Computed Tomography Coronary Angiography findings associated with Left Ventricular Non-Compaction in patients with reduced LV systolic dysfunction: observations from a registry.

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Authors: C. Martini, E. Maffei, T. Arcadi, F. Cademartiri; Monastier di Treviso/IT  
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Purpose

1. Ventricular noncompaction (LVNC) is an unclassified cardiomyopathy in the World Health Organization classification of cardiomyopathies [1]. Its clinical manifestations and outcomes are highly variable, ranging from no symptoms to sudden death [2] and usually associated with significant ventricular dysfunction.

2. Echocardiography is the primary imaging method to diagnose LVNC [3]. Recently, coronary CT angiography (CTCA) is evolving complementary noninvasive diagnostic modalities to image cardiac structures.

3. The purpose of this study was to evaluate the role of coronary CT angiography (CTCA) in the detection of abnormalities of Left Ventricle as described in LVNC and relate them to LV systolic function, referring to our registry.
Methods and Materials

Materials:

We retrospectively review the Institutional CTCA database to screened morphological CTCA findings of 112 consecutive subjects (76 men, 36 women; mean age±SD = 64±13 years) with an echocardiographic diagnosis of systolic dysfunction (EF<45%) of unknown etiology and without diagnosed LVNC, who were referred for CT Coronary Angiography (CTCA) for coronary artery evaluation (CAD), between October 2006 and March 2010. Demographic details of the enrolled subjects as well as associated cardiovascular risk factors and details of disease prevalence (Table 1). Because this study is a retrospective one, no ethics committee approval was required.

Patient preparation before CT

Patients with pre-scan HR>65bpm received a single intravenous dose of 5 mg atenolol 10 min before CT under ECG and blood pressure control. Immediately before CT, all patients were administered sub-lingual isosorbide dinitrate (0.3 mg).

CT protocol

All CTCA were performed using a 64-slice MDCT (Sensation 64 Cardiac, Siemens, Forchheim, Germany). For the unenhanced CT a standard protocol described elsewhere was applied [1]. For the contrast-enhanced CT, all patients were administered a 100-ml bolus of a contrast medium containing a high concentration of iodine (iomeprol, lomeron 400, 400 mgl/ml; Bracco, Milan, Italy). Contrast medium was injected into an antecubital vein at a rate of 5 ml/s. The CT was triggered using a bolus tracking technique.

CT image reconstruction

For CTCA, a retrospective ECG-gated technique was used for the reconstruction of images. Data acquired during a single heartbeat were used. Datasets were reconstructed during the mid-to-end diastolic phase (reconstruction windows set at -300 to -450ms) and the mid-to-end systolic phase (reconstruction windows set at -300 to -450ms). The reconstructed slice thickness was 0.75 mm with an increment of 0.4 mm. All the CT datasets were filtered with a medium-soft convolution kernel. The CT images were evaluated by two experienced readers in consensus who were blinded to the patient clinical and pathological characteristics. Evaluation of images [axial images, oblique and curved multiplanar reformats, maximum intensity projection (MIP) reformats, and volume rendered (VR) reformats] was performed on a dedicated Workstation (MMWP, Siemens, Forchheim, Germany).
CT image evaluation

A complete CT data was obtained for all patients. The CT images were exported and transferred to a separate workstation with dedicated software (Leonardo, Siemens).

To diagnosis LVNC, the data were re-evaluated according to echocardiographic criteria for LVNC (Jenni Criteria) [1]:

1. Absence of coexisting cardiac abnormalities.
2. Evidence of excessively thickened myocardial wall with a two-layered structure comprising a thin compacted layer on the epicardial side and a much thicker non-compacted layer of prominent trabeculations and deep intertrabecular recesses on the endocardial side.
3. Evidence of deep-perfused intertrabecular recesses, due the intrabeculart spaces filled by direct blood flow from the ventricular cavity.
4. Predominant localization of the noncompacted myocardial segment mainly in the apical and mid-lateral and mid-inferior regions of the left ventriclel and typically show a two-layered structure with an endsystolic ratio (ESR) greater than two between the non compacted subendocardial layer of prominent trabeculations and deep intertrabecular recesses on the endocardial side and the subepicardial layer on the epicardial side.

According on the recommendations of the America Heart Association on standardized myocardial segmentation, a 17-segment model was used [2].

First, for qualitative analysis, short axis end-systolic datasets were assessed to identify the distribution and pattern of abnormalities of the sub-endocardial trabeculae LV. Then, the linear ratio of non compacted to compacted myocardium (NC/C ratio) was measured by measuring the site of maximal thickness of noncompaction and the corresponding radial compacted area. The measurements was performed in the 3-chamber view at the end-systolic phase of the cardiac cycle for optimal visualization of the two layers.

Patients without significant abnormalities of the sub-endocardial trabeculae were excluded. Patients were classified based on both the NC/C ratio and LV systolic function (Table 2). The severity of non compaction by NC/C ratio was arbitrarily classified as mild (1<NC/C#2), moderate (2<NC/C#3), and severe (NC/C#3). While, LV functional parameters were calculated using a dedicated software (Argus, Leonardo, Siemens, Forchheim, Germany). In particular, the parameters calculated were the following: left ventricle ejection fraction (LV EF), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and end-diastolic wall mass of the left ventricle (ED wall mass). Based on this, patients were divided in 3 sub-groups according to their EF: group 1 EF<25% (Gr1), group 2 EF=25-35% (Gr2), and group 3 EF=35-45% (Gr3). Correlation between the NCs and EF were assessed. Patients with EF>45% were excluded.
### Table 1: Population study demographics, cardiovascular RF and details of disease prevalence of patient with an echocardiographic diagnosis of LV systolic dysfunction

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Table 2: Classification Criteria. Population study was classified on basis of NC/C ratio (a) and CT findings of LV systolic dysfunction (b).

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Results

After the collection of parameters, we analysed a continuous series of 33 patients affected by abnormalities of the LV sub-endocardial trabeculae (i.e. LVNC) (Table 3). The main symptom was dyspnoea and hypertension in 67% (in all of these patients, however, a concomitant ischemic cardiomyopathy was demonstrated). The average age of the registry was 67.3±9.3 years (range 41-81 years), considering 18 males and 15 females. HR during CTCA was 70±18 bpm. In 33, we found a LV systolic dysfunction with an average EF of 28±11%. While, the average NC/C was 3±1.4 (range 1.2-6). The clinical CT features of suspected LVNC population and relate sub-groups was showed in Table 4, according to their EF.

Patients with mild (n. 7) moderate (n.12) and severe (n.14) NC/C, showed LVEF of 30±15%, 28±10% and 28±11%, respectively (R²=0.53 - Graph 1). While, none correlation between LVEF and degree of NC/C and was demonstrated (Graph 2). In LVNC population, 30(91%) showed LV systolic dysfunction (EF ≤45%) (Table 5). In Gr 1 (n.14), NC/C was 2.9±1.0, in Gr2 (11) 3.1±1.6 and in Gr3 (5) 2.6±0.9 (R²=0.50 - Graph 3). Patient with decreased systolic dysfunction (Gr3) showed a correlation between NC/C ratio and EF (r=0.59), and LVEDV (r=-0.62) (Graph 4). None significant differences between degree of NC/C and LV systolic dysfunction was found.
### Table 3: LVNC Population

Population Demographics, cardiovascular risk factors and details of disease prevalence of patients with CT findings of LVNC (NC/C ratio>2). The LVNC population was clustered base on NCs classification

<table>
<thead>
<tr>
<th>Population</th>
<th>67.3±9.3 (81-41)</th>
<th>70±3.2 (75-65)</th>
<th>66.6±10.1 (81-48)</th>
<th>66.6±10.9 (77-41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (BMI &gt;30kg/m²)</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Known CAD</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>22</td>
<td>3</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Bundle Branch block</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>FA</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25</td>
<td>5</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Family history</td>
<td>14</td>
<td>4</td>
<td>5</td>
<td>5</td>
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<tr>
<td>ICD</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ventricular Thrombi</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Aortic disease</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>LV ejection Fraction (%)</td>
<td>28±11</td>
<td>30±15</td>
<td>28±10</td>
<td>28±11</td>
</tr>
</tbody>
</table>

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Table 4: LVNC Population characteristics. The Table show the demographic characteristics and EF of CT findings of LVNC and relate sub-groups.

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<table>
<thead>
<tr>
<th>Age (yrs; mean±SD)</th>
<th>50.9±9.9</th>
<th>70.0±3.2</th>
<th>66.6±10.1</th>
<th>66.6±10.9</th>
</tr>
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<tbody>
<tr>
<td>EF</td>
<td>58 ± 5.5</td>
<td>30 ± 15</td>
<td>28 ± 10</td>
<td>28 ± 11</td>
</tr>
</tbody>
</table>

Fig. 1: NCs Classification. The Graph shows the relation between LV systolic dysfunction and degree of NC/N. We found a moderate correlation between EF reduction and degree
of NC/C. The increase of sub-endocardial LV trabecolae not involves in a higher systolic dysfunction.

**Fig. 2:** Correlation between NCs and LVEF. The Graph a shows the relation between LVNC and LVEF. The Graph b shows the relation between degree of NC/C and EF.

<table>
<thead>
<tr>
<th>Age (yrs; mean±SD)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>68.4±8.3</td>
<td>69.1±7.7</td>
<td>66.6±10.1</td>
<td>67.8±13.9</td>
</tr>
<tr>
<td>NC/C</td>
<td>3.0±1.4</td>
<td>2.9±1.0</td>
<td>3.1±1.6</td>
<td>2.6±0.9</td>
</tr>
</tbody>
</table>

**Table 5:** LV systolic dysfunction in patients with Suspected LVNC. The Table show the demographic characteristics and NC/C ratio of patients with CT findings of LV systolic dysfunction.
Fig. 3: EFs Classification. The Graph shows the relation between NC/C ratio and the degree of LV systolic dysfunction. We found a moderate correlation between EF reduction and degree of NC/C. The increase of LV systolic dysfunction is not associated to severity of LVNC.

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**Fig. 4:** Correlation between LV systolic Dysfunction and NC/C. The Graph shows the relation between degree of LV systolic dysfunction and NC/C

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Conclusion

New CT technologies have opened the way to perform CTCA using a reasonably low dose [4], providing a comprehensive evaluation of coronary artery disease, and morphological and functional features of the LV. However, as compared with echocardiography and cardiac MR imaging, only few reports related the CT as non invasive imaging tool for the differential diagnosis of ventricular noncompaction, including prominent trabeculations (fewer than three in normal variants), hypertrophic cardiomyopathy, endocardial fibroelastosis, dilated cardiomyopathy, restrictive cardiomyopathy, apical thrombosis, and endomyocardial fibrosis [5-7]. Our study showed that CTCA provided clinically relevant information in patients with pattern of abnormalities of the LV sub-endocardial trabeculae, such as morphological and functional differences based on the degree of left ventricular noncompaction. The occurrence of trabeculated myocardium might be due to a different pathophysiological mechanism. We believe that correct diagnosis of ventricular noncompaction may be readily made by recognizing characteristic morphological features on cardiac CT imaging.
References


Personal Information

Dr.ssa Chiara Martini, RT
Cardio-Vascular Imaging Unit - Giovanni XXIII Hospital
Via Giovanni XXIII, 7 - 31050 - Monastier di Treviso (TV) - Italy
Tel. +39 0422 896377
Tel. +39 0422 896310 (direct)
Cel +39 340 1633219
Fax. +39 0422 896507

e-mail: chiaramartini10@gmail.com
Profilo BiomedExpert