in interventricular septum motion, prolongs the pre-ejective and relaxation periods, shortens left ventricular filling time and, finally, deteriorates stroke volume. (22-24) Studies have reported that the development of LBBB during the follow-up of patients with moderate to severe ventricular failure predicts functional class impairment and the need of HTx. (25)

In this study of patients with LVNC, LBBB was observed in 22.7% of patients (5/22); these five patients had severe left ventricular dysfunction. None of the patients with preserved EF had LBBB. The incidence of LBBB in our patients with LVNC and left ventricular dysfunction was 26% (5/19), similar to the one previously published; however, none of the patients who developed major events (SD, ICD and HTx), presented LBBB. In these patients with LVNC, LBBB was associated with HF but did not predict the development of fatal events.

**Echocardiography**

Transthoracic echocardiography is useful to evaluate left ventricular systolic and diastolic function and the presence of intraventricular thrombi. In our study, 13.6% of the population had preserved systolic function (EF ≥ 50%). In contrast, 86.4% had ventricular dysfunction (EF < 50%), which was mild in 32% of patients (49-40%), moderate in 10% (39-30%) and severe in 58% (≤ 29%). The diastolic filling pattern was normal in 27.3% of patients and was impaired in 72.7%; prolonged in 9.1%, pseudonormal in 13.6% and restrictive in 50%.

In this series, the noncompacted segments were more frequent in the mid and apical inferior, posterior and lateral segments. The explanation why the basal segments were not compromised is found in the embryological development of the heart. During the first month of pregnancy, the myocardium is formed by a thin meshwork of spongy-like muscle fibers with a trabecular appearance alternating with deep recesses communicating with the ventricular cavity. A gradual compaction from the epicardium to the endocardium and from base to apex starts between the fifth and eighth week of intrauterine development and the recesses become capillary vessels. (26, 27) The arrest of this process would explain the absence of noncompaction of the basal segments and the occasional finding of coronary artery fistulas (Figure 3).
CONCLUSIONS
In the population studied with LVNC, female gender prevailed, weight and BMI were lower compared with the general population and dyspnea was the most common symptom. The ECG showed sinus rhythm, conduction disturbances and repetitive ventricular arrhythmia. Transthoracic echocardiography detected different degrees of systolic and diastolic left ventricular dysfunction with areas of myocardial non-compaction in the mid and apical inferior, posterior and lateral segments, in some cases complicated with intraventricular thrombi and occasionally associated with coronary artery thrombi.

RESUMEN
Presentación clínica y características ecocardiográficas de pacientes con miocardio no compacto

Introducción
El miocardio no compacto es una miocardiopatía genética primaria ocasionada por la detención de la embriogénesis normal del endocardio y el miocardio. Esta anomalía se asocia frecuentemente con arritmias, insuficiencia cardíaca y eventos embólicos.

Objetivos
El presente estudio se llevó a cabo con el objetivo de describir la modalidad de presentación clínica y las características electrocardiográficas y ecocardiográficas en portadores de esta miocardiopatía.

Material y métodos
Se analizaron 22 pacientes con diagnóstico de miocardio no compacto detectados en el laboratorio de ecocardiografía entre julio de 2004 y abril de 2009. Toda la población en estudio fue analizada mediante electrocardiograma y eco-Doppler cardíaco transtorácico y en 12 casos se registró Holter de 24 horas. Se determinaron el peso, la altura y el índice de masa corporal, que se compararon contra 66 pacientes distribuidos en tres grupos de 22 pacientes cada uno: 1) grupo control de personas sin cardiopatías, 2) portadores de miocardiopatía hipertrófica y 3) pacientes con miocardiopatía dilatada idiopática.

Resultados y conclusiones
En la población estudiada con miocardio no compacto predominó el sexo femenino y se observó menor peso e índice de masa corporal en relación con los grupos comparados y el síntoma preponderante fue la disnea. El electrocardiograma mostró ritmo sinusal con trastornos de conducción y arritmia ventricular repetitiva. El eco transtorácico mostró diferentes grados de disfunción ventricular izquierda sistólica y diastólica con áreas de miocardio no compacto predominantes en los territorios medial y apical de los segmentos inferior, posterior y lateral, en algunos casos complicados con trombos intraventriculares y ocasionalmente asociados con fistulas coronarias.

Palabras clave > Ecocardiografía - Cardiomiopatías Índice de masa corporal

CONCLUSIONS
In the population studied with LVNC, female gender prevailed, weight and BMI were lower compared with the general population and dyspnea was the most common symptom. The ECG showed sinus rhythm, conduction disturbances and repetitive ventricular arrhythmia. Transthoracic echocardiography detected different degrees of systolic and diastolic left ventricular dysfunction with areas of myocardial non-compaction in the mid and apical inferior, posterior and lateral segments, in some cases complicated with intraventricular thrombi and occasionally associated with coronary artery thrombi.

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