Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction†

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Aims
To describe a method for measuring trabeculated left ventricular (LV) mass using cardiac magnetic resonance imaging and to assess its value in the diagnosis of left ventricular non-compaction (LVNC).

Methods and results
Between January 2003 and 2008, we prospectively included 16 patients with LVNC. During the mean period, we included 16 patients with dilated cardiomyopathy (DCM), 16 patients with hypertrophic cardiomyopathy (HCM), and 16 control subjects. Left ventricular volumes, LV ejection fraction, and trabeculated LV mass were measured in the four different populations. The percentage of trabeculated LV mass was almost three times higher in the patients with LVNC (32±10%), compared with those with DCM (11±4%, P<0.0001), HCM (12±4%, P<0.0001), and controls (12±5%, P<0.0001). A value of trabeculated LV mass above 20% of the global mass of the LV predicted the diagnosis of LVNC with a sensitivity of 93.7% [95% confidence interval (CI), 71.6–98.8%] and a specificity of 93.7% (95% CI, 83.1–97.8%; k=0.84).

Conclusion
The method described is reproducible and provides an assessment of the global amount of LV trabeculation. A trabeculated LV mass above 20% of the global LV mass is highly sensitive and specific for the diagnosis of LVNC.

Keywords
Left ventricular non-compaction • Magnetic resonance imaging • Cardiomyopathy • Trabeculae

Introduction
Left ventricular non-compaction (LVNC) is a cardiomyopathy characterized by a thin, compacted epicardial layer and an extremely thick endocardial layer with prominent trabeculation and deep recesses that communicate with the LV cavity but not with the coronary circulation.1–3 Left ventricular non-compaction has been classified as a primary cardiomyopathy of genetic origin with a predominantly autosomal dominant inheritance pattern and has been linked to several gene mutations.4–6 Left ventricular non-compaction can lead to heart failure, thrombo-embolism, malignant arrhythmia, and can occur as an isolated anomaly or associated with other congenital heart diseases.7,8 Echocardiography is considered to be the gold standard method for diagnosing LVNC and three different diagnostic criteria have to date been published, although there is no universally accepted definition of LVNC at present.1,3,8 Furthermore, Kohli et al.9 showed that there was a poor correlation between the three echocardiographic
definitions of LVNC. There has been an exponential rise in the number of reports describing LVNC. In a recent paper, investigators showed that 23.6% of the patients explored by echocardiography for LV systolic impairment had one or more of the echocardiographic definitions of LVNC. Investigators suggest that the current diagnostic criteria using echocardiography are too sensitive for the diagnosis of LVNC.

High-resolution imaging techniques such as cardiac magnetic resonance imaging (CMR) have been successfully used to distinguish myocardial trabeculation within the LV cavity. Furthermore, CMR yields images with a higher spatial resolution than echocardiography in the LV apex and lateral wall. The CMR diagnosis criteria for LVNC are based on a ratio of the thickness of non-compacted to compacted myocardial layers, measured in the diastolic phase and on an adapted version of the existing echocardiographic criteria; they therefore have the same limitations. The aim of this study is to describe a method for measuring trabeculated LV mass using CMR and to assess its value in the diagnosis of LVNC. For this purpose, the distribution of trabeculated LV mass was studied in four different populations: patients for whom a diagnosis of LVNC was established on echocardiographic criteria (n = 16), patients with dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM), and control subjects.

**Methods**

**Study population**

This study complies with the Declaration of Helsinki and was approved by our institutional review board, and written informed consent was obtained from all patients. Between January 2003 and 2008, 16 consecutive patients for whom a diagnosis of LVNC was established on echocardiographic criteria were enrolled. Each patient was clinically assessed by echocardiography first and CMR studies were performed in the course of the same week.

The echocardiographic criteria for LVNC diagnosis include all patients fulfilling Jenni et al.’s criteria. These specific echocardiographic diagnostic criteria are (in the absence of co-existing cardiac anomalies): a typical two-layered myocardial structure with a thin, compacted outer (epicardial) band and a much thicker, non-compacted inner (endocardial) layer consisting of trabecular meshing with deep endocardial spaces, a maximum end-systolic NC/C ratio >2, and colour Doppler evidence of deeply perfused intertrabecular recesses. Among the 16 patients included, 12 fulfilled all Jenni et al.’s criteria. We also included four patients with a maximum NC/C ratio ≤2 in whom LVNC was strongly suspected because of the presence of a marked two-layered structure associated with more than three prominent trabeculations and a family history of LVNC.

The remaining subjects were patients drawn from groups given a potential differential diagnosis for LVNC and control patients. During the same period, we prospectively included 16 patients with DCM, 16 patients with HCM, and 16 control subjects without any family history of cardiovascular disease. The diagnosis of DCM was made on the basis of impaired global LV function (<40% on echocardiography), LV chamber dilatation, and exclusion of other cause of LV dysfunction. Patients with HCM were diagnosed on the basis of family history, standard ECG, and echocardiographic findings in the absence of a secondary cause of hypertrophy. All these patients were treated according to the current international guidelines for patient’s care.

**Cardiac magnetic resonance imaging**

All imaging was performed on a 1.5 T MR scanner (Symphony TIM, Siemens, Erlangen, Germany, with a 12-element phased-array cardiac coil and Achieva, Philips, Best, The Netherlands, with a 5-element phased-array cardiac coil). A standard CMR method was used to assess global LV function and structure. Cine steady-state free precession sequences were acquired on long-axis two-chamber, four-chamber, and short-axis views to cover the whole LV without any gap between images. For both scans, we used cine sequences with retrospective cardiac gating adjusted as follows: TR/TE = 40/1.8 ms, slice thickness = 6 mm, no gap between slice, flip angle = 65°, matrix = 148 × 256, field of view = 350 × 350 mm, and temporal resolution = 35 ms for the Siemens scan; and TR/TE = 35/1.5 ms, slice thickness = 6 mm, no gap between slice, flip angle = 60°, matrix = 148 × 256, field of view = 350 × 350 mm, and temporal resolution = 35 ms for the Philips scan.

**Cardiac magnetic resonance imaging analysis**

All examinations were transferred to a dedicated workstation, and LV volumes, ejection fraction (EF), LV mass, and LV trabeculation were determined using Argus post-processing software (Siemens) adapted from a previously published method. The cine loops were reviewed, and the end-diastolic (ED) and end-systolic (ES) frames were identified. Basal image positions were defined in ED and ES. Epicardial and endocardial contours were outlined in a semi-automatic fashion, and the papillary muscles were included in the myocardial mass. If the papillary muscles could not be clearly distinguished from the trabeculation on the long- and short-axis images, they were treated as trabeculation. Left ventricular trabeculation was defined at the end-diastolic phase as myocardium protruding from the LV wall into the LV cavity. Right ventricular trabeculation was excluded from our measurements. To assess LV volumes, LV EF, and compacted LV mass, the endocardial border was drawn to include papillary muscle and exclude LV trabeculation. To assess global LV mass, the endocardial border was drawn to include LV papillary muscles and LV trabeculation. In patients with a highly trabeculated LV, the endocardial contour was positioned at the outer edges of the trabeculation net to assess the global LV mass (Figure 1). Compacted and global LV mass were measured only at the end-diastolic phase. The trabeculated LV mass was calculated as follows: trabeculated LV mass = global LV mass − compacted LV mass. Left ventricular volumes, compacted LV mass, and trabeculated LV mass are given indexed to the body surface to account for the variations in body weight between subjects. The distribution of myocardial trabeculation was assessed by qualitative analysis of all 17 segments for the presence or absence of any degree of trabeculation (i.e. for a distinct two-layered appearance of segments of trabeculated and compacted myocardium). A segment was regarded as trabeculated if the visual appearance suggested the presence of two myocardial layers with different degrees of tissue compaction. These measurements were performed in all groups by two readers (A.J. and F.T.).

**Statistical analysis**

All values are given as mean ± SD. A P-value <0.05 was considered significant. The statistical analysis was performed using SPSS for Windows 15.0 (Chicago, IL, USA). Patient group characteristics were compared by the Kruskal–Wallis non-parametric tests, and then, when significant, by the Mann–Whitney U non-parametric tests for post hoc analysis. In this case, to ensure an overall type I error rate of 5%, the Bonferroni correction was applied and an adjusted P < 0.05/3 = 0.016 was considered significant. The distribution of the
two-layered structure between the groups was assessed and compared using a Fisher’s exact probability test. The inter-observer reproducibility was assessed using intra-class correlation and Bland–Altman analysis by calculating the bias (mean difference) and the 95% limits of agreement (1.96 SD around the mean difference).

We used receiver operating characteristics (ROC) curves to determine the optimal cut-off values of trabeculated mass. Comparison of the area under the ROC curves was performed using the method described by Hanley et al.16

Results

The study population comprised 64 patients and was homogeneous in terms of its ethnic origin (Caucasian). There were no significant differences between the LVNC patients and the three other groups in terms of gender or age distribution (Table 1). Furthermore, all groups were comparable in terms of height, weight, and body surface. The patterns of distribution of the two-layered structure were not significantly different between groups.

Figure 1 Illustration of the described method for measuring the global and trabeculated left ventricular masses in patients with left ventricular non-compaction, dilated cardiomyopathy, hypertrophic cardiomyopathy, and controls. Column A shows the short-axis end-diastolic cine images used for measurement without contouring, Column B shows the inclusion of papillary muscles and the exclusion of left ventricular trabeculation for the measurements of the compacted left ventricular mass. Column C shows inclusion of papillary muscles and trabeculation for the measurements of global left ventricular mass.
Trabeculation was more common on the apical segment than on the medial and basal segments.

**Distribution of the percentage of trabeculated left ventricular mass and reproducibility**

In the patients with LVNC, the percentage of trabeculated LV mass was three times higher (32 ± 10%) than in DCM (11 ± 4%, P < 0.0001), HCM (12 ± 4%, P < 0.0001), and controls (12 ± 5%, P < 0.0001) (Figure 3 and Table 2). The mean trabeculated mass was also higher in LVNC (43 ± 19 g/m²) than in DCM (11 ± 5 g/m², P < 0.016), HCM (14 ± 24 g/m², P < 0.016), and the controls (9 ± 24 g/m², P < 0.016). However, the LV compacted mass was the same for LVNC (88 ± 29 g/m²), DCM (95 ± 24 g/m²; P = NS), and controls (66 ± 11, P = NS). The compacted LV mass was lower in the LVNC compared with the HCM (108 ± 30 g/m², P < 0.016). The percentage of trabeculated LV mass was the same in DCM, HCM, and the controls. Furthermore, in all four groups of our study, the distribution of the percentage of trabeculated LV mass was Gaussian in all the populations. We were able to measure trabeculated LV mass in all cases with a high degree of inter-observer reproducibility and an intra-class correlation coefficient equal to 0.95 [95% confidence interval (CI), 0.89–0.97; \( \kappa = 0.87 \) with \( P < 0.001 \)]. There was a slight bias (0.3 ± 4.4), but no tendency and only 2/32 values slightly outside the limits of agreement, and the intra-class

**Table 1 Patient characteristics**

<table>
<thead>
<tr>
<th></th>
<th>LVNC</th>
<th>DCM</th>
<th>HCM</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>48 ± 17</td>
<td>59 ± 15 (P = NS)</td>
<td>45 ± 20 (P = NS)</td>
<td>42 ± 17 (P = NS)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>10/16</td>
<td>11/16 (P = NS)</td>
<td>8/16 (P = NS)</td>
<td>10/16 (P = NS)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68 ± 11</td>
<td>71 ± 7 (P = NS)</td>
<td>69 ± 6 (P = NS)</td>
<td>65 ± 13 (P = NS)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169 ± 7</td>
<td>172 ± 7 (P = NS)</td>
<td>170 ± 6 (P = NS)</td>
<td>170 ± 8 (P = NS)</td>
</tr>
<tr>
<td>Body surface (m²)</td>
<td>2 ± 0</td>
<td>2 ± 0 (P = NS)</td>
<td>2 ± 0 (P = NS)</td>
<td>2 ± 0 (P = NS)</td>
</tr>
</tbody>
</table>

LVNC, left ventricular non-compaction; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy. P-value was calculated in comparison with values obtained in LVNC patients.

(Figure 2). Trabeculation was more common on the apical segment than on the medial and basal segments.

**Figure 2** Graph showing the patterns of distribution of the left ventricular two-layered structure in all patient groups. There were no statistical differences between left ventricular non-compaction and other patient groups in the repartition of the two-layered structure.
correlation coefficient was strong (equals to 0.95 with 95% CI, 0.89–0.97).

**Value of the percentage of trabeculated left ventricular mass in left ventricular non-compaction diagnosis**

Receiver operating characteristics analysis identified the end-diastolic trabeculated mass as a valuable parameter for distinguishing highly trabeculated myocardium (LVNC patients) from patients with a normal amount of trabeculation in the LV (DCM, HCM, and controls) (Figure 4A). If our echocardiographic diagnosis criteria for LVNC are considered as the gold standard for LVNC diagnosis, a value of trabeculated LV mass above 20% of the total LV mass is predictive of LVNC with a sensitivity of 91.6% (CI, 64.6–98.5%) and a specificity of 86.5% (CI, 74.7–93.3%; \( \kappa = 0.65 \)).

The technique we describe was compared with the previous gold standard CMR technique defined by Petersen et al.\(^1\) If a value of trabeculated LV mass above 20% is applied, the sensitivity and specificity for the diagnosis of LVNC based on Petersen et al.’s criteria as the standard of reference would be: 78.5% (CI, 52.4–92.4%) and 72.2% (CI, 49.1–87.5%), respectively (\( \kappa = 0.50 \)). An ROC analysis was performed using our echocardiographic diagnosis criteria for LVNC as a reference to classify the patients and describe the performance of Petersen et al.’s criteria (Figure 4B). The area under the ROC curves describing the performance of Petersen et al.’s criteria was measured at 0.94 (CI, 0.87–1.0) and was slightly lower compared with the area under the ROC curves describing the performance of the percentage of trabeculated LV mass [0.98 (CI, 0.96–1.0), \( P = 0.88 \)].

**Discussion**

The main findings of this study were: (i) the measurement of LV trabeculation using CMR, expressed as a percentage of LV mass, is feasible and highly reproducible in LVNC patients as well as in DCM, HCM, and controls. (ii) Patients with an LV trabeculated mass above 20% of the total LV mass should be considered as hypertrabeculated LV patients with a high probability of LVNC.

**Quantification of left ventricular trabeculation using cardiac magnetic resonance imaging**

Left ventricular non-compaction is characterized by numerous prominent trabeculations in the LV, and our technique permits global quantification of LV trabeculation without the need to select a view or a segment of the LV. Quantification of LV mass and volume with or without LV trabeculation has already been described and validated.\(^10\) Papavassiliu et al.\(^10\) assessed the effect of including or excluding LV trabeculation in LV volumes and mass. Investigators found that trabeculation significantly affected the measurement of LV mass and the mean difference between these measurements, including or excluding trabeculation, was measured at 10 ± 3% in healthy volunteers and at 14 ± 6% in patients with impaired LV systolic function. These results were

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Table 2  **Cardiac magnetic resonance imaging findings**

<table>
<thead>
<tr>
<th></th>
<th>LVNC</th>
<th>DCM</th>
<th>HCM</th>
<th>Controls</th>
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<tbody>
<tr>
<td>LVEF (%)</td>
<td>33 ± 20</td>
<td>26 ± 11 (( P = ) NS)</td>
<td>71 ± 13*</td>
<td>69 ± 7*</td>
</tr>
<tr>
<td>EDV (mL/m²)</td>
<td>112 ± 43</td>
<td>115 ± 26 (( P = ) NS)</td>
<td>71 ± 18*</td>
<td>71 ± 11*</td>
</tr>
<tr>
<td>ESV (mL/m²)</td>
<td>80 ± 47</td>
<td>84 ± 24 (( P = ) NS)</td>
<td>21 ± 11*</td>
<td>25 ± 7*</td>
</tr>
<tr>
<td>Compacted LV mass (g/m²)</td>
<td>88 ± 29</td>
<td>95 ± 24 (( P = ) NS)</td>
<td>108 ± 30*</td>
<td>66 ± 11 (( P = ) NS)</td>
</tr>
<tr>
<td>Trabeculated mass (g/m²)</td>
<td>43 ± 19</td>
<td>11 ± 5*</td>
<td>14 ± 5*</td>
<td>9 ± 4*</td>
</tr>
<tr>
<td>Trabeculated mass (% of LV)</td>
<td>32 ± 10</td>
<td>11 ± 4*</td>
<td>12 ± 4*</td>
<td>12 ± 5*</td>
</tr>
</tbody>
</table>

LVNC, left ventricular non-compaction; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume. \( P \)-value was calculated in comparison with values obtained in LVNC patients and \( * P < 0.016 \).
in line with our results in the controls and in the DCM, showing that trabeculation is a normal constituent of the LV anatomy. Furthermore, our measurement was highly reproducible in LVNC, DCM, and HCM as well as in the controls, thereby confirming the excellent reproducibility of this technique as described previously. The technique we describe is based on measuring the total amount of LV trabeculation and establishing a cut-off value above which an LVNC diagnosis is highly probable. It does not depend on partial volume effect or slice selection. This is one of the major advantages of our method over the other previously described techniques that focus on only one echocardiographic view, 3,8,11 or two echocardiographic views. 1 The other advantage of our method is that CMR is capable of assessing the whole LV myocardium, especially the apical and lateral parts, with a high degree of spatial resolution. Rickers et al.12 showed previously that CMR was capable of identifying regions of the LV that were not readily recognized by echocardiography in HCM. Echocardiography remains a very useful and simple bedside examination, but with well-known limitations. Cardiac magnetic resonance imaging probably has a role to play as a second-line examination when an LVNC is suspected after echocardiographic examination.

**Diagnostic criteria for left ventricular non-compaction**

Left ventricular trabeculation is a normal constituent of the LV chamber anatomy and prominent trabeculation can be found in normal subjects. Kohli et al.9 recently published a paper showing a lack of consistency in the various different echocardiography techniques described for diagnosing LVNC. The investigators sought to determine the prevalence of LVNC using the existing echocardiographic criteria in 199 patients referred for heart failure. Interestingly, 23.6% of the patients fulfilled one or more echocardiographic definition of LVNC, which is much higher than the previously published prevalence in adults (<0.3%).7,17,18 Furthermore, for these 23.6%, only 29.8% fulfilled all three echocardiographic definitions of LVNC. This can be explained by differences in the definition of abnormal trabeculation, echocardiographic planes, the cardiac phase selected for measurement, and the subjectivity of some criteria. The CMR criteria for LVNC were based on an adapted version of Jenni et al.’s echocardiographic criteria and have the same limitations. We feel that CMR could be a reliable technique for assessing LV trabeculation and diagnosing LVNC, which is characterized by excessive, prominent trabeculations inside the LV cavity.

**Clinical implications**

Accurate diagnostic criteria for LVNC are clinically important as LVNC is associated with severe LV dysfunction, a high incidence of ventricular arrhythmia, and thrombo-embolic complications.7 Furthermore, clinical studies suggest that LVNC is often a familial disorder, inherited predominantly via an autosomal dominant pattern; this emphasizes the importance of an early diagnosis.6,7 Our method permits the measurement of LV trabeculation but does not assess the severity of the disease. Oechslin et al.7 described the characteristics and outcomes of patients with LVNC. The investigators found a high incidence of mortality and morbidity in this population, including thrombo-embolism, ventricular arrhythmia, and heart failure. Dodd et al.19 showed that the amount of delayed trabecular hyper-enhancement correlated significantly with LVEF and was an independent predictor of LVEF. This retrospective study included 9 patients with LVNC and 10 control subjects. The investigators assessed the presence of delayed trabecular enhancement by measuring the ratio of trabecular signal intensity to myocardial signal intensity >3. The presence of delayed enhancement within the LV trabeculation is induced by fibrosis which is probably of bad prognosis in this disease. Further longitudinal studies will be needed to assess the predictive indicators of outcome in such populations.
Limitations
The main limitation of this study is the lack of genetic diagnosis for LVNC; a genetic diagnosis would provide a more powerful means of validating our method. Also, the percentage of trabeculated mass was measured in only one ethnic group, and our method needs to be validated in other ethnic groups such as a black African population. The value of the non-compacted LV mass should also be validated in a larger cohort of patients to confirm its diagnostic value. Furthermore, we expressed our measurements as a percentage of LV mass but clearly there is a substantial blood pool in the trabeculated region, especially in non-compacted patients. However, we finally decided to use LV mass rather than LV volume to be more consistent with the previous studies, and to be able to compare trabeculated mass with compacted mass.

Conclusion
The method we describe is highly reproducible and provides an assessment of the global amount of LV trabeculation. A trabeculated LV mass above 20% of the total LV mass assessed using CMR is highly sensitive and specific in the diagnosis of LVNC.

Conflict of interest: none declared.

References