CLINICAL RESEARCH

Assessment of left ventricular non-compaction in adults: Side-by-side comparison of cardiac magnetic resonance imaging with echocardiography

Évaluation de la non-compaction isolée du ventricule gauche chez l’adulte : comparaison de l’imagerie par résonance magnétique nucléaire avec l’échographie cardiaque

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KEYWORDS
Non-compaction; Cardiomyopathy; Echocardiography; Cardiac magnetic resonance

Summary
Background. — Two-dimensional echocardiography images obtained at end-diastole and end-systole and cardiac magnetic resonance (CMR) images obtained at end-diastole represent the three imaging methodologies validated for diagnosis of left ventricular non-compaction (LVNC). No study has compared these methodologies in assessing the magnitude of non-compaction.
Aims. — To compare two-dimensional echocardiography with CMR in the evaluation of patients with suspected LVNC.

Abbreviations: C, compacted epicardial layer thickness; CMR, cardiac magnetic resonance; LV, left ventricular; LVNC, left ventricular non-compaction; NC, non-compacted endocardial layer thickness; Echo-2D, two-dimensional echocardiography.

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Introduction

Left ventricular non-compaction (LVNC) is a recently recognized cardiomyopathy characterized by a distinctive (“spongy”) morphological appearance of the left ventricular (LV) myocardium [1]. Prominent LV trabeculae and deep intertrabecular recesses are present and the myocardial wall is often thickened with a thin compacted epicardial layer and a thickened non-compacted endocardial layer. In some patients, LVNC is associated with LV dilatation and systolic dysfunction, leading to heart failure, ventricular arrhythmia and thrombo-embolic complications [2–8]. This myocardial disorder has been described by two-dimensional echocardiography (Echo-2D) and although many echo criteria have been proposed [4,8,9], a poor correlation exists between them [10]. These discrepancies may be explained by differences not only in the definition of abnormal trabeculation, but also in the echo planes and phase of the cardiac cycle in which they are applied (end-diastole and end-systole) [10]. Thus, there is no clear consensus for LVNC diagnosis. Moreover, Echo-2D evaluation can be limited by poor acoustic windows. Recently, cardiac magnetic resonance (CMR) imaging has been proposed for the diagnosis of LVNC [11–13] and new criteria have been proposed [14]. This technique has the

Methods. — Sixteen patients (48 ± 17 years) with LVNC underwent echocardiography and CMR within the same week. Echocardiography images obtained at end-diastole and end-systole were compared in a blinded fashion with those obtained by CMR at end-diastole to assess non-compaction in 17 anatomical segments.

Results. — All segments could be analyzed by CMR, whereas only 238 (87.5%) and 237 (87.1%) could be analyzed by echocardiography at end-diastole and end-systole, respectively (p = 0.002). Among the analyzable segments, a two-layered structure was observed in 54.0% by CMR, 42.9% by echocardiography at end-diastole and 41.4% by echocardiography at end-systole (p = 0.006). Similar distribution patterns were observed with the two echocardiographic methodologies. However, compared with echocardiography, CMR identified a higher rate of two-layered structures in the anterior, anterolateral, inferolateral and inferior segments. Echocardiography at end-systole underestimated the NC/C maximum ratio compared with CMR (p = 0.04) and echocardiography at end-diastole (p = 0.003). No significant difference was observed between CMR and echocardiography at end-diastole (p = 0.83). Interobserver reproducibility of the NC/C maximum ratio was similar for the three methodologies.

Conclusion. — CMR appears superior to standard echocardiography in assessing the extent of non-compaction and provides supplemental morphological information beyond that obtained with conventional echocardiography.

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capability of acquiring tomographic images of the LV chambers, with border definition that is often superior to that achievable by echocardiography. However, while Echo-2D criteria have been validated either at end-diastole [8,9,15] or end-systole [4], CMR criteria have only been validated at end-diastole [14]. Thus, no previous study has compared the two imaging techniques at different times of the cardiac cycle in the assessment of patients with suspected LVNC. The aim of the present study was to compare standard Echo-2D with CMR in the evaluation of patients with isolated LVNC.

Materials and methods

Patient selection

Between January 2003 and January 2008, 16 consecutive patients for whom diagnosis of LVNC was suspected on echocardiographic criteria and without CMR contraindications were enrolled. Each patient was assessed clinically by echocardiography first and CMR studies were performed during the same week.

Among the 16 patients included, 12 fulfilled Jenni’s criteria [4,5]. These specific echocardiographic diagnostic criteria are (in the absence of coexisting 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 non-compacted epicardial layer thickness/compacted epicardial layer thickness (NC/C) ratio >2;
- colour Doppler evidence of deeply perfused intertrabecular recesses.

Four other patients were also included, despite having a maximum NC/C ratio <2. In these patients, LVNC was highly suspected due to the presence of a marked two-layered structure associated with more than three prominent trabeculations [8] and a family history of LVNC.

This study complies with the declaration of Helsinki and was approved by our institutional review board. Written informed consent was obtained from all patients.

Two-dimensional echocardiographic imaging

Echo-2D were obtained using commercially available instruments (GE Medical Systems, Milwauke, Wis) with 3.5-MHz transducers equipped with harmonic imaging. Images were acquired in the long-axis parasternal view, the three short-axis views (basal, mid, apical), and the 2-, 3- and 4-chamber apical views. These views were used to visualize all 17 segments according to American Heart Association recommendations [16]. Offline analysis was then performed on digitally stored images (EchoPAC, GE Vingmed, Horthen, Norway).

CMR 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). Cine steady-state free precession sequences were acquired on long-axis, 2-chamber, 4-chamber and short-axis views to cover the whole left ventricle without any gap between images. For both scans, cine sequences with retrospective cardiac gating were used with the following parameters:

- TR/TE = 40 ms/1.8 ms, slice thickness = 6 mm, no gap between slice, flip angle = 65°, matrix = 148 × 256, field of view = 350 mm × 350 mm, temporal resolution = 30 ms
- TR/TE = 35/1.5 ms, slice thickness = 6 mm, no gap between slice, flip angle = 60°, matrix = 148 × 256, field of view = 350 mm × 350 mm, temporal resolution = 30 ms, for the Siemens and Philips scans, respectively.

All examinations were transferred to a dedicated workstation. LV volumes, ejection fraction and LV trabeculation were determined using Argus™ post-processing software (Siemens, Erlangen, Germany). The cine loops were reviewed and the end-diastolic and end-systolic frames were identified.

Image analysis

Qualitative and quantitative analyses of all 17 segments were performed using the three imaging methodologies: Echo-2D at end-diastole, Echo-2D at end-systole and CMR at end-diastole. CMR analysis was not performed at end-systole because, in most cases, the trabeculations and two-layered structure could not be visualized at this time in the cardiac cycle and because the measurements were validated at this point by a previous study. For each segment (n = 272), the following criteria were assessed with the three imaging methodologies: analysable segment (yes/no), two-layered structure (yes/no) and NC/C maximum ratio. A segment was considered to be non-analysable if the imaging methodology failed to assess the presence or absence of the two-layered structure. The two-layered structure was assessed with one of the long- or short-axis views. The NC/C ratio was measured in short-axis views when possible, but long-axis views were used in some cases (Fig. 1). Only segment 17 was always measured using 2- or 4-chamber views. For each patient and each imaging methodology, only the maximal NC/C ratio was used for subsequent analysis.

LV volumes and LV ejection fractions were calculated by Echo-2D from the 2- and 4-chamber images using the biplane Simpson’s rule and by CMR from the short-axis views using the disks method.

The same observer performed the entire analysis for each imaging methodology and was blinded to the data obtained for the alternative imaging test.

Pathological analysis

Pathological analysis was performed in the three patients who underwent cardiac transplantation. After perfusion and fixation of the hearts with formalin, the macroscopic preparations were analysed.

Statistical analysis

All continuous variables are expressed as means ± standard deviations; non-continuous variables are presented as per-
centages. Comparisons between non-continuous variables were performed by the $\chi^2$-test. Comparisons of NC/C maximum ratios between the imaging methodologies (CMR at end-diastole, Echo-2D at end-diastole and Echo-2D at endsystole) were performed using a Friedman test and then, when significant, by the Wilcoxon rank sum test for post hoc analysis. In this case, to ensure an overall type I error rate of 5%, Bonferroni correction was applied and an adjusted $p < 0.05/3 = 0.016$ was considered significant.

Agreement in the NC/C maximum ratio between the imaging methodologies was determined by Bland-Altman analysis.

Two observers reviewed each imaging modality (Echo-2D and CMR) independently in all patients. The two observers were senior cardiologists who were experienced in echocardiography and CMR. All NC/C maximum ratio measurements were repeated by these two observers who were blinded to the previous results. The intraclass correlation coefficient and Bland-Altman analysis were used to assess the interobserver reproducibility for each imaging methodology. Bias was estimated by the mean difference between two measurements and paired $t$-tests were used to evaluate significance.

A two-sided $p$-value of <0.05 was established as the level of statistical significance for all tests. All analyses were performed with SPSS for Windows 15.0 (Chicago, IL, USA).

### Results

**Patient characteristics**

Our sample consisted of 16 consecutive patients aged 48 ± 17 years with LVNC. No patient had symptoms or signs of neuromuscular disease. Only one patient had LV thrombosis, which was identified by both CMR and Echo-2D. Patient characteristics are reported in Table 1.

### Analysable segments

CMR assessed significantly more segments than Echo-2D. Among the 272 segments, all (100%) could be assessed by CMR, whereas only 238 (87.5%) and 237 (87.1%) could

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**Table 1** Characteristics of the 16 patients with definite diagnosis or suspicion of left ventricular non-compaction.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex (M/F)</th>
<th>Family history</th>
<th>LBBB</th>
<th>NYHA class</th>
<th>LVEF (%) (Echo-2D)</th>
<th>LVEF (%) (CMR)</th>
<th>LVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>F</td>
<td>−</td>
<td>+</td>
<td>III/IV</td>
<td>65</td>
<td>36</td>
<td>−</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>F</td>
<td>−</td>
<td>+</td>
<td>I/II</td>
<td>42</td>
<td>45</td>
<td>−</td>
</tr>
<tr>
<td>3a</td>
<td>29</td>
<td>M</td>
<td>−</td>
<td></td>
<td></td>
<td>44</td>
<td>59</td>
<td>−</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>F</td>
<td>+</td>
<td></td>
<td>III/IV</td>
<td>44</td>
<td>53</td>
<td>−</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>M</td>
<td>−</td>
<td>+</td>
<td>I/II</td>
<td>34</td>
<td>21</td>
<td>−</td>
</tr>
<tr>
<td>6</td>
<td>41</td>
<td>M</td>
<td>−</td>
<td></td>
<td>III/IV</td>
<td>43</td>
<td>34</td>
<td>−</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>M</td>
<td>+</td>
<td></td>
<td>III/IV</td>
<td>5</td>
<td>8</td>
<td>−</td>
</tr>
<tr>
<td>8</td>
<td>42</td>
<td>M</td>
<td>−</td>
<td>+</td>
<td>III/IV</td>
<td>65</td>
<td>63</td>
<td>−</td>
</tr>
<tr>
<td>9</td>
<td>45</td>
<td>M</td>
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<td>+</td>
<td>I/II</td>
<td>20</td>
<td>32</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>III/IV</td>
<td>25</td>
<td>25</td>
<td>−</td>
</tr>
<tr>
<td>11</td>
<td>51</td>
<td>M</td>
<td>−</td>
<td></td>
<td>III/IV</td>
<td>18</td>
<td>18</td>
<td>−</td>
</tr>
<tr>
<td>12</td>
<td>54</td>
<td>M</td>
<td>+</td>
<td></td>
<td>III/IV</td>
<td>45</td>
<td>45</td>
<td>−</td>
</tr>
<tr>
<td>13</td>
<td>70</td>
<td>F</td>
<td>+</td>
<td></td>
<td>I/II</td>
<td>73</td>
<td>74</td>
<td>−</td>
</tr>
<tr>
<td>14a</td>
<td>71</td>
<td>M</td>
<td>−</td>
<td></td>
<td>III/IV</td>
<td>27</td>
<td>27</td>
<td>−</td>
</tr>
<tr>
<td>15a</td>
<td>72</td>
<td>M</td>
<td>+</td>
<td></td>
<td>I/II</td>
<td>44</td>
<td>10</td>
<td>−</td>
</tr>
<tr>
<td>16a</td>
<td>74</td>
<td>F</td>
<td>−</td>
<td></td>
<td>III/IV</td>
<td>13</td>
<td>11</td>
<td>−</td>
</tr>
</tbody>
</table>

CMR: cardiac magnetic resonance; F: female; LBBB: left bundle branch block; LVEF: left ventricular ejection fraction; LVT: left ventricle thrombosis; M: male; NYHA: New York Heart Association; Echo-2D: two-dimensional echocardiography.

a Patients not fulfilling all Jenni echocardiography criteria.
be analysed by Echo-2D at end-diastole and end-systole ($p = 0.002$), respectively. These segments were more difficult to analyse by Echo-2D due to poor acoustic windows. No significant difference was observed between Echo-2D at end-diastole and Echo-2D at end-systole ($p = 0.90$). The differences between CMR and Echo-2D were observed mainly for the anterior, anterolateral and inferolateral segments (Fig. 2).

**Extent of the two-layered structure**

CMR identified significantly more segments with a two-layered structure. Among the analysable segments, a two-layered structure was observed in 54.0% of cases by CMR, 42.9% by Echo-2D at end-diastole and 41.4% by Echo-2D at end-systole ($p = 0.006$). No significant difference was observed between Echo-2D at end-diastole and Echo-2D at end-systole ($p = 0.74$). Fig. 3 illustrates the distribution of the two-layered structure according to the imaging methodology used. Similar distribution patterns were observed with the two echocardiographic methodologies. However, compared with echocardiography, CMR identified a higher rate of two-layered structures in the anterior, anterolateral, inferolateral and inferior segments.

**Assessment of the NC/C maximum ratio**

The NC/C maximum ratio was higher when measured by CMR at end-diastole compared with Echo-2D at end-diastole and Echo-2D at end-systole ($p = 0.01$) (Table 2). Echo-2D at end-systole underestimated the NC/C maximum ratio compared with CMR ($p = 0.04$) and Echo-2D at end-diastole ($p = 0.003$) (Table 2 and Fig. 4). No significant difference was observed between CMR and Echo-2D at end-diastole ($p = 0.83$) (Table 2 and Fig. 4).

The interobserver variability of the NC/C maximum ratio was assessed in all patients, with similar correlation and agreement observed for the three imaging methodologies (Table 3 and Fig. 5).

Fig. 6 shows a representative example of the comparison between the three imaging methodologies and the pathological examination.

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**Table 2** NC/C maximum ratio according to the imaging methodologies.

<table>
<thead>
<tr>
<th>Imaging methodology</th>
<th>NC/C maximum ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± standard deviation</td>
</tr>
<tr>
<td>CMR at end-diastole</td>
<td>3.91 ± 2.29</td>
</tr>
<tr>
<td>Echo-2D at end-diastole</td>
<td>3.60 ± 1.60</td>
</tr>
<tr>
<td>Echo-2D at end-systole</td>
<td>2.81 ± 0.83</td>
</tr>
</tbody>
</table>

Global comparison between the three imaging methodologies, $p = 0.01$. CMR at end-diastole vs Echo-2D at end-diastole, $p = 0.83$. CMR at end-diastole vs Echo-2D at end-systole, $p = 0.04$. Echo-2D at end-diastole vs Echo-2D at end-systole, $p = 0.003$. C: compacted layer thickness; CMR: cardiac magnetic resonance; NC: non-compacted layer thickness; Echo-2D: two-dimensional echocardiography.

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**Table 3** Interobserver NC/C maximum ratio according to the imaging methodologies.

<table>
<thead>
<tr>
<th>Observer</th>
<th>Observer 2</th>
<th>Mean difference (95% CI)</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR at end-diastole</td>
<td>3.91 ± 2.29</td>
<td>4.36 ± 2.0</td>
<td>$-0.45 (−1.18$ to $0.29)$</td>
</tr>
<tr>
<td>Echo-2D at end-diastole</td>
<td>3.60 ± 1.60</td>
<td>4.30 ± 2.03</td>
<td>$-0.70 (−1.19$ to $−0.21)$</td>
</tr>
<tr>
<td>Echo-2D at end-systole</td>
<td>2.81 ± 0.83</td>
<td>3.39 ± 1.38</td>
<td>$-0.58 (−1.04$ to $−0.12)$</td>
</tr>
</tbody>
</table>

C: compacted layer thickness; CI: confidence interval; CMR: cardiac magnetic resonance; ICC: interclass correlation coefficient; NC: non-compacted layer thickness; Echo-2D: two-dimensional echocardiography.

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*Data are mean ± standard deviation.*

* $p < 0.05.$
Figure 3. Distribution of the two-layered structure according to the imaging methodology used. The bars represent the percentage of patients in each imaging methodology with a two-layered structure in the indicated segments. CMR: cardiac magnetic resonance; Echo-2D: two-dimensional echocardiography.
Discussion

This is the first study to compare the three validated imaging methodologies for the diagnosis of LVNC. We showed that, in patients with suspected LVNC, CMR provides a more accurate and reliable evaluation of the extent of non-compacted myocardium than Echo-2D images performed either at end-diastole or end-systole. Moreover, this work revealed a good agreement between Echo-2D at end-diastole and CMR measurements.

Study rationale

LVNC is a cardiomyopathy for which various diagnostic criteria have been proposed [4,8,9,14]. These criteria are based on imaging data provided by different techniques at different times during the cardiac cycle. Thus, among the three Echo-2D definitions published, two have attempted to describe non-compaction at end-diastole [8,9] and one at end-systole [4]. A recent study has validated a CMR criterion by using an adapted version of existing Echo-2D criteria.
Figure 6. Short-axis, 4-chamber and 2-chamber views of a patient with a definite diagnosis of isolated left ventricular non-compaction. Each view is compared according to the three imaging methodologies and the pathological specimen after transplantation (white arrow shows the defibrillator lead). The two-layered structure and trabeculations are best visualized by cardiac magnetic resonance at the level of the anterior and anterolateral segments, particularly in the short-axis views. CMR: cardiac magnetic resonance; Echo-2D: two-dimensional echocardiography.

at end-diastole [14]. There is a lack of data comparing the three imaging methodologies (Echo-2D at end-diastole, Echo-2D at end-systole and CMR at end-diastole), hence no consensus exists as to which is the best method for evaluating LVNC.

Only one previous work reported better delineation of the extent of abnormal trabeculation by CMR compared with Echo-2D [11]. However, this study had several limitations, such as inclusion of only four paediatric patients, evaluation of only nine LV segments and measurements performed exclusively at end-systole. Our study offers the advantage of comparing for the first time, in a larger sample size, the data obtained using CMR at end-diastole, Echo-2D at end-diastole and Echo-2D at end-systole.

Two-dimensional echocardiography vs cardiac magnetic resonance

In the present study, when the two-layered structure was evaluated as a criterion of LVNC, no significant differences between Echo-2D at end-diastole and Echo-2D at end-systole were observed with regard to the number of analysable segments, extent of non-compaction and inter-observer reproducibility. However, the NC/C maximum ratio obtained by Echo-2D at end-diastole was obviously higher than that obtained at end-systole. This result implies that the measurements of the NC cannot be performed equally at end-diastole and end-systole.

Two-dimensional echocardiography at end-diastole vs end-systole

In the present study, when the two-layered structure was evaluated as a criterion of LVNC, no significant differences between Echo-2D at end-diastole and Echo-2D at end-systole were observed with regard to the number of analysable segments, extent of non-compaction and inter-observer reproducibility. However, the NC/C maximum ratio obtained by Echo-2D at end-diastole was obviously higher than that obtained at end-systole. This result implies that the measurements of the NC cannot be performed equally at end-diastole and end-systole.
CMR should remain a technique of second intention after Echo-2D. Moreover, in some cases, CMR can overlook non-compaction as a consequence of respiration and cardiac movement artifacts or atrial fibrillation [21]. Therefore, CMR might be indicated in the case of poor acoustic windows or subnormal Echos-2D in first-degree relatives of patients with typical LVNC. In addition, it is not clear whether the extent of non-compaction or the NC/C ratio has prognostic value; however, CMR might be an appropriate technique for testing this hypothesis.

Limitations

The relatively small sample size limits the statistical power of the analysis. Moreover, only adults were included in this study and a few patients had a minor form of LVNC. Because Echo-2D was used to screen patients for study entry, we were not able to define whether CMR is superior to Echo-2D in screening for LVNC among a large population of patients.

We did not analyse LVNC according to the three morphological groups described previously [22] (spongy, meshwork, prominent trabeculations only) because there is considerable subjectivity in defining such patterns [10]. We preferred to consider the two-layered structure aspect, which we found to be an easier and more reproducible criterion for defining the extent of non-compaction.

Finally, contrast echocardiography was not performed in this work. This technique could have been helpful for improving the visualization of endocardial borders and may have allowed for a clearer analysis of the extent of non-compaction [23].

Conclusions

In summary, both echocardiography and CMR are useful for the assessment of patients with LVNC. Echocardiography must be used as a screening method due to its large availability and because it allows a similar assessment of the distribution of the non-compacted segments compared with CMR. CMR appears superior to standard Echo-2D in assessing the extent of non-compaction and provides supplemental morphological information beyond that obtained from conventional Echo-2D studies. For this reason, we suggest that CMR should be performed in all patients with LVNC diagnosed by echocardiography to better assess the extent of non-compaction, and in all patients in whom the diagnosis of LVNC remains doubtful after an echocardiographic study, or in patients with a poor acoustic window.

Finally, the good agreement between Echo-2D at end-diastole and CMR measurements justifies the use of end-diastolic measurements, whatever the technique. Whether CMR is superior to standard echocardiography for the diagnosis of LVNC requires further large prospective studies including genetic and/or pathological correlations.

Conflict of interest statement

None.

References


