Kawasaki’s Disease and Coronary Abnormalities

Magnetic Resonance Angiography Is Equivalent to X-Ray Coronary Angiography for the Evaluation of Coronary Arteries in Kawasaki Disease

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OBJECTIVES
The purpose of this study was to compare the results of magnetic resonance angiography (MRA) with X-ray coronary angiography (XCA) in a pediatric population.

BACKGROUND
Coronary artery abnormalities in Kawasaki disease (KD) develop in about 15% to 25% of young patients, mostly in the form of aneurysms.

METHODS
Thirteen patients (12 male), age three to eight years, were studied. The maximal diameter and length of the aneurysm were recorded. Coronary MRA was performed using a 1.5 T Philips Intera CV magnetic resonance scanner with an electrocardiographically triggered pulse sequence. It was a three-dimensional segmented k-space gradient-echo sequence (TE = 2.1 ms, TR = 7.5 ms, flip angle = 30°, slice thickness = 1.5 mm) employing a T2-weighted preparation pre-pulse and a frequency selective fat-saturation pre-pulse. Data acquisition was performed in mid-diastole. All scans were carried out with the patient free breathing using a two-dimensional real-time navigator beam. All patients underwent XCA within a week.

RESULTS
In six patients, aneurysms of the coronary arteries were identified, while coronary ectasia alone was present in the remaining seven patients. Magnetic resonance angiography and XCA diagnosis of coronary artery aneurysm agreed completely. Maximal aneurysm diameter and length and ectasia diameter by MRA and XCA were similar. No stenotic lesion was identified by either technique.

CONCLUSIONS
In conclusion, MRA is a reliable diagnostic tool, equivalent to XCA for coronary artery aneurysm identification in patients with KD. Magnetic resonance angiography may prove to be of great value for the serial non-invasive evaluation of these patients. (J Am Coll Cardiol 2004;43:649–52) © 2004 by the American College of Cardiology Foundation

Kawasaki disease (KD) is an acute vasculitis of unknown etiology usually occurring in children younger than five years of age. Infants and children may show myocarditis and/or pericarditis with coronary artery aneurysms (CAAs) developing in approximately 15% to 25% of untreated cases (1,2) that cause both short- and long-term morbidity and mortality (3). Approximately half of the children with coronary aneurysms during the acute phase of the disease have normal-appearing vessels by angiography one to two years later (4). Coronary artery aneurysms may rupture, thrombose, or develop stenotic lesions. Serial evaluation of size and location of CAAs is necessary for further treatment. Transthoracic echocardiography is usually sufficient for this purpose in children, but it is deficient in adolescents (5).

Noninvasive coronary magnetic resonance angiography (MRA) has been successfully used in the diagnosis of anomalous origin of the coronaries (6), coronary artery disease (7), and bypass graft evaluation (8). The purpose of this study was to compare the results of coronary MRA with those of X-ray coronary angiography (XCA) in a pediatric population with KD.

METHODS

Patient population. Thirteen patients (12 males), age three to eight years, were included in the study. All were referred for diagnostic coronary angiography for the evaluation of KD. Patients were ineligible for enrollment if they had a known contraindication for magnetic resonance imaging. Patients’ families gave informed consent, and the study was approved by the local ethics committee.

All patients underwent XCA, which confirmed CAA or ectasia. After XCA, coronary MRA was performed. The mean interval between the two examinations was 25 days (range: 5 to 60). Both XCA and MRA were completed without complications, while no clinical events were manifested between the two examinations. The imaging protocols were accomplished without the use of nitrates.

XCA. X-ray contrast enhanced coronary angiography was performed using a transfemoral arterial approach. Quantitative information was provided by an experienced investigator who was blinded to the MRA results. The selected end-diastolic frames were magnified, digitized, and analyzed off-line with the QCA imaging system.
(CMS, MEDIS, Leiden, The Netherlands). Automatic contour detection was performed with the geometric edge-differentiation technique according to a previously validated method (9).

MRA. Coronary MRA was performed using a 1.5 T Philips Intera CV MR scanner (Philips Medical Systems, Best, The Netherlands). A commercial, five-element, cardiac phased array receiver coil was used for signal acquisition. All patients were examined with four electrocardiographic (ECG) electrodes (10) on the anterior left hemithorax and during free breathing. Sedation was used in 5 of 13 patients. Propofol 2 to 3 mg/kg was given intravenously for sedation. Heart rate was increased 8% to 10% from baseline. All patients were free breathing, and to compensate for respiratory motion artifacts, a prospective two-dimensional real-time navigator beam was properly placed on the patients’ right hemidiaphragm for slice tracking and end-expiratory gating (11). The R wave of the ECG was used as a trigger for data acquisition, and all images were acquired in mid-diastole.

The “white blood” sequence used (12) was a three-dimensional, segmented k-space, gradient-echo sequence (TE = 2.1 ms, TR = 7.5 ms, flip angle = 30°, reconstructed slice thickness = 1.5 mm, in-plane image resolution = 0.7 mm × 1.0 mm) employing a T2-weighted preparation pre-pulse and a frequency selective fat-saturation pre-pulse. For the right coronary artery (RCA), a double oblique volume was imaged with use of the coordinates prescribed by a three-point planscan tool (13). For the left coronary artery system, a transverse volume was scanned centered on the origin of the left main coronary artery.

**Image analysis.** X-ray and MRA images were analyzed independently. For coronary MRA, semiautomatic multiplanar reformatting of the three-dimensional data was performed using a workstation (Easy Vision 4.0, Philips Medical Systems, Best, the Netherlands) by an investigator blinded to the X-ray results. X-ray measurements were calibrated to catheter size. Epicardial coronary arteries were assessed for the presence of aneurysms. A coronary aneurysm was diagnosed if the internal lumen diameter was >4.0 mm. A coronary artery ectasia was defined as a distension of a part of a coronary vessel of up to one and a half times the diameter of an adjacent normal segment (14). The intraobserver variability for minimal lumen diameter was 0.19 mm for the catheter studies (15) and 0.22 mm for the magnetic resonance imaging study.

**Statistical analysis.** All measurements were expressed as mean ± SD. Statistical significance of the differences between the examined methods was investigated with the paired Student t test. Correlation between XCA and MRA data was sought with Pearson’s correlation coefficient. Statistical significance was considered for p < 0.05. A Bland-Altman analysis was also used to assess the agreement between XCA and MRA methods. In Bland-Altman analysis, the difference (MRA - XCA) is plotted versus the mean (MRA + XCA)/2 for diameter and length measurements.

**RESULTS**

Magnetic resonance angiography measurements were obtained from all patients participating in this study, because good image quality was achieved for all ectatic or aneurysmatic segments examined. Total MR imaging time did not exceed 1 h for any of the patients. Navigator efficiency was

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**Abbreviations and Acronyms**

- CAA = coronary artery aneurysm
- ECG = electrocardiogram/electrocardiographic/electrocardiography
- KD = Kawasaki disease
- LAD = left anterior descending coronary artery
- MRA = magnetic resonance angiography
- RCA = right coronary artery
- XCA = X-ray coronary angiography

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**Figure 1.** Magnetic resonance angiography (A) and X-ray coronary angiography (B) image of a left anterior descending coronary artery aneurysm (LAD an) in a patient with Kawasaki disease. LV = left ventricle; R. Atrium = right atrium; RCA = right coronary artery.
in the range of 35% to 55%. Examples of a coronary MRA and a corresponding XCA in a patient with a left anterior descending coronary artery (LAD) aneurysm are shown in Figure 1.

The average lengths of continuously visualized left main coronary artery with LAD, left circumflex, and RCA by MRA were $4.8 \pm 0.8$, $3.2 \pm 1.0$ and $8.9 \pm 1.2$ cm, respectively.

In six patients, aneurysms of the coronary arteries were identified, while coronary ectasia alone was present in the remaining seven patients. Right coronary artery and LAD ectasia was present in one patient, while RCA and LAD aneurysms were also present in one patient. Both ectasia and aneurysm were present in one patient.

Magnetic resonance angiography and XCA diagnosis of coronary artery ectasia or aneurysm agreed completely. The distance of the lesions from the coronary ostia with MRA and XCA was not significantly different ($4.55 \pm 1.29$ mm, $p = NS$). Maximal aneurysm diameter and length and ectasia diameter by MRA and XCA were similar (Table 1). No stenotic lesion was identified by either technique. Slow flow or thrombi were not detected in any patient, because all of them were receiving anti-thrombotic treatment.

Comparison between measurements obtained with MRA and XCA, using a paired Student $t$ test, showed no statistically significant differences. A statistically significant correlation was observed between magnetic resonance angiography and X-ray coronary angiography measurements of vessel diameter and length.

### Table 1. Patients With Kawasaki Disease: MRA and XCA Measurements

<table>
<thead>
<tr>
<th>Patients</th>
<th>Lesions</th>
<th>MRA (mm)</th>
<th>XCA (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>RCA aneurysm</td>
<td>$14 \times 7.6$</td>
<td>$14.4 \times 7.8$</td>
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<td></td>
<td>LAD ectasia</td>
<td>$3.8$</td>
<td>$3.9$</td>
</tr>
<tr>
<td>Case 2</td>
<td>RCA aneurysm</td>
<td>$8.5 \times 5.7$</td>
<td>$8.6 \times 5.7$</td>
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<tr>
<td></td>
<td>LAD aneurysm</td>
<td>$13.3 \times 8.1$</td>
<td>$13.5 \times 8.2$</td>
</tr>
<tr>
<td>Case 3</td>
<td>LAD aneurysm</td>
<td>$16 \times 9$</td>
<td>$16.2 \times 9$</td>
</tr>
<tr>
<td>Case 4</td>
<td>RCA aneurysm</td>
<td>$7 \times 4$</td>
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<tr>
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<td>LAD aneurysm</td>
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<td>Case 5</td>
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<tr>
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<td>$3.9$</td>
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<td>Case 9</td>
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</tr>
<tr>
<td></td>
<td>LAD ectasia</td>
<td>$4.3$</td>
<td>$4.1$</td>
</tr>
</tbody>
</table>

LAD = left anterior descending coronary artery; MRA = magnetic resonance angiography; RCA = right coronary artery; XCA = X-ray coronary angiography.

Figure 2. (A) A statistically significant correlation was observed in patients with Kawasaki disease between magnetic resonance angiography (MRA) and X-ray coronary angiography (XRA) measurements of vessel diameter and length (Pearson coefficient $r = 0.99$, $p < 0.001$ for both diameter and length).
through Bland–Altman analysis, and the results are graphically illustrated in Figure 3. No systematic differences were observed for the two methods over the whole range of vessel diameter values encountered.

**DISCUSSION**

Our study evaluated the ability of coronary MRA to identify CAA and ectasia in KD using XCA as the reference standard. Magnetic resonance angiography accurately detected all lesions, and their dimensions agreed well with XCA results. No stenotic lesion was identified by either technique.

Kawasaki disease is the most common cause of acquired heart disease in children. The use of intravenous gamma globulin reduces the incidence of coronary lesions. However, coronary abnormalities in the form of aneurysms may still develop as the result of treatment failure or late diagnosis. Some of these children undergo coronary bypass operation (15). The dimensions of aneurysm play an important role in the development of coronary artery stenosis and myocardial ischemia. Moreover, slow blood flow in the ectatic coronary artery may be a causative factor for thrombosis (16). Aneurysm size also correlates with the risk of coronary thrombosis (17). Serial evaluation of aneurysm dimensions is essential to guide anti-thrombotic and patient follow-up.

To our knowledge, this is the largest series so far of pediatric patients with KD evaluated by both techniques. In early childhood, trans-thoracic echocardiography is adequate to visualize the coronaries. As children grow, follow-up is hampered by the need for serial coronary angiography, which is an invasive procedure. Magnetic resonance angiography has been successfully used for the detection of aneurysms in KD (18,19).

In our experience, MRA was feasible in all patients studied and was safely accomplished without any complications. Quality of the images was good enough to permit dimension measurements for comparison with X-ray angiography. There was good agreement between the two techniques for the measurement of ectasia and aneurysm dimensions, and Bland-Altman analysis showed no over- or under-estimation over the whole range of aneurysm diameter and length values encountered in this study.

Cardiovascular magnetic resonance imaging is a fast-evolving field. The addition of flow quantification using magnetic resonance imaging will provide functional information about the flow in ectatic or aneurysmatic coronary arteries (20). Furthermore, the use of spiral MRA may improve the resolution and shorten the acquisition time, with excellent sensitivity and specificity compared with X-ray angiography (21).

Consequently, MRA appears promising for the non-invasive evaluation and serial follow-up of patients with KD.

**REFERENCES**