Anatomical and functional evaluation of the cardiovascular system in Marfan syndrome
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CHAPTER
Magnetic resonance imaging of the main pulmonary artery: reliable assessment of dimensions in Marfan patients on a simple axial spin echo image

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Abstract

Objective:
To investigate if a simple axial spin echo (SE) image can be used for reliable assessment of pulmonary artery dimensions in patients with Marfan syndrome.

Methods:
Fifty Marfan patients (mean age 33 ± (10 years; 34 men, 16 women) and 15 normal subjects (mean age 28 ± 4 years; 9 men, 6 women) underwent cardiac magnetic resonance imaging (MRI). Pulmonary artery dimensions were obtained on axial spin echo images at two different levels: 1) the level of the pulmonary artery root, and 2) the level of the pulmonary artery bifurcation. To evaluate the accuracy of axial plane measurements 10 Marfan patients also underwent contrast enhanced MR angiography (CE-MRA).

Results:
In the 10 Marfan patients who also underwent CE-MRA, the mean diameter at the pulmonary bifurcation assessed with CE-MRA (31.5 ± 3.6 mm) was almost equal to mean diameter assessed with axial SE (30.7 ± 3.6 mm). Agreement of methodology according to Bland and Altman analysis showed a 95% confidence interval ranging from -2.6 to +4.4 mm for all distances of the pulmonary artery root. In Marfan patients the mean right-left diameter measured on both axial SE images and CE-MRA was approximately 2.5 mm larger than the anterior-right and anterior-left diameters (p<0.001).

Conclusions:
Axial SE MR imaging is a reliable and easy acquisition to measure pulmonary artery dimensions in patients with Marfan syndrome, and could be used for follow-up, especially in patients with severe involvement of the cardiovascular system. Not only the pulmonary artery trunk but also the asymmetric pulmonary root should be measured, although the clinical relevance of the asymmetric root is not yet known.
Introduction

The Marfan syndrome is an autosomal dominant inherited disorder of connective tissue with variable manifestations in primarily skeletal, ocular and cardiovascular organ systems. Diagnosis is based on a combination of major and minor clinical features classified in 1986 (Berlin nosology) and revised by an experts' consensus (Ghent nosology 1996). Although dilatation of the main pulmonary artery is a criterion for establishing diagnosis, until recently little was known about the pulmonary artery in Marfan syndrome. Since normal values for the pulmonary artery diameter were not available at that time, it was advised in the Ghent criteria to detect dilatation provisionally by echocardiography, computed tomography (CT) or magnetic resonance imaging (MRI) using nomograms for the aorta.

Normal values for pulmonary artery bifurcation have been assessed from axial scans in a small number of patients. In a very recent study, it was shown that in normal subjects, as well as in Marfan patients, dimensions measured at the pulmonary artery root were significantly larger than dimensions measured at the pulmonary artery bifurcation on axial SE MR images. In that study, it was also shown that Marfan patients had significantly larger pulmonary artery dimensions than normal subjects.

Simple assessment of pulmonary artery diameters is useful in individuals who are referred for screening on the Marfan syndrome and for follow-up of Marfan patients. With the increased survival of patients with aortic complications, pulmonary artery dilatation might become of clinical relevance in the future.

The aim of the present study was to investigate if a simple axial spin echo (SE) image can be used for reliable assessment of pulmonary artery dimensions in patients with Marfan syndrome.

Methods

Study population

Fifty consecutive Marfan patients (mean age 33 ± 10 years; 34 men, 16 women) underwent routine cardiac MR imaging in the Academic Medical Center, Amsterdam and the University Medical Center St Radboud, Nijmegen. Diagnosis of Marfan syndrome had been established according to the Ghent Criteria. Thirty-five patients had undergone an aortic root replacement. Pulmonary artery dilatation had not been previously diagnosed in any of the patients with Marfan syndrome, nor did they have a history of left-right shunt, pulmonary arterial hypertension, or pulmonary or tricuspid valvular regurgitation.

The normal group consisted of 15 age-and-sex matched healthy subjects (mean age 28 ±
4 years; 9 men, 6 women). The study was approved by the local ethical committee and individual oral and written informed consent was obtained in each patient.

**Magnetic resonance imaging and analysis**

Imaging was performed on a Siemens Magnetom Vision 1.5 Tesla MR system (Siemens Medical Systems, Erlangen, Germany). The aorta was imaged in axial and oblique sagittal planes using a standard ECG-gated T1-weighted spin echo (SE) sequence. Repetition time equalled the R-R interval, echo time was 12 ms, imaging matrix was 256 x 256, field of view 350 mm, slice thickness was 6-8 mm and there was a slice gap depending on patient size with a maximum of 0.5 mm. Typical acquisition time was 4-5 minutes depending on the R-R interval. Additional conventional breath-hold contrast-enhanced-3D gradient-echo MR angiography (CE-MRA) was performed in 10 patients. Repetition time was 4.60 ms, echo time 1.80 ms, flip angle 20°, imaging matrix was 512 x 512, field of view 500 mm and there was no slice gap.

For analysis the MR imaging software tool MASS® (Medis, Leiden, The Netherlands) was used. Two trained observers who reached a consensus on each measurement performed all measurements.

**Measurement of main pulmonary artery and accuracy of measurements**

Main pulmonary artery dimensions were assessed on axial SE images at two levels: 1) the level of the pulmonary artery root, and 2) the level of the pulmonary artery bifurcation. The region of the ascending aorta and pulmonary artery was magnified to full screen size. Pulmonary sinuses were named by their relationship to the aortic valve: right, left and anterior (nonseptal)12. Three distances were obtained from the inner contours of the pulmonary artery root according to the aortic root measurements by Meijboom et al.13: 1) from the anterior to the right sinus, 2) from the anterior to the left sinus, and 3) from the right to the left sinus. Figure 1 shows a representative image demonstrating the two levels at which the main pulmonary artery was measured.

To evaluate the accuracy of axial plane measurements, in 10 patients who also underwent CE-MRA, the pulmonary artery was reconstructed double oblique using multi planar reconstruction (Figure 2). The pulmonary root was measured in the three defined directions. The pulmonary artery bifurcation diameter was assessed perpendicular to the pulmonary trunk just proximal to the bifurcation. To assess partial volume effects on axial SE images, correlation between angle of the pulmonary root in the coronal and sagittal plane and the distances measured on axial planes were investigated.
Figure 1 Levels of measurement on axial SE planes in a Marfan patient: (A – D) is from cranial to caudal: (B) main pulmonary artery diameter measurement at the level of pulmonary artery bifurcation, (D) pulmonary artery root measurements: anterior-right diameter, anterior-left diameter and right-left diameter.

Figure 2 CE-MRA of the pulmonary artery. (A): Level of the main pulmonary artery diameter measurement at the level of pulmonary artery bifurcation. (B): image used for multiplanar reconstruction. C: image perpendicular to the pulmonary artery root. Ant.= anterior.

Statistics
Data are given as mean ± SD. Differences between the groups were assessed by the unpaired Student’s t test. The 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

All main pulmonary artery dimensions measured on axial SE planes in normal subjects and Marfan patients are shown in Figure 3.

In the 10 Marfan patients who also underwent CE-MRA, the mean diameter at the pulmonary bifurcation assessed with CE-MRA (31.5 ± 3.6 mm) was almost equal to mean diameter assessed with axial SE (30.7 ± 3.6 mm). Agreement of methodology according to Bland and Altman analysis showed a 95% confidence interval ranging from –2.6 to +4.4 mm for all distances of the pulmonary artery root (Figure 4).

The mean angle of the pulmonary artery root measured on oblique sagittal planes was 33 degrees (range 20 - 42) and was not different in normal subjects and Marfan patients. No correlation between this angle and the difference between anterior-right and right-left diameter was found. The angle measured on coronal planes was minimal and never exceeded six degrees.
In contrast to normal subjects in whom the three diameters of the pulmonary artery root were not different, in Marfan patients the mean right-left diameter measured on both axial SE images and CE-MRA was approximately 2.5 mm larger than the anterior-right and anterior-left diameters (p<0.001) (Figure 3). The anterior-right diameter appeared to be the direction that, measured on both axial SE images and CE-MRA, showed the smallest difference and the smallest variability between the two MR sequences compared to the anterior-left and right-left diameters (Figure 5).

A good correlation was found between pulmonary artery and aortic root diameter in non-operated Marfan patients (Figure 6).

**Figure 5**
Difference between pulmonary artery root measurements on MRA and on axial SE plane for the three directions. Boxes extend from the 25th to the 75th percentile, with a horizontal line at the median (50th percentile). Whiskers extend down to the smallest value and up to the largest.

**Figure 6**
Correlation between pulmonary artery root diameter and aortic root diameter in 15 non-operated Marfan patients.

**Discussion**
In the present study it was shown that diameters measured on axial SE images were not significantly different from diameters measured after double-oblique reconstruction on CE-MRA at both the pulmonary artery root and bifurcation. It was also shown that in Marfan patients the mean right-left diameter of the pulmonary artery root measured on both axial SE images and CE-MRA was approximately 2.5 mm larger than the anterior-right and anterior-left diameters.
Comparing imaging methods
The available methods to image the pulmonary arteries include color-Doppler-echocardiography, pulmonary angiography, CT and MR imaging. In this study we compared SE with CE-MRA for several reasons. Color-Doppler-echocardiography is limited by only being able to depict the intramediastinal course of the vessels\textsuperscript{14}. Pulmonary angiography was thought to be the “gold standard” for the measurement of pulmonary artery. However its invasive nature carries a small risk of morbidity and mortality\textsuperscript{15,16}. Compared with both CT and pulmonary angiography, CE-MRA is a noninvasive imaging technique for assessing great vessels and pulmonary vessels without the need for ionizing radiation or iodinated contrast material\textsuperscript{17,18}.

Accuracy of measurements
Diameters of the pulmonary artery measured at both levels corresponded very well between the two methods (SE and CE-MRA). Although the axial SE images were not perpendicular to the pulmonary root and partial volume effects could be expected, these effects did not influence the accuracy of measurement, since no significant correlation between angles of the pulmonary root measured in the oblique sagittal plane and difference between diameters was found.

Measurement of main pulmonary artery
In Marfan patients the mean right-left diameter measured on both axial SE images and CE-MRA images was approximately 2.5 mm larger than the anterior-right and anterior-left diameters (p<0.001). Asymmetry of the main pulmonary artery, observed in this study, has also been described by Sloth et al., as it has been shown for the aortic root by various authors\textsuperscript{13,19,20}. Further follow-up studies are needed to examine the clinical significance of the asymmetric pulmonary root.

Pulmonary artery dilatation and aneurysms are rare pathologic conditions that may be caused by congenital heart disease, infection, pulmonary hypertension and are occasionally idiopathic\textsuperscript{21-26}. In 1947 Deterling et al. reviewed 109.571 autopsy studies and concluded that only eight cases of pulmonary artery aneurysms had been documented\textsuperscript{27}. Until now, only two cases of pulmonary artery dissection in Marfan syndrome have been reported\textsuperscript{28,29}. One case report of pulmonary artery dissection in bovine Marfan syndrome has been described\textsuperscript{30}.

A uniform approach for pulmonary aneurysm is not yet available, because little is known
about natural history and long-term outcome following medical or surgical treatment. Some investigators argue that surgical repair is recommended when an aneurysm is discovered\textsuperscript{31,32}. Others believe that surgery should only be considered for large aneurysms if the patient has an acceptably low operative risk\textsuperscript{22}.

In a recent study it was suggested that dilatation of the pulmonary root increased with progressive involvement of the cardiovascular system in Marfan patients. Although main pulmonary artery aneurysm and dissection have been reported only rarely in the past, they could become of more clinical relevance in the near future because of increased longevity in Marfan patients\textsuperscript{11}.

Conclusions

Axial SE MR imaging is a simple and reliable acquisition method to measure pulmonary artery dimensions in patients with Marfan syndrome, and could be used for follow-up, especially in patients with severe involvement of the cardiovascular system. Not only the pulmonary artery trunk, but also the asymmetric pulmonary root should be measured, although the clinical relevance of the asymmetric root is not yet known.
References