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Assessment of aortic root dimensions in patients with suspected Marfan syndrome: Intraindividual comparison of contrast-enhanced and non-contrast magnetic resonance angiography with echocardiography

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ABSTRACT

Purpose: Our purpose was to evaluate intraindividually the performance of contrast-enhanced magnetic resonance angiography (MRA) and non-contrast MRA for aortic root diameter measurements and to compare the results with routinely performed echocardiography in patients with suspected Marfan syndrome.

Methods and materials: Aortic roots were examined prospectively in 51 consecutive patients with suspected Marfan syndrome by using contrast-enhanced MRA and non-contrast MRA at 1.5 T. Two readers independently measured aortic root diameters at the annulus, sinuses of Valsalva and sinutubular junction in both data sets and compared results with echocardiographic data. Intraclass correlation coefficient, Pearson correlation coefficient, Bland–Altman, and two-sided t-test were used to assess agreement between observers and methods.

Results: 38 (74.5%) of the 51 patients (25 female, 26 male; mean age 37.1 ± 13.7 years) had Marfan syndrome. Both, contrast-enhanced MRA and non-contrast MRA measurements of the sinuses of Valsalva revealed a strong correlation with echocardiography ($r = 0.850$ and $r = 0.893$, respectively). Intraclass correlation was markedly better for non-enhanced MRA ($r = 0.904$) when compared to contrast-enhanced MRA ($r = 0.690$). Image quality ($p < 0.001$) as well as interobserver agreement ($p < 0.0042$) of measurements of the sinuses of Valsalva was significantly better for non-enhanced MRA than for contrast-enhanced MRA.

Conclusion: Non-contrast MRA was more reliable and more valid than contrast-enhanced MRA for assessment of aortic root dimensions in patients with suspected Marfan syndrome. Therefore contrast agents can be omitted for establishing the diagnosis of aortic involvement in Marfan syndrome.

1. Introduction

Marfan syndrome is a hereditable disorder of connective tissue that causes several distinct cardiovascular abnormalities, including aortic regurgitation, dissection, and aneurysm [1]. The prevalence of Marfan syndrome ranges between 1 and 2 in 10,000 [2]. It is the most common syndromic presentation of ascending aortic aneurysm with a high risk of aortic dissection, rupture and pericardial tamponade [1,2]. Current therapy for the cardiovascular complications of Marfan syndrome consists of medical management in order to slow down the rate of aortic root dilatation, and surgery to prevent dissection when the aortic root reaches a diameter of 4.5 cm or is growing at a rate of more than 0.5 cm per year [1–5].

A reliable, accurate, reproducible and operator-independent imaging technique for assessing the exact diameter of the aortic root, specifically at the level of the sinuses of Valsalva is needed to improve the selection of candidates for elective operation [3,5]. Longitudinal progression of aortic root dilatation and appropriate timing for surgery are usually derived from serial non-invasive imaging studies [3]. An ideal imaging modality will rapidly and precisely detect aneurysm formation and progression. Of the non-invasive imaging methods, echocardiography, computed tomography (CT), and magnetic resonance imaging (MRI) have become diagnostic options [3]. However, echocardiography has limited value for evaluation of the entire aorta and an experienced operator is needed for image acquisition and interpretation [3]. CT has the advantage of rapid image acquisition but the disadvantage of ionizing radiation and the use of iodinated contrast, which is especially of concern in young patients and patients subject to serial imaging [3,6,7].

Magnetic resonance angiography (MRA) has developed from a complementary to a competing imaging modality for the thoracic aorta [8,9]. With neither ionizing radiation nor iodinated contrast

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required, MRA is ideal for patients with contrast allergies or patients with multiple follow-up scans, such as patients with Marfan syndrome. Until recently, contrast-enhanced MRA was considered ideal in renal failure. However, discovery of nephrogenic systemic fibrosis (NSF) in patients with renal dysfunction receiving gadolinium has renewed the interest in non-contrast MRA [10–12]. Previous studies have compared the image quality of non-contrast MRA and contrast-enhanced MRA for imaging of the thoracic aorta and concluded that non-contrast MRA achieves diagnostic image quality of the thoracic aorta [10,13]. However, these studies comprised only small and unselected study populations and were of retrospective nature [14,15]. Neither of the previously performed studies focused on patients with known or suspected Marfan syndrome nor assessed intraobserver and interobserver variability when comparing non-contrast MRA and contrast-enhanced MRA at the level of the aortic root. More importantly, none of the studies compared the diameters obtained by MRA with results from echocardiography to assess whether these imaging modalities can be used comparatively for aortic root dimensions.

To our knowledge, non-contrast MRA has not yet been used for aortic root measurements at all three recommended aortic root levels (annulus, sinuses of valsalva, sinutubular junction) in a larger series of selected patients with suspected Marfan syndrome to assess the reproducibility of this imaging technique. The main focus of our study was the exact assessment of the diameter at the level of the sinuses of Valsalva, since this diameter is critical in clinical practice for the indication of surgical aortic root replacement [1,2,5]. We compared intraobserver and interobserver agreement of measurements of aortic root diameters assessed with non-contrast MRA and contrast-enhanced MRA and compared the results with routinely performed echocardiography. The purpose of our prospective study was to determine the most reproducible MRA technique for screening patients with suspected Marfan syndrome and for follow-up of patients with known Marfan syndrome.

2. Materials and methods

2.1. Study collective

The prospective study was approved by the local ethics committee, and all patients provided written informed consent. 54 consecutive patients suspected with Marfan syndrome were included between November 2009 and January 2011. Marfan syndrome was established with the criteria of the current Ghent-2 nosology with sequencing of the FBN1 gene in all individuals [16,17]. All 54 patients underwent the routine echocardiographic examination, which is included in the standard clinical protocol for patients with known or suspected Marfan syndrome in our Universitary Marfan Centre. All 54 included patients were in stable clinical conditions and underwent an MR-examination of the thoracic aorta the same day of the echocardiographic examination. Indications for study inclusion compromised suspected or known Marfan syndrome. Patients were excluded from the study if they had contraindications to MR imaging such as implanted pacemakers or severe claustrophobia.

2.2. MR imaging

MR imaging was performed using a 1.5 T scanner (Magnetom Symphony, Siemens, Erlangen, Germany) Software VA30 with a four-element phased array coil. Before positioning the patient inside the magnetic bore, a 20-gage cannula was placed into an antecubital vein and connected to a power injector via an extendable tube. For cardiac triggering ECG-leads were placed in a standardized manner. At the beginning of every examination, scout images were performed in axial, coronal and sagittal orientation.

2.3. Non-contrast 3D MRA

A 3D steady-state free precision (SSFP) sequence was used for non-contrast MRA. Image acquisition was triggered to the end-diastolic phase of the cardiac cycle to minimize cardiac motion artifacts. The FOV was selected to cover the thoracic aorta and source images were obtained in para-sagittal orientation. A free-breathing, navigator-gated acquisition scheme was used to minimize respiratory motion artifacts [10]. A 5-mm respiratory gating window was implemented, which tracked the stable respiratory phase throughout the scan. Imaging parameters for the 3D SSFP sequence were chosen as follows: TR/TE: 140/2.4 ms; flip angle: 20°; FOV: 400 × 262 mm; acquisition matrix, 384 × 252; pixel size: 1.1 × 1.1 mm; slice thickness: 1.5 mm; number of slices: 36; acquisition time: 8.3 ± 2.4 min (depending on patient's heart rate and breathing frequency).

2.4. Contrast-enhanced 3D MRA

A 3D contrast-enhanced MRA of the thoracic aorta was performed after automatic injection (2 ml/s) of gadobenate dimeglumine (MultiHance, Bracco, Singen, Germany) at a dose of 0.1 mmol/kg bodyweight using a para-sagittal gradient-echo T1-weighted sequence: TR/TE, 3.6/1.3 ms; flip angle, 25°; FOV, 470 × 382 mm; matrix, 512 × 424; pixel size 0.9 × 0.9 mm; slice thickness, 1.3 mm; number of slices, 36. In order to determine scan delay and to optimize contrast bolus timing, a 2-ml test bolus was used. Imaging was started at the time of contrast material arrival in the descending aorta and patients were asked to hold their breath in expiration. Two post-contrast datasets were acquired with a 10-second respiration interval.

2.5. MR image evaluation

Anonymized images of non-contrast MRA and contrast-enhanced MRA examinations were presented to two radiologists, P.B (4 years of experience) and M. G. (5 years of experience) in random order. For measurements taken by MR imaging, the external diameter of the aorta was measured perpendicular to the blood flow [3]. For detailed evaluation of aortic root diameters, three independent measurements of the aortic annulus, sinuses of valsalva and sinutubular junction [3] were performed in each patient using either non-contrast MRA images or contrast-enhanced MRA source images in para-sagittal orientation as displayed in Fig. 1. For assessment of intraobserver agreement, two measurements were performed by P.B., with an interval of 4 weeks between the first and second measurement. For assessment of interobserver agreement, a third measurement was performed by M.G. For detailed evaluation of image quality, the aortic root was evaluated in consensus by both radiologists according to a 3-point-scale regarding the visibility, sharpness of the aortic root and presence and severity of motion artifacts: 3 = excellent image quality; 2 = moderate image quality; 1 = poor image quality. A standard window level was applied for all measurements and image quality evaluation.

2.6. Echocardiographic examination

All patients underwent a comprehensive routine 2D-transthoracic echocardiographic examination, which was performed by an experienced cardiologists, either by M.R (10 years of experience) or by S.S. (6 years of experience). Echocardiography was performed with a commercially available ultrasound system (Sonos 2000, Hewlett Packard, Andover, MA, USA). Wall thickness, left ventricular end-diastolic diameter and end-systolic diameter, left atrial diameter, left ventricular ejection fraction, left ventricular mass, and classic mitral valve prolapse were routinely assessed on 2D images. Aortic root diameters were determined at the level of the aortic annulus, sinuses of Valsalva and sinutubular junction [18].

2.7. Statistical analysis

Intraclass correlation coefficient was calculated to investigate intraobserver and interobserver agreement between measurements obtained from non-contrast MRA and contrast-enhanced MRA data sets. Bland–Altman analysis was used to assess intra- and interobserver agreement between measurements obtained from 3D SSFP and contrast-enhanced MRA. A two-sided t-test was performed for comparison of mean differences and F-test for comparison of variances. Comparisons of image quality of the aortic root using 3D SSFP and contrast-enhanced MRA were performed using the Wilcoxon matched-pair test.

Pearson's correlation was calculated to determine the correlation between diameters assessed by reading 3D SSFP or contrast-enhanced MRA and diameters assessed by echocardiography. Correlation coefficients greater than 0.8 indicated a strong correlation. Coefficients ranging from 0.5 to 0.8 indicated a moderate correlation whereas coefficients ranging from 0.3 to 0.49 indicated a weak correlation and coefficients smaller than 0.3 were interpreted as an almost nonexistent correlation. Bland–Altman analysis was used to assess agreement between measurements obtained from 3D SSFP and contrast-enhanced MRA data sets versus measurements obtained from echocardiography. A two-sided paired t-test was used to determine if there was a significant difference between the measurements obtained from the non-contrast MRA or contrast-enhanced MRA-sequence and measurements obtained from echocardiography. $P < 0.05$ indicated statistical significance. Statistical analysis was performed using commercially available software (MedCalc for Windows, Mariakerke, Belgium and Excel, Microsoft Corporation, Redmond WA USA). Data are presented as means ± standard deviations.

3. Results

3.1. Patients

Non-contrast MRA and contrast-enhanced MRA examinations were performed successfully in 51 patients (25 female, 26 male; mean age, 37.1 ± 13.7 years) (94.4%) of the initially included 54