Coronary Artery Imaging in Grown Up Congenital Heart Disease
Complementary Role of Magnetic Resonance and X-Ray Coronary Angiography

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Background—There is a high incidence of anomalous coronary arteries in subjects with congenital heart disease. These abnormalities can be responsible for myocardial ischemia and sudden death or be damaged during surgical intervention. It can be difficult to define the proximal course of anomalous coronary arteries with the use of conventional x-ray coronary angiography. Magnetic resonance coronary angiography (MRCA) has been shown to be useful in the assessment of the 3-dimensional relationship between the coronary arteries and the great vessels in subjects with normal cardiac morphology but has not been used in patients with congenital heart disease.

Methods and Results—Twenty-five adults with various congenital heart abnormalities were studied. X-ray coronary angiography and respiratory-gated MRCA were performed in all subjects. Coronary artery origin and proximal course were assessed for each imaging modality by separate, blinded investigators. Images were then compared, and a consensus diagnosis was reached. With the consensus readings for both magnetic resonance and x-ray coronary angiography, it was possible to identify the origin and course of the proximal coronary arteries in all 25 subjects: 16 with coronary anomalies and 9 with normal coronary arteries. Respiratory-gated MRCA had an accuracy of 92%, a sensitivity of 88%, and a specificity of 100% for the detection of abnormal coronary arteries. The MRCA results were more likely to agree with the consensus for definition of the proximal course of the coronary arteries (P<0.02).

Conclusions—For the assessment of anomalous coronary artery anatomy in patients with congenital heart disease, the use of the combination of MRCA with x-ray coronary angiography improves the definition of the proximal coronary artery course. MRCA provides correct spatial relationships, whereas x-ray angiography provides a view of the entire coronary length and its peripheral run-off. Furthermore, respiratory-gated MRCA can be performed without breath holding and with only limited subject cooperation. (Circulation. 2000;101:1670-1678.)

Key Words: magnetic resonance imaging ■ arteries ■ heart disease, congenital ■ angiography

The incidence of anomalous coronary arteries in patients with normal cardiac anatomy is ~0.3% to ~0.9%.1-4 It is important to identify coronary anomalies, because arteries that pass between the aorta and pulmonary artery (PA) may be associated with myocardial ischemia and sudden death.1-3 The identification of anomalous coronary arteries can be difficult with conventional x-ray angiography, because of the lack of 3-dimensional (3-D) information that relates the course of the coronary arteries to the great vessels.3,6 Recently, magnetic resonance (MR) coronary angiography (MRCA) was used to define anomalous coronary artery origins and proximal course. In several cases, the diagnosis made with the use of x-ray coronary angiography was changed with the use of information derived from MRCA.10-12 To date, all MRCA studies of anomalous coronary arteries have been performed on patients with otherwise normal cardiac morphology.

In patients with congenital heart disease, the identification of anomalous coronary arteries may be important for several reasons. First, there is a higher incidence of anomalous coronary arteries in patients with congenital heart disease (3% to 36%).13,14 Second, patients with congenital heart disease often undergo operative procedures, and detailed information regarding coronary anatomy is necessary to avoid damage to the arteries. In particular, in patients with tetralogy of Fallot, an anomalous artery or a large conus branch may pass over the right ventricular outflow tract and may be severed during ventriculotomy.15,16 Finally, identification of the relationship of the coronary arteries to abnor-
mally related great vessels with the use of x-ray angiography is more difficult than it is for normal cardiac anatomy, because the exact 3-D position of the aorta and PA may be difficult to determine.14,17

We performed a controlled, blinded comparative study in which we compared the use of x-ray angiography and MRCA for identification of the coronary artery origin and proximal course in adults with a variety of congenital heart abnormalities.

Methods
Study Protocol
The study included 25 subjects with congenital heart disease (mean age 38±11 years). Subjects were selected after x-ray coronary angiography, and their conditions included a variety of congenital heart diseases, with both normal and abnormal coronary anatomy, as defined with x-ray coronary angiography (Table). Eighteen consecutively patients with coronary artery anomalies admitted or seen in the Jane Somerville Grown Up Congenital Heart Unit were recruited, of which 16 underwent an MR study. Two patients did not undergo an MR study because of the presence of pacemakers. The patients with coronary anomalies were recruited consecutively, but the control subjects were selected nonconsecutively in an attempt to match subjects with normal and abnormal coronary anatomy and the same underlying congenital heart abnormality. The following congenital anomalies were included: tetralogy of Fallot (n=10), bicuspid aortic valve (n=3), tricuspid atresia (n=2), congenital mitral stenosis (n=2), congenital cardiomyopathy (n=2), congenitally corrected transposition of the great arteries (atrioventricular and ventriculoarterial discordance) (n=2), transposition of the great arteries (ventriculoarterial discordance) (n=1), ventricular septal defect (n=1), pulmonary atresia (n=1), and subaortic stenosis (n=1). Both subjects with mitral stenosis had controlled atrial fibrillation (subjects 10 and 22).

The MRCA investigators were blinded to all clinical details, including the patient name on the review images, except for the underlying congenital diagnosis. The MRCA investigators were also blinded to the x-ray angiography coronary anatomy diagnosis. All subjects had x-ray coronary angiography performed before MRCA. For 10 subjects, MRCA was performed within 3 days of x-ray angiography; for 11 subjects, MRCA was performed within 11 months of x-ray angiography; and for the remaining 4 subjects, MRCA were performed within 9 years of x-ray angiography. The Royal Brompton Hospital Ethical Committee approved the study, and all subjects gave informed consent.

Conventional X-Ray Coronary Angiography Procedure
Conventional x-ray coronary angiograms were performed as part of a clinically indicated assessment with an integrated digital cardiac catheter imaging system (Siemens). The majority of x-ray coronary angiograms were performed by 1 investigator (S.A.T., 18 subjects), and 2 investigators (S.A.T. and M.B.R.) reported all of the x-ray angiograms, in consensus. All subjects had selective coronary intubation, but in some subjects, aortic root injections were necessary to help locate the coronary origins. Both of the x-ray investigators were blinded to the MRCA results. A formal report was written for each subject that defined the coronary artery origin and proximal course.

MRCA Procedure
MRCA was performed with a Picker Edge 1.5-T scanner with a phased-array receiver coil (4 coils: 2 anterior and 2 posterior). Images were acquired during free respiration using an NE to monitor diaphragm motion during free respiration. A coronal pilot study was first performed to establish the correct position of the subject within the magnet and the correct position of the receiver coil on the subject. A set of transaxial pilot studies were then performed to identify the dome of the right hemidiaphragm. The NE column was placed on the dome of the right hemidiaphragm. The NE column was defined by the intersection of 2 orthogonal slice-selective 90° and 180° RF pulses, and an edge-detection algorithm was implemented to detect the diaphragm. The acquisition parameters for the NE pulse were 4-ms pulse duration, 512-mm field of view along the column length, 512 readout points, 10-ms data sampling time, column area 4 cm², and NE repeat time 500 ms. Once the NE was positioned, the subject was asked to breathe quietly and to not sleep.19

MRCA was initially performed with a 3-D segmented-FLASH (fast low-angle shot) imaging sequence in combination with the phase-reordering algorithm hybrid ordered phase encoding (HOPE).19,20 The following sequence parameters were used: TE 2.6 ms, TR 6, incremental flip angle 35° to 90°, slice thickness 5 mm, field of view 24×24 cm, read 256, phase 256, in-plane resolution 0.9×0.9 mm, slab thickness 20 mm with 8 secondary phase encode steps, reconstructed slice thickness 2.5 mm, and number of excitations 1. NE diaphragm monitoring was performed for 30 seconds at the start of each 3-D scan to define a 10-mm NE acceptance window around end expiration. The final 3-D image data set was visualized as a cine loop of the 8 reconstructed image slices.

If the subject’s respiratory pattern was too erratic or drifted significantly throughout the 3-D scans, shorter-duration, respiratory-gated 2-D segmented-FLASH MRCA images were acquired. The following sequence parameters were used: TE 2.6 ms, TR 6, incremental flip angle 35° to 90°, slice thickness 5 mm, field of view 24×24 cm, read 256, phase 256, number of excitations 1, and number of views per segment 8. A 5-mm NE acceptance window was positioned around end expiration and was shifted for each scan to compensate for changes in diaphragm position over time.

For all of MRCA images, data were acquired with ECG gating during mid to late diastole and late saturation. The NE pulse sequence was performed before image data acquisition, and data were accepted only if the NE was within the NE acceptance window. MRCA images were initially obtained in a transaxial plane. Oblique planes were then applied to obtain in-plane images of coronary anatomy as necessary. All scans were performed by a single investigator (A.M.T.) and were reported by 2 investigators (A.M.T. and D.J.P.) in consensus. Both investigators were experienced in MRCA imaging of normal coronary arteries but had limited experience with MR imaging of congenital heart disease. A formal report was written for each subject that defined the coronary artery origin and proximal course.

Consensus Reporting
The formal reports from each imaging modality were compared, all images were reviewed by 2 investigators (A.M.T. and S.T.), and a consensus report was written. Normal coronary anatomy was defined as follows:

- Left main stem arises from the left coronary sinus and divides into an LAD and a circumflex (LCx) artery.
- The LAD passes posterior to the main PA into the anterior interventricular groove.
- The LCx passes posteriorly into the posterior atrioventricular groove.
- The RCA arises from the right coronary sinus and passes into the anterior atrioventricular groove.

Any deviation from the above definition was considered to be abnormal coronary artery anatomy; this includes subjects in whom the coronary artery anatomy may be considered normal for that anomaly13 but differs from the anatomy of those with normal cardiac morphology.

Fisher’s exact test was used to compare the accuracy of MRCA and x-ray coronary angiography in the definition of the proximal coronary artery course. A value of P<0.05 was regarded as statistically significant.

Results
No significant complications occurred in any subject during the study. The mean total scan time for MRCA was...
14.3 minutes. A complete 3-D data set was acquired in 13 subjects, with 12 subjects requiring imaging with 2-dimensional (2-D) MRCA. The results for all subjects are shown in the Table (Figures 1 and 2). With the use of MRCA in combination with x-ray coronary angiography, the coronary artery origin and proximal course were diagnosed for all subjects in the study population.

Nine subjects with normal coronary artery anatomy were included in the study. With MRCA, we could identify all of these subjects, whereas with x-ray coronary angiography, 1 subject was misdiagnosed as having an abnormal right coronary artery (RCA) origin (subject 7). Abnormal coronary artery anatomy was identified by consensus for the remaining 16 subjects. Eighteen coronary anomalies were seen in these subjects: single coronary artery (n=4), coronary artery/pulmonary fistulas (n=3), anterior left coronary artery with posterior RCA (in subjects with transposition) (n=3), circumflex from the RCA (n=2), abnormal RCA origin alone (n=3), abnormal left anterior descending coronary artery (LAD) origin alone (n=2), and LAD from RCA (n=1) (Table).

With the use of MRCA, we correctly identified abnormal coronary anatomy in 14 subjects (sensitivity 88%, specificity 100%, and accuracy 92%). In subject 4, the LAD was assumed to have arisen from the left coronary sinus. With x-ray angiography, we demonstrated retrograde filling of the LAD from the RCA, with an LAD-to-PA anastomosis. Retrospective analysis of the MRCA images confirmed the

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<th>Subject</th>
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PDA indicates patent ductus arteriosus; TGA, transposition of the great arteries; CM, cardiomyopathy; LMS, left main stem; Ant, anterior; Ao, aorta; Post, posterior; RV, right ventricles; NC, no course defined by x-ray angiography; AV, atrioventricular groove; and IV, interventricular groove.
Figure 1. Coronary artery anatomy in a subject with congenitally corrected transposition of great arteries (subject 11). a. X-ray coronary angiogram (anterior posterior view) shows left coronary system (LAD and LCx). b and c. Transaxial MRCA images demonstrate anterior origin of left main stem, dividing into an LAD, which passes to left, anterior to aorta, and an LCx, which passes to right, anterior to PA. RCA arises from posterior aorta. d. Schematic. This pattern of coronary anatomy is seen in 60% of subjects with congenitally corrected transposition.
direct connection between the LAD and PA (Figure 3). In subject 18, an RCA was identified in the anterior atrioventricular groove, but the origin could not be visualized because of an MR artifact secondary to a umbrella device in the interatrial septum. At x-ray coronary angiography, selective intubation of only the left coronary artery had been possible, and the RCA was thought to be absent. However, by viewing the x-ray and MR coronary angiograms together, it was possible to identify the RCA from the x-ray aortogram and to define an abnormal posterior origin for the RCA.

One further incorrect x-ray diagnosis was made. In subject 1, the left main stem was described as passing between the aorta and the PA. MRCA demonstrated an anterior left main stem course, over the right ventricular outflow tract. This diagnosis was confirmed at surgery. Thus, x-ray coronary angiography was used to correctly identify abnormal coro-

Figure 2. Left main stem (LMS) coronary–to-PA fistula in a subject with congenitally corrected transposition of great arteries (subject 16). a, Aortogram (anterior posterior view) shows a large LMS artery. A blush of contrast was seen in PA, confirming the fistula. b, Coronal MRCA image demonstrates pulmonary-LMS connection. c and d, Transaxial MRCA image and schematic show entire LMS fistula connecting aorta and PA.
Figure 3. Single coronary artery arising from anterior aortic (Ao) sinus in a subject with a bicuspid aortic valve and patent ductus arteriosus (subject 4). a, X-ray coronary angiogram (right anterior oblique view) shows that LCx artery arises from RCA. LAD fills retrogradely and forms a fistula with PA. b, Insertion of LAD into PA was missed on original viewing of this transaxial MRCA image. However, retrospective analysis confirms x-ray angiography findings. c, Transaxial MRCA image of LCx arising from proximal RCA. LV indicates left ventricle; RA, right atrium. d and e, Aortogram (right anterior oblique view) and sagittal MRCA image showing retroaortic progression of LCx from RCA.
Figure 4. Separate origin of a large conus branch in a subject with tetralogy of Fallot (subject 20). a to c, X-ray coronary angiograms (right anterior oblique views) show separate origin of conus artery, superior to main RCA. d to f, Transaxial MRCA images and schematic (d inferior to e) demonstrating separate origins of RCA and conus artery. GCV indicates great cardiac vein; LMS, left main stem. Conus artery did not pass over right ventricular outflow tract.
nary artery anatomy in 14 subjects. However, with the conventional x-ray angiography technique used in the present study, it was not possible to assess the proximal coronary course in 7 of these subjects. MRCA was used to define the proximal coronary course in all of these subjects \( (P=0.02) \). Retrospective analysis of the proximal coronary course with the x-ray images was, however, possible in combination with the MRCA images.

For 8 of the 10 subjects with tetralogy of Fallot whom we investigated, a large anterior coronary artery was identified. For 7 subjects, this right ventricular artery was a large conus branch; of these subjects, 4 had a separate origin to the RCA (Figure 4), and in 1 subject, the right ventricular artery was an anomalous anterior LAD (subject 1). In 3 subjects, this anterior coronary artery was seen to pass over the right ventricular outflow tract.

**Discussion**

The role of MR imaging in congenital heart disease is well defined. In combination with echocardiography and cardiac catheterization, a complete anatomic and functional assessment can be made to guide patient management. Abnormal coronary artery anatomy is common in patients with congenital heart disease. The diagnosis of these anomalies is important because they may be associated with myocardial ischemia or be damaged during operative procedures. Because images are 2-D projections and other cardiac structures and great vessels are not visualized. Several x-ray angiography and noninvasive techniques have been used to address these problems; however, all have limitations. A more promising noninvasive technique is MRCA, with which coronary artery anomalies can be accurately and reliably identified. Breath holding can be difficult for subjects with congenital heart disease secondary to the underlying cardiac condition or associated skeletal abnormalities. It has become possible to monitor the position of the diaphragm with an intrinsic MR sequence known as a navigator echo (NE). NE respiratory-gated MRCA enables images to be acquired during free respiration with limited subject cooperation. In the present study, we used respiratory-gated MRCA to define the coronary artery origin and proximal course in patients with congenital heart disease. MRCA was superior to conventional x-ray coronary angiography for definition of the proximal course, but a consensus of the 2 investigations defined the coronary artery anatomy in all subjects. MRCA provides tomographic information, which is useful in determination of the 3-D spatial relationship between the proximal coronary arteries and the great vessels and other cardiac structures, whereas x-ray angiography provides an assessment of the entire coronary tree and the peripheral run-off (eg, into the PA, as in 3 patients in this study). When viewed together, the interpretation of all images was much improved.

Finally, it should be noted that there is a learning curve in image interpretation of the MRCA studies of hearts with abnormal anatomy, despite previous experience with normal coronary anatomy. A large part of this learning curve was related to familiarization with the wide range of possible anomalies in subjects with congenital heart disease rather than with the actual interpretation of the MRCA image data.

**Study Limitations**

The sensitivity of x-ray angiography for the detection of proximal coronary artery course could have been improved with the use of an end-on aortic view. This view is not routinely performed at our institution for the investigation of adults with anomalous coronary anatomy, and the normal x-ray angiographic protocol was not altered before the present study.

Although PA catheterization may assist in the definition of the 3-D relationships of the anomalous coronary arteries, this was not performed at our institution because of concerns regarding the small but recognized complication rate of thromboembolism in these patients. Thus, although PA catheterization was performed in 21 of the subjects, the duration was kept to a minimum and the catheter was removed before the left heart and coronary studies.

MRCA is still under development, and it is widely anticipated that further improvements in image quality may occur with the use of T2 preparation pulses, intravascular contrast agents, and novel ultrafast imaging sequences. Furthermore, MR phase velocity mapping was not used in this study. This technique may have helped in the MR identification of the LAD-to-PA anomaly in patient 4. Phase mapping in this situation may have demonstrated LAD blood flow away from the apex into the PA.

Finally, though all of investigators thought that a conclusive diagnosis was reached in all subjects, further surgery or autopsy study would be necessary for absolute confirmation of the diagnoses. Of the 25 subjects investigated in this study, 23 had undergone a previous operation, but an operative note of the coronary artery anatomy was recorded in only 4 subjects (patients 1, 14, 15, and 22). Importantly, the consensus MRCA/x-ray coronary angiography report was in agreement with the operative findings in the 4 subjects.

**Conclusions**

At experienced centers, MRCA is useful as an adjunct to x-ray coronary angiography for the correct definition of coronary anomalies in patients with congenital heart disease. It should be used after the identification of coronary anomalies with routine x-ray angiography in the preoperative assessment to avoid accidental coronary artery damage at surgery. It could also be used as a first-line test to identify coronary anomalies, if this is the sole question under consideration and if this is clinically relevant.

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