Anatomical and functional evaluation of the cardiovascular system in Marfan syndrome
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CHAPTER
Comparison of aortic elasticity in patients with the Marfan syndrome with and without aortic root replacement

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Introduction

Aortic elasticity has been identified as a potential risk factor for aortic complications. Groenink et al. demonstrated decreased aortic elasticity determined by measurement of local distensibility and flow wave velocity (FWV) with magnetic resonance (MR) imaging in patients with Marfan syndrome who did not undergo operation. Aortic elasticity after aortic root replacement (ARR) has not yet been investigated, but Imawaki et al. demonstrated decreased aortic distensibility in patients with the Marfan syndrome after surgery of the abdominal and thoracic aorta.

This study investigates the feasibility of MR imaging for assessing aortic elasticity in patients with the Marfan syndrome after elective ARR, and compares aortic elasticity in these patients with the aortic elasticity of patients with Marfan syndrome who did not undergo surgery using MR imaging.

Methods

Patient group

In all, 133 consecutive patients with the Marfan syndrome without previous aortic dissection (mean age 32, age range 16-55 years) underwent cardiac MR imaging from September 1996 to April 2001. The diagnosis of the Marfan syndrome had been established according to the Ghent Criteria. After initial inclusion, 16 (12%) patients were excluded because of triggering problems during image acquisition or poor image quality. The remaining 117 patients were divided into 2 groups: 1) 78 patients with Marfan syndrome without ARR (mean age 31 ± 8 years, age range 18-50 years), and 2) 39 patients with Marfan syndrome with elective ARR (mean age 32 ± 11 years, age range 16-55 years). Of the 39 patients who underwent surgery, 36 had composite valve graft replacements; the remaining 3 underwent aortic valve-sparing operations. The study was approved by the local ethical committee, and individual oral and written informed consent was obtained in each patient.

Magnetic Resonance imaging

MR Imaging was performed with a 1.5 Tesla MR system (either Philips ACS NT15, Philips Medical Systems, Best, the Netherlands; Signa, GE Medical systems, Milwaukee, Wisconsin, USA; or Magnetom Vision, Siemens Medical Systems, Erlangen, Germany) using similar pulse sequences. Image acquisition was triggered on the electrocardiogram. The entire aorta was imaged in the transverse and oblique sagittal planes by using a standard spin-echo pulse sequence. Next, a high resolution gradient echo pulse sequence with a velocity encoding gradient was applied perpendicular to the aorta at 4 levels.
Figures 1: (A) MR image showing the aorta in the long axis view of a patient with Marfan syndrome with an aortic root replacement in which the graft is drawn. (B) Levels perpendicular to the aorta applied for gradient echo MR imaging with velocity encoding. Distensibility and diastolic diameter were assessed at these 4 levels. Flow wave velocity between these levels was calculated.

(Figure 1): 1) the ascending aorta, 2) descending aorta at the level of the bifurcation of the pulmonary artery, 3) descending aorta at the level of the diaphragm, and 4) just above the aortic bifurcation. Maximal velocity encoding was chosen at 150 cm/sec and was increased to a maximum of 250 cm/s when aliasing occurred. This resulted in multi-phase image pairs of modulus and velocity encoded images with a temporal resolution of approximately 25 ms through the cardiac cycle and a spatial resolution of approximately 1 pixel/mm. Distances between the levels were measured on the console of the MR system by drawing a line through the middle of the aortic lumen on the oblique sagittal images. During each flow measurement, the brachial artery systolic and diastolic blood pressure was measured by means of a sphygmomanometer cuff.

A workstation (Sparc Ultra; Sun Microsystems; Mountain View, Calif.) and the FLOW® image analysis software (Medis, Leiden, The Netherlands) were used for image analysis. Aortic contours were drawn manually on the modulus images of all cardiac phases and flow (ml/s) through each aortic level was calculated using the areas on the modulus images and the velocity values of the corresponding velocity encoded images.

Flow wave velocity (FWV, meters per second) was calculated as the ratio of distance between 2 levels and the time difference between arrival of the flow wave at these levels. The flow wave was considered to arrive at a certain level when the flow reached half of its maximum value. Consequently, FWV was determined in the entire aorta distal to the aortic root (from level 1 to level 4, FWV 1 to 4) and in 3 segments of the aorta: aortic arch (level 1 to level 2, FWV 1 to 2), descending thoracic aorta (level 2 to level 3, FWV 2 to 3) and abdominal aorta (level 3 to level 4, FWV 3 to 4).
Distensibility at the 4 levels was calculated by means of the following equation:

\[
D = \frac{(A_{\text{max}} - A_{\text{min}})}{A_{\text{min}} \cdot (P_{\text{max}} - P_{\text{min}})}
\]

\(D\) = distensibility \((10^{-3} \text{ mmHg}^{-1})\), \(A_{\text{max}}\) = maximal (systolic) aortic area \((\text{mm}^2)\), \(A_{\text{min}}\) = minimal (diastolic) aortic area \((\text{mm}^2)\), \(P_{\text{max}}\) = systolic blood pressure \((\text{mmHg})\) and \(P_{\text{min}}\) = diastolic blood pressure \((\text{mmHg})\).

Statistical analysis

Data are given as mean ± SD. Differences between the groups were assessed by the unpaired Student’s t test. Statistical analysis was performed with the SPSS statistical package (SPSS Inc, Chicago, Illinois, USA). The level of significance was set at \(p < 0.05\).

Results

There were no significant differences in clinical characteristics between patients with Marfan syndrome with and without ARR (Table 1). No significant differences in Marfan-related phenotypic features, or in familial involvement could be demonstrated between the 2 groups.

Table 1 Clinical characteristics of the patients with Marfan syndrome.

<table>
<thead>
<tr>
<th></th>
<th>Nonoperated ((n=78))</th>
<th>Operated ((n=39))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>46 (59%)</td>
<td>29 (74%)</td>
</tr>
<tr>
<td>Female</td>
<td>32 (41%)</td>
<td>10 (26%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31 ± 8</td>
<td>32 ± 11</td>
</tr>
<tr>
<td>Body surface area ((\text{m}^2))</td>
<td>2.01 ± 0.19</td>
<td>2.08 ± 0.23</td>
</tr>
<tr>
<td>Mean blood pressure ((\text{mmHg}))</td>
<td>80 ± 8</td>
<td>81 ± 11</td>
</tr>
<tr>
<td>Beta-blocker use</td>
<td>53 (68%)</td>
<td>31 (80%)</td>
</tr>
<tr>
<td>Family history of the Marfan syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>30 (38%)</td>
<td>21 (54%)</td>
</tr>
<tr>
<td>positive</td>
<td>13 (17%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>positive for dissection</td>
<td>35 (45%)</td>
<td>15 (38%)</td>
</tr>
</tbody>
</table>

Note.-For comparisons of all characteristics, \(p\) values were greater than 0.05.

Table 2 lists data on aortic diameters. The differences in aortic diameter between both groups were only marginally significant at levels 1 and 2 (both \(p<0.05\)). Furthermore, at level 1, differences were assessed between the fixed diameter of the tube graft and the diameter of the native ascending aorta. At the other 2 levels no significant differences in diameter were observed.

No significant difference in distensibility between patients with and without ARR was
Table 2  Aortic diameters and aortic elasticity patients with Marfan syndrome with and without aortic root replacement.

<table>
<thead>
<tr>
<th></th>
<th>Nonoperated patients (n=78)</th>
<th>Operated patients (n=39)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>30.9 ± 3.2</td>
<td>29.5 ± 4.0†</td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>Level 2</td>
<td>23.3 ± 2.3</td>
<td>24.4 ± 2.6</td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>Level 3</td>
<td>20.3 ± 2.6</td>
<td>21.0 ± 4.0</td>
<td>ns</td>
</tr>
<tr>
<td>Level 4</td>
<td>18.2 ± 3.4</td>
<td>17.9 ± 3.9</td>
<td>ns</td>
</tr>
<tr>
<td>Distensibility (10³ mmHg⁻¹)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>3.0 ± 2.6</td>
<td>2.0 ± 0.8†</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Level 2</td>
<td>3.4 ± 1.9</td>
<td>3.4 ± 2.0</td>
<td>ns</td>
</tr>
<tr>
<td>Level 3</td>
<td>5.1 ± 2.0</td>
<td>5.5 ± 2.4</td>
<td>ns</td>
</tr>
<tr>
<td>Level 4</td>
<td>3.8 ± 2.2</td>
<td>4.4 ± 2.2</td>
<td>ns</td>
</tr>
<tr>
<td>Flow wave velocity (m/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 1-2</td>
<td>4.4 ± 1.1</td>
<td>4.8 ± 1.5</td>
<td>ns</td>
</tr>
<tr>
<td>Level 2-3</td>
<td>6.7 ± 2.2</td>
<td>6.6 ± 2.8</td>
<td>ns</td>
</tr>
<tr>
<td>Level 3-4</td>
<td>5.5 ± 1.5</td>
<td>5.5 ± 2.4</td>
<td>ns</td>
</tr>
<tr>
<td>Level 1-4</td>
<td>5.2 ± 0.8</td>
<td>5.2 ± 1.3</td>
<td>ns</td>
</tr>
</tbody>
</table>

* Difference significant. Values are expressed as mean value (SD).
† Assessed in the graft. ns = not significant.

shown at all native aortic levels (Table 2). Distensibility in the tube graft (level 1) was significantly lower than ascending aortic distensibility in patients without ARR. No significant differences in FWV between patients with and without ARR were demonstrated (Table 2 and Figure 2).

In patients with Marfan syndrome with ARR, a positive correlation between age and FWV in both the aortic arch (r = 0.61) and the entire aorta (r = 0.68) was observed (Figure 3). Correlation in the descending thoracic aorta and abdominal aorta was r = 0.52 and r = 0.26, respectively. In patients with Marfan syndrome without ARR no correlation between age and FWV was observed.

![Figure 2](image)

Difference in flow wave velocity assessed in the aortic arch (FWV 1-2) between patients with Marfan syndrome with and without an aortic root replacement.
Figure 3 Graphs showing the linear correlation between age and flow wave velocity in the aortic arch (A), and the entire aorta (B). The 95% confidence limits of the true regression line are indicated with dashed lines.

Discussion

In the present study we used MR imaging to compare aortic elasticity of patients with Marfan syndrome with elective ARR with aortic elasticity of patients with Marfan syndrome who did not undergo surgery. We demonstrated no significant differences in aortic elasticity between patients with Marfan syndrome with and without ARR. Furthermore, a positive correlation between age and flow wave was shown only in patients who underwent surgery. To our knowledge, this is the first study on aortic elasticity in patients with Marfan syndrome after elective root replacement.

Noninvasive techniques such as echocardiography and MRI have been used to determine aortic elasticity. In previous studies, MRI has proved to be a very accurate technique to detect abnormal aortic elasticity, with good interobserver and intraobserver reproducibility (differences < 5.5 %). Aortic elasticity of the 78 patients with Marfan syndrome who did not undergo surgery was decreased compared with matched controls, as has been previously reported. Also in patients with Marfan syndrome with elective ARR, aortic elasticity was decreased. This underscores the finding that patients with Marfan syndrome after ARR are at considerable higher risk of dissection and recurrent aneurysms than patients with another etiology of aortic disease. The most significant predictor of subsequent vascular complications is aortic dissection, acute or chronic, present at the time of initial operation. Finkbohner et al. demonstrated no difference in incidence of aneurysm or dissection in the thoraco-abdominal aorta between electively operated and non-operated patients with Marfan syndrome during a follow-up period of > 25
years\textsuperscript{12}. This is in agreement with our findings of comparable aortic elasticity in non-operated and electively operated patients, suggesting that patients after an elective ARR may not be at higher risk for aortic complications in the residual aorta than non-operated patients.

In patients with ARR, a positive correlation was found between age and FWV in both the aortic arch and entire aorta. In the descending thoracic and abdominal aorta this correlation was lower, which was also observed in a recent study by Rogers et al.\textsuperscript{14}. Age is an important determinant of arterial elasticity and it is generally accepted that arterial elasticity tends to decrease with age\textsuperscript{14,15,16,17}.

In conclusion, MR imaging enables the assessment of aortic elasticity in patients with Marfan syndrome with elective aortic root replacement. Aortic elasticity between patients with Marfan syndrome with and without aortic root replacement did not show any differences.
References


