The impact of maximal septal end-diastolic wall thickness (SEDWT) value on clinical outcome in hypertrophic cardiomyopathy (HCM)

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Purpose

Hypertrophic cardiomyopathy (HCM) is a common disease, occurring in 500 of the general population and clinically diagnosed by the presence of left ventricular (LV) hypertrophy without a specific cause (such as associated with specific cardiac or systemic disorders, for example infiltrative disease) [1]. HCM is characterized by extreme heterogeneity with regard to phenotypic expression, pathophysiology, and clinical course [2,3].

HCM is the most common cause of sudden cardiac death in young people, but also a major cause of heart failure disability and important disease-related complications that impact clinical outcome at any age [4, 5, 6]. HCM annual mortality rates is between 3 to 6% [7].

Cardiovascular magnetic resonance (CMR) imaging is a non-invasive imaging modality capable of providing high-resolution images of the heart in any desired plane and is considered the gold standard for in-vivo determination of LV mass and volumes. Furthermore it enables precise quantification of posterior and septal wall thickness. Moreover Late-Gadolinium-Enhancement Cardiac Magnetic Resonance (LGE-CMR) imaging is the standard of reference to detect myocardial viability, used for non-invasive tissue characterization and it can detect as well foci of fibrosis in the myocardium of HCM patients, due to the accumulation of contrast media in interstitial space [8].

The aim of the present study is to determine the association between SEDWT and the occurrence of major adverse cardiac events (MACE) in HCM patients.
Methods and Materials

Study population:

It’s a non-randomized single centre study with prospective evaluation, performed between August 2005 and August 2011 at the Radiology Department, University Hospital of Modena, Italy. Local ethic committee approved the study.

The study population is composed by 62 patients (mean age: 55.6±16.0; 67.7% males) with the diagnosis of HCM based on history, clinical examination, echocardiography, coronary angiography and 24 h ECG Holter-monitoring and familiar History (Fig. 1).

Indications for LGE-CMR were to confirm the diagnosis and to determine mass and volumes data of LV.

Exclusion criteria: clinical history of atherosclerotic coronary artery disease, systemic or specific cardiac cause of hypertrophy, general MR imaging contraindications.

Written Informed consent was obtained by all subjects.

LGE-CMR acquisition:

LGE-CMR examinations were performed on 1.5 Tesla whole body imaging system (Achieva, Philips Medical System, Best, The Netherlands). A dedicated five-element, phase-array body coil was used. Images were acquired during repeated end-expiratory breath-hold that was of 10-15 s, depending on the heart-rate. To evaluate functional parameters, ECG-gated cine images were then acquired using Balanced-Turbo Field Echo (b-TFE) sequence on multiple cardiac phases.

Subsequently, LGE-CMR images were obtained in the same long and short axis orientation, 15 minutes after intravenous administration of 0.1 mmol/ kg gadolinium DOTA (Dotarem, Guerbet S.A., Cedex, France), using a breath-hold 3D Inversion-Recovery TurboField Echo (IR-TFE-3D) sequence acquired in the same views as the cine images. The inversion recovery time was adjusted per patient to optimally null the signal from normal myocardium (typically 230-350 ms) [9] (Fig. 2).

Total acquisition time averaged 40 minutes.

Images analysis, determination of ventricular and atrial parameters and wall thickness:

Ventricular function was analyzed off-line from the serial short-axis using a dedicated commercially available software (ViewForum 3.2, Philips Medical System, Best, The Netherlands) by two experienced investigators. Volume and mass values were obtained applying the Simpson's method and were indexed to body surface area [10] (Fig. 3).
In addition to volumetric measurements, one dimensional measurements of left ventricular end-diastolic diameter, posterior wall thickness and maximum inter-ventricular septum wall thickness were measured from ED short axis views (Fig. 4).

**Follow up:**

During follow-up the occurrence of major adverse cardiac events was recorded by interviewing patients and their reference cardiologists.

MACE considered were: sustained ventricular tachyarrhythmias (SVT), atrial fibrillation (AF), implantable cardioverter defibrillator shock (ICDS), progression into NYHA functional classes III or IV, surgery for obstructive HCM (myomectomy and mitral valve replacement), unscheduled hospitalization, death from heart failure and sudden cardiac death (SCD).

**Statistical analysis:**

The statistical correlations between SEDWT value and the occurrence of MACE was performed with university and multivariate analysis. All results were considered statistically significant when p<0.05.
### Demographics and Clinical Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (n.62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD), years</td>
<td>55.6±16.0</td>
</tr>
<tr>
<td>Males (%)</td>
<td>43 (69.4%)</td>
</tr>
<tr>
<td>Familiar forms of HCM (%)</td>
<td>24 (38.7)</td>
</tr>
<tr>
<td>Dyspnea (%)</td>
<td>23 (37.1)</td>
</tr>
<tr>
<td>Angina (%)</td>
<td>11 (17.7)</td>
</tr>
<tr>
<td>NYHA III-IV Class (%)</td>
<td>4 (6.5)</td>
</tr>
<tr>
<td>LVOT Obstruction (%)</td>
<td>29 (46.8)</td>
</tr>
</tbody>
</table>

**Fig. 1:** Table with demographics and clinical parameters.

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Fig. 2: Septal thickening and LGE pattern of a patient with hypertrophic cardiomyopathy. Thickness is obtained by using B-TFE sequence in short axis view and LGE with IR-TFE sequence, acquired in the same view.

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Fig. 3: Spatial distribution of the mean values for segmental wall thickness, wall thickening and myocardial motion represented as colour maps in patients with HCM.

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Fig. 4: Bidimensional measurements of posterior and septal wall thickness and left and right ventricular diameters in short axis view.

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Results

The mean maximal SEDWT was 20.5±4.4 mm (Fig. 5).

Volumes and masses measured with LGE-CMR are reliable and reproducible because they are calculated on images obtained with b-TFE sequence in the short axis, by using the Simpson's method. This approach is independent of geometric assumptions that affect and make less reliable the parameters derived by echocardiography.

There were no statistically significant differences in LV-function and volumes between high- and low- thickened septum wall.

During 32.1±11.2 months of follow-up, 15 patients (24,2%) had AF, 12 (19,3%) SVT, 4 (6,5%) ICD shock, 8 (12,9%) progression into NYHA classes III or IV, 10 (16,2%) unscheduled hospitalization, 1 (1,6%) death from heart failure, there were no SCD.

One or more MACE occurred in 26 (41.9%) patients and two or more MACE in 14 (22.5%). There was no association between maximal SEDWT and SVT (9), ICDS (4), progression of NYHA (8), surgery for obstructive HCM (4), unscheduled hospitalization (10), death from heart failure (1) and SCD (0).

However there was a relation between SEDWT and AF (15; p-value=0.004) and overall MACE (48).

In particular, patients who presented one or more MACE had significantly higher value of SEDWT compared to those without: 22.1±4 mm vs 19.4±4.4 mm, p=0.008 (Fig. 6).

Moreover patients who presented two or more MACE had significantly higher value of SEDWT compared to those with only one or without MACE: 22.9±3.1 mm vs. 19.8±4.5 mm, P=0.009 (Fig. 7).
Fig. 5: Table with CMR parameters.

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Fig. 6: Distribution of SEDWT in patients with or without MACE.

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Fig. 7: Distribution of SEDWT in patients with MACE 0-1 and patients with MACE # 2.

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Conclusion

Coming to conclusions, it can be stated that SEDWT value is a significant predictor for the occurrence of MACE in HCM patients.

Our results show that the maximal SEDWT value is a strong predictor of prognosis in patients with hypertrophic cardiomyopathy.

In the absence of other generally accepted risk factors, patients with a higher maximal SEDWT have a higher long-term risk for MACE.
References


10. Society of Cardiovascular Magnetic Resonance, see http://www.scmr.org/technologists/ protocols.html, consulted on 10-08-2011].