Elastic aortic properties in hypertrophic cardiomyopathy: a single center echocardiographic evaluation

E. VIZZARDI, E. SCIATTI, I. BONADEI, S. GELSONINO¹, R. LORUSSO², M. METRA

Abstract. – OBJECTIVE: Previous studies revealed that hypertrophic cardiomyopathy (HCM) patients have impaired aortic elastic properties with contrasting data about aortic dimensions. We aimed to extend our knowledge about this topic, considering tissue Doppler imaging (TDI) and tissue strain.

PATIENTS AND METHODS: 25 HCM patients and 25 healthy volunteers matched for age and sex were enrolled. They underwent transthoracic echocardiography to measure aortic dimensions at four levels (Valsalva sinuses, sinotubular junction, tubular tract, aortic arch), elastic properties (i.e., distensibility, stiffness, M-mode strain, tissue strain), and TDI aortic wall velocities (S', E', A' waves).

RESULTS: Aortic dimensions differed between the two groups only at sinotubular junction (18 ± 6 vs. 15 ± 3 mm/m²; p = 0.039) and aortic arch levels (19 ± 5 vs. 11 ± 8 mm/m²; p < 0.001). Aortic stiffness was significantly higher among patients (16.4 ± 23.2 vs. 5.9 ± 3.4; p = 0.034), and TDI waves greater (S': 5.2 ± 1.9 vs. 8.0 ± 2.7 cm/s, p < 0.001; E': -5.3 ± 2.4 vs. -7.2 ± 2.7 cm/s, p = 0.012; A': -5.3 ± 1.6 vs. -8.6 ± 4.5 cm/s, p = 0.002). M-mode and tissue strains, and aortic distensibility did not reach statistical significance, although showing a tendency to altered values in the HCM group.

CONCLUSIONS: Patients affected by HCM show a larger aorta and altered aortic elastic properties compared with healthy volunteers. These findings could help to investigate treatment response and prognosis of these alterations.

Key Words:
Hypertrophic cardiomyopathy, Aortic stiffness, Aortic distensibility, Aortic strain, Tissue Doppler imaging.

Introduction

Hypertrophic cardiomyopathy (HCM) is a genetic cardiac disease with high heterogeneity in clinics and phenotype. It affects at about 1 out of 500 adult subjects and it is recognized as the most common cause of sudden death in young people, especially in athletes

Boonyasirinan et al demonstrated that HCM patients show an increased aortic stiffness measured by means of pulse wave velocity (PWV) calculated on cardiac magnetic resonance imaging (MRI) acquisitions. Moreover, aortic elastic properties could also be assessed by echocardiography measuring the pulsatile changes in ascending aortic diameter and conventional left brachial arterial systolic (SBP) and diastolic blood pressure (DBP) values. Boonyasirinan et al revealed that aortic distensibility, stiffness and M-mode strain are impaired in HCM patients than healthy controls; these alterations are similar to those of hypertensive subjects with LV hypertrophy. The aim of the present study was to completely evaluate echocardiographically-derived aortic dimensions and elastic properties in HCM patients, including tissue Doppler imaging (TDI) waves and tissue strain of ascending aorta, in comparison to healthy subjects.
Patients and Methods

Subjects
We enrolled 25 patients affected by HCM, followed by the Cardiologic Day Service, University Civil Hospital of Brescia, Italy. Diagnosis of HCM was confirmed in all patients according to the guidelines. They were carefully selected without left ventricular outflow tract obstruction and not on medical therapy. They were compared with 25 healthy volunteers matched for age and sex. We state that our study complies with the Declaration of Helsinki and that informed consent has been obtained from the subjects (or their guardians). Everyone underwent blood pressure measurement and transthoracic echocardiography.

Blood Pressure Measurement
Blood pressure was assessed using a standard, calibrated sphygmomanometer. The mean of three sitting and standing blood pressure was recorded. The arm in which the highest sitting diastolic pressures was found was the arm used for all subsequent readings throughout the study. Every effort was made to have the same staff member obtain blood pressure measurements in each individual patient, at the same time of day, using the same equipment. Systolic blood pressure (SBP) was recorded when the initial sound is heard (Phase I of the Korotkoff sound), while diastolic blood pressure (DBP) at the disappearance of the sound (Phase V of the Korotkoff sound). The cuff was deflated at a rate not greater than 2 mmHg/s.

Transthoracic Echocardiography
Echocardiographic examinations (M-mode, 2D, color-Doppler and tissue Doppler) was performed using Vivid 7 machine (GE Healthcare, Milwaukee, WI, USA) with a 3.5 MHz transducer. Digital loops were stored on the hard disk of the echocardiograph for on-line and off-line analyses and transferred to a workstation EchoPac, Vingmed (GE Healthcare, Milwaukee, WI, USA) for off-line analysis. Participants were studied in the left lateral decubitus position according with the standardization of the American Society of Echocardiography and images acquired from standard parasternal and apical windows. All studies were read by two echocardiologists blinded to all patient informations.

Elastic aortic properties measured with conventional and Tissue Doppler Imaging (TDI) measurements were taken in five consecutive cycles and the means were used for statistical comparison. Aortic size was assessed at four levels: Valsalva sinuses (Ys), sinotubular junction (STJ), tubular tract (TT), and aortic arch (AAr), at the end of diastole. Aortic elastic indexes distensibility (DIS, cm² × dyn⁻¹), and stiffness index were calculated from the echocardiographically-derived thoracic aortic diameters (mm²/m²). Aortic elasticity was assessed on the basis of a 2D guided M-mode recording of systolic (AoS) and diastolic (AoD) aortic diameters, 3 cm above the aortic valve. AoD was obtained at the peak of the R wave at the simultaneously recorded ECG, and AoS was measured at the maximal anterior motion of the aortic wall; five measurements were averaged for each diameter. The following indexes of aortic elasticity were calculated: M-mode strain = (AoS – AoD)/AoD; aortic distensibility = [2 × (AoS – AoD)/AoD × (PP) (mmHg⁻¹]]; aortic stiffness index (SI) = ln(SBP/DBP)/[(AoS – AoD)/AoD] (pure number) where pulse pressure (PP) is calculated as SBP-DBP, and ln(SBP/DBP) refers to the natural logarithm of the relative pressure. A sample volume was placed in the region of interest on the anterior aortic wall (3 cm above the aortic valve at the same position as in M-mode measurements). TDI wall velocities during systole (S’), early relaxation (E’) and atrial systole (A’) were measured in the two groups. Velocity data sets were analyzed off-line using the same dedicated software, and peak systolic strain was measured from the resulting deformation curves.

Statistical Analysis
All analyses were done using IBM SPSS Statistics 20 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were tested for normality with Kolmogorov-Smirnov test and represented by mean ± standard deviation, while categorical variables as frequency (n) and percentage of the sample. Independent-samples Student’s t test was performed to analyze the difference between means for continuous variables and Fisher’s exact test for the difference between proportions for dichotomic ones. For all statistical tests, probability values < 0.05 were considered significant.

Results
Demographic and clinical characteristics are shown in Table I. Patients and controls did not differ in age, sex distribution, and body surface
area (BSA). All people in the study population were normotensive. SBP was not statistically different between the two groups, as well as DBP and heart rate.

Echocardiographic examination of LV and aorta are resumed in Table II, respectively. LVEF and LVEDV index were not different between cases and controls. Aortic dimensions, instead, were significantly larger in the HCM group only at the level of STJ (18 ± 6 vs. 15 ± 3 mm/m²; p = 0.039) and AAR (19 ± 5 vs. 11 ± 8 mm/m²; p < 0.001). Aortic distensibility was lower among patients than controls, being 3.7 ± 2.6 vs. 5.3 ± 3.9 mmHg⁻¹ (p = 0.108), while stiffness higher (16.4 ± 23.2 vs. 5.9 ± 3.4; p = 0.034), M-mode strain greater (8.2 ± 5.7 vs. 11.1 ± 8.1%; p = 0.149) as well as tissue strain (−19.9 ± 9.7 vs. -24.3 ± 9.1; p = 0.109). Finally, TDI evaluation of aortic wall velocities revealed every wave reached a statistic significant difference, being reduced in the HCM group (S’ wave: 5.2 ± 1.9 vs. 8.0 ± 2.7 cm/s, p < 0.001; E’ wave: -5.3 ± 2.4 vs. -7.2 ± 2.7 cm/s, p = 0.012; A’ wave: −5.3 ± 1.6 vs. −8.6 ± 4.5 cm/s, p = 0.002). No patients had an echocardiographic diagnosis of either a bicuspid aortic valve or severe aortic valve stenosis or regurgitation.

### Discussion

The present study demonstrated that patients affected by HCM show a larger aorta and altered aortic elastic properties compared with healthy volunteers. This is not completely coherent with previous findings. In fact, Boonyasirinant et al.⁹ found no statistically significant differences between patients and controls in aortic dimensions measured at cardiac MRI¹⁰, while Jain et al.¹⁶ revealed aortic dilation at VS in proportions similar to general population, but at TT more than twice. Our patients, although being normotensive, presented significantly larger aortas at STJ and AAR levels, thus confirming and extending Jain et al.

### Table I. Demographic and clinical characteristics of the study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HCM (n = 25)</th>
<th>Healthy controls (n = 25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35 ± 15</td>
<td>32 ± 9</td>
<td>0.507</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>14 (56.0%)</td>
<td>9 (36.0%)</td>
<td>0.256</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.78 ± 0.17</td>
<td>1.73 ± 0.19</td>
<td>0.388</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>122 ± 13</td>
<td>122 ± 15</td>
<td>0.960</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>75 ± 8</td>
<td>77 ± 12</td>
<td>0.378</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>76 ± 11</td>
<td>75 ± 15</td>
<td>0.688</td>
</tr>
</tbody>
</table>

BSA = body surface area; DBP = diastolic blood pressure; HCM = hypertrophic cardiomyopathy; HR = heart rate; SBP = systolic blood pressure.

### Table II. Results from transthoracic echocardiography.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HCM (n = 25)</th>
<th>Healthy controls (n = 25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV index (mL/m²)</td>
<td>62 ± 12</td>
<td>57 ± 14</td>
<td>0.212</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>65 ± 4</td>
<td>64 ± 5</td>
<td>0.374</td>
</tr>
<tr>
<td>VS index (mm/m²)</td>
<td>12 ± 4</td>
<td>12 ± 4</td>
<td>0.901</td>
</tr>
<tr>
<td>STJ index (mm/m²)</td>
<td>18 ± 6</td>
<td>15 ± 3</td>
<td>0.039</td>
</tr>
<tr>
<td>TT index (mm/m²)</td>
<td>16 ± 6</td>
<td>16 ± 3</td>
<td>0.574</td>
</tr>
<tr>
<td>AAR index (mm/m²)</td>
<td>19 ± 5</td>
<td>11 ± 8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Distensibility (mmHg⁻¹)</td>
<td>3.7 ± 2.6</td>
<td>5.3 ± 3.9</td>
<td>0.108</td>
</tr>
<tr>
<td>Stiffness</td>
<td>16.4 ± 23.2</td>
<td>5.9 ± 3.4</td>
<td>0.034</td>
</tr>
<tr>
<td>M-Mode strain (%)</td>
<td>8.2 ± 5.7</td>
<td>11.1 ± 8.1</td>
<td>0.149</td>
</tr>
<tr>
<td>Tissue strain (%)</td>
<td>-19.9 ± 9.7</td>
<td>-24.3 ± 9.1</td>
<td>0.109</td>
</tr>
<tr>
<td>S’ wave (cm/s)</td>
<td>5.2 ± 1.9</td>
<td>8.0 ± 2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E’ wave (cm/s)</td>
<td>-5.3 ± 2.4</td>
<td>-7.2 ± 2.7</td>
<td>0.012</td>
</tr>
<tr>
<td>A’ wave (cm/s)</td>
<td>-5.3 ± 1.6</td>
<td>-8.6 ± 4.5</td>
<td>0.002</td>
</tr>
</tbody>
</table>

AAR = aortic arch; HCM = hypertrophic cardiomyopathy; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; STJ = sinotubular junction; TT = tubular tract; VS = Valsalva sinuses.
findings. The discrepancy with Boonyasirinant et al\textsuperscript{9} may be explained considering that they measured aorta by means of cardiac MRI at not well specified mid-ascending and mid-descending level.

Regarding aortic elastic properties, we agree with Gavallà et al\textsuperscript{13}, showing impaired distensibility, stiffness and M-mode strain in HCM patients. Moreover, we extend these findings revealing that even S', E' and A' waves of ascending aorta wall velocity at TDI were significantly reduced in these subjects. Of note, the two groups were similar regarding SBP and DBP.

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In addition to the hypothesized genetic common pathway, several factors have been included in the possible explanations of impaired aortic function in HCM: neurohormonal disturbances (because of increased LV pressure and activation of renin-angiotensin-aldosterone system and nor epinephrine release), endothelial dysfunction, abnormal LV baroreceptor response, atherosclerotic process (frequently found in HCM patients)\textsuperscript{9}. Moreover, an intrinsic aortic fibrosis similar to ventricle one could also be hypothesized, as previous studies have shown a role for transforming growth factor-\(\beta\) (TGF-\(\beta\)) in the development of fibrosis and hypertrophy in HCM, as well as aortic aneurism and dissection\textsuperscript{[8-11, 13, 14]}.

Concerning pathophysiological implications, impaired aortic function may negatively affect an already stiff ventricle, thus impairing ventriculo-arterial coupling (thus, performance and energetics). This phenomenon leads to an even stiffer ventricle and could aggravate symptoms and prognosis.

Conclusions

We can speculate about an hypothetical utility of aortic elastic properties and dimensions in clinical risk stratification for HCM. Furthermore, further studies may aim to test whether pharmacological treatment or surgical interventions (i.e., septal ablation, myectomy) improve aortic elastic properties, and then prognosis. We are lacking data about medical treatment of HCM patients. Moreover, blood pressure for distensibility and stiffness formulae have been measured at brachial instead of aortic level.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References


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