Ultrafast Three-Dimensional Contrast-Enhanced Magnetic Resonance Angiography and Imaging in the Diagnosis of Partial Anomalous Pulmonary Venous Drainage

Victor A. Ferrari, MD, FACC,* Craig H. Scott, MD, FACC,* George A. Holland, MD,†‡ Leon Axel, PhD, MD,† Martin St. John Sutton, FRCP, FACC*

Philadelphia, Pennsylvania

OBJECTIVES
The purpose of our study was to evaluate patients with suspected anomalous pulmonary veins (APVs) and atrial septal defects (ASDs) using fast cine magnetic resonance imaging (MRI) and ultrafast three-dimensional magnetic resonance angiography (MRA).

BACKGROUND
Precise anatomic definition of anomalous pulmonary and systemic veins, and the atrial septum are prerequisites for surgical correction of ASDs. Cardiac catheterization and transesophageal echocardiography (TEE) are currently used to diagnose APVs, but did not provide complete information in our patients.

METHODS
Twenty consecutive patients with suspected APVs were studied by MRA after inconclusive assessment by catheterization, TEE or both. The MRI images were acquired with a fast cine sequence and a novel ultrafast three-dimensional sequence before and after contrast injection.

RESULTS
Partial anomalous pulmonary venous drainage was demonstrated in 16 of 20 patients and was excluded in four patients. Magnetic resonance imaging correctly diagnosed APVs and ASDs in all patients (100%) who underwent surgery. For the diagnosis of APVs, the MRI and catheterization results agreed in 74% of patients and the MRI and TEE agreed in 75% of patients. For ASDs, MRI agreed with catheterization and TEE in 53% and 83% of patients, respectively.

CONCLUSIONS
Fast cine MRI with three-dimensional contrast-enhanced MRA provides rapid and comprehensive anatomic definition of APVs and ASDs in patients with adult congenital heart disease in a single examination. (J Am Coll Cardiol 2001;37:1120–8) © 2001 by the American College of Cardiology

Recent studies have underscored the importance of accurate assessment of the number and the course of anomalous pulmonary veins (APVs) in patients with atrial septal defects (ASDs), especially of the sinus venous type (1–3). Definitive diagnosis of anomalous pulmonary venous drainage (APVD) may be difficult by cardiac catheterization from oximetry or levophase angiography, even when using selective pulmonary artery injection techniques (4,5). Diagnostic difficulties are also encountered with transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) (1,6); adults provide a greater challenge than children due to more limited echocardiographic windows (7). Detection rates for APVs using TEE have varied widely (1,4,8). While conventional magnetic resonance imaging (MRI) or computed tomography techniques can aid in detection of these abnormalities (9–11), recent advances in MRI sequences have increased the speed of image acquisition and improved the diagnostic utility of MRI (12).

Magnetic resonance angiography (MRA) methods were adapted to the thorax and permitted noninvasive assessment of vessel size, course and location in a multiplanar manner. Initial MRA approaches used noncontrast-enhanced images at lower field strength to evaluate APVs (13). Further improvements in pulse sequence and gradient design now permit high resolution three-dimensional (3D) examination of the entire mediastinum in a single 10- to 30-s breath-hold at 1.5-Tesla field strengths (14). Contrast-enhanced MRA improves delineation of vessel borders and enables 3D reconstruction of the heart and great vessels, which can establish unequivocally the presence of APVs and identify their entire course through the lung parenchyma and mediastinum and their sites of drainage.

Magnetic resonance imaging, which is an established method for evaluation of ASDs, has proven useful using both spin echo and conventional cine gradient echo techniques (15–17). In addition, recent advances have led to precise identification of the size and shape of ASDs using phase-contrast cine MRI methods (18). The advent of rapid imaging using segmented k-space techniques has reduced data acquisition time dramatically, allowing dynamic cine MRI at a desired slice location in a single breath-hold, which aids in localization of intracardiac shunts (19).
Precise anatomic knowledge of the drainage of APVs, location of associated ASDs and the presence of abnormal systemic venous connections are important prerequisites for planning optimal surgical repair (20).

The aim of this prospective study was to use these new technologic developments in MRI and ultrafast 3D MRA to define the anatomy of the pulmonary venous circulation and the atrial septum in 20 consecutive adult patients with suspected APVD and ASDs, in whom inconclusive diagnostic information was obtained at cardiac catheterization, TTE and/or TEE.

**METHODS**

**Patient population.** We studied 20 consecutive adult patients (9 male and 11 female) aged 22 to 68 years (mean 42 ± 13), with suspected APVD and/or ASDs. All were referred specifically for ultrafast MRI and MRA to determine the presence of APVs and ascertain the presence and anatomic location of the ASDs, because prior cardiac catheterization data, TEE or both had proved inconclusive.

The most common presenting symptoms were dyspnea on exertion (75%), palpitations (40%) and fatigue (30%). Two patients presented with atypical chest pain, and two patients were seen in follow-up for a heart murmur. Two patients had documented paroxysmal atrial fibrillation. Two patients (10%) had multiple skeletal abnormalities including short humeri, distal radio-ulnar synostoses, abnormal carpal bones and bilateral digitization of the thumbs, consistent with the hand-heart or Holt-Oram syndrome (21), and one patient (5%) had Swyer-James syndrome with atresia of the right pulmonary artery (22) (Table 1).

All patients were in sinus rhythm and were screened for contraindications to MRI and MRA.

**Magnetic resonance imaging and angiography.** MR imaging. All MRI was performed on a 1.5-T Signa scanner (General Electric Medical Systems [GEMS], Milwaukee, Wisconsin), using an enhanced gradient system.
(maximal gradient strength = 2.3 Gauss/cm in 150 μs). We used a custom torso multicoil array surface coil set to improve signal-to-noise ratio (23). Following scout imaging, a set of interleaved $T_1$-weighted spin echo images (5-mm thickness with 5-mm skip) was acquired from just cephalad to the manubrium to the level of the hepatic veins.

**ASD IMAGING.** We used a combination of techniques for the assessment of ASD location, size and direction of shunt flow. An ultrafast ECG-gated multiphase segmented k-space gradient-echo sequence was used to assess the structure and potential flow across the interatrial septum, providing 10 to 14 frames through the cardiac cycle at each imaging plane (24). Single breath-hold periods of 13 to 18 s were required at each slice location. Imaging variables included 26 to 32 cm field of view; 256 × 128 acquisition matrix interpolated to 256 × 256; 6-mm slice thickness; echo time (TE) 1.8 to 2.3 ms, repetition time (TR) 6.7 to 8.3 ms; 6 to 8 k-space lines per cardiac frame; number of signal averages = 1, digital receiver bandwidth ± 32 kHz; excitation flip angle = 30°. Imaging commenced at the site of potential communication between a suspected APV (based on spin echo images) and the superior vena cava (SVC), brachiocephalic vein or other structure, and continued through the entire interatrial septum. The presence of a consistent flow disturbance (signal void or moving blood) from the left atrium to the right atrium at the level of the high interatrial septum defined a sinus venous ASD (SVASD). A flow disturbance associated with a defect in the interatrial septum at the level of the fossa ovalis defined a secundum ASD. If the diagnosis of ASD was uncertain, the TE and TR of the segmented k-space sequence was lengthened to at least twice the nominal values and then repeated at the level of the most suspicious site. If this was still unrevealing, a conventional cine gradient echo sequence was performed (TE approximately 13 ms, TR approximately 33 ms), followed by a phase-contrast cine MRI sequence to permit more sensitive flow detection. Quantitative assessment of the ASD size was determined from the maximum defect size noted on the cine images. The ASD sizes were designated as follows: small, < 1 cm; moderate, 1 to 1.5 cm; and large, > 1.5 cm.

**MR ANGIOGRAPHY.** We modified a fast 3D spoiled gradient (SPGR) sequence to minimize TE and TR by decreasing the width of the radiofrequency pulse used for slice excitation (TE) in a standard fast SPGR sequence from 3.20 to 1.28 ms (14). In addition, first-order gradient-moment nulling was eliminated and an asymmetric echo was used. Coronal ultrafast 3D SPGR (UF-3DSPGR) imaging was performed using the conventional body coil before and after intravenous administration of a gadolinium-based contrast agent (gadopentetate dimeglumine, “Magnevist,” Berlex Laboratories, Cedar Knolls, New Jersey; or gadoteridol, “Prohance,” Bracco Diagnostics, Princeton, New Jersey) with the following parameters: TR = 4.8 to 7 ms; flip angle 60°; matrix size 256 × 128; slice thickness 2 to 4 mm; receiver bandwidth 64 kHz; and acquisition time 18 to 34 s. A field of view of 26 to 38 cm was used to include the majority of the thorax. The patients’ arms were positioned above the head (coronal plane imaging) or on the abdomen (sagittal plane imaging) to avoid aliasing. Scans were completed in 18 to 34 s. Scan time was reduced in those patients who could not sustain breath-holds for 30 s despite hyperventilation and oxygen by nasal cannula at up to 4 liters/min. Later software improvements allowed the TE to be reduced to 1.11 ms (final three patients).

**INJECTION.** Patients underwent imaging before, during and twice after intravenous injection of contrast. All patients received 20 to 40 ml of contrast agent administered intravenously, with injections performed by hand using a stopwatch. Injection rate was modified based on the acquisition time of the scan to obtain as uniform an arterial contrast concentration as possible throughout the image acquisition. Scanning commenced approximately 10 s after contrast injection in patients with normal right and left ventricular function (assessed from cine or multiphase GRE images), and approximately 20 s after injection in patients with moderate or severe right or left ventricular dysfunction.

**IMAGE ANALYSIS.** Images were analyzed on an Advantage Windows workstation (GEMS; Milwaukee, Wisconsin) featuring interactive 3D reformatting, variable reconstructed slice thickness and oblique and multiaxis reconstruction (Fig. 1), and displayed using the maximum intensity projection algorithm (25).

**Cardiac catheterization.** Nineteen of the twenty patients (95%) underwent cardiac catheterization to obtain right and left heart chamber pressures and oxygen saturations. Pulmonary (Qp) and systemic (Qs) blood volume flows and shunt fractions (Qp/Qs) were calculated. Attempts were made to cross the interatrial septum with a catheter in all patients. Selective contrast angiography by hand injection was used to identify the site of drainage of any suspected APV.

**Transesophageal Echocardiography.** Transesophageal echocardiograms were obtained in 12 patients. Images of the right and left heart chambers (including sizes and function) were obtained, and attempts were made to define the entire interatrial septum, all the pulmonary veins, the vena cavae and coronary sinus in all patients from multiple views. Doppler color flow mapping and peripheral venous contrast injections of agitated saline solution were performed to establish the presence, size, location and direction of blood flow across the interatrial septum.

**Comparative data.** Data were analyzed by an agreement analysis that compared the number of instances in which the different techniques agreed or disagreed for a given test situation (26). This analytical approach was the most appropriate since not all patients underwent imaging with each technique, and not all patients underwent surgical correction. An overall comparison was performed among MRI, cardiac catheterization and TEE for detection of APVs and ASDs.
RESULTS

Magnetic resonance imaging and angiography. Fast cine MRI with UF-3DSPGR contrast-enhanced MRA was performed in all 20 patients without complication. Total time per patient for completion of all imaging was 58 ± 12 min. Partial APVD was demonstrated in 16 of 20 patients and was definitively excluded in four patients. The region of lung drained by APV involved one pulmonary lobe in four patients (Fig. 2), two lobes in 10 and the complete right lung in two. Fifteen APVs were right-sided and one was left-sided. Drainage of the APV was supracardiac in 13 and infracardiac in three. These latter three patients had scimitar syndrome, which consisted of drainage of the whole right lung (in two) and two lobes of the right lung (in one) via an APV to the inferior vena cava (IVC) (27) (Fig. 3). One of these patients (not the subject of Fig. 3) was described in a previous report (28). Four patients had normal pulmonary venous drainage, of whom one had Eisenmenger’s syndrome with a nonrestrictive ventricular septal defect (VSD), one had a restrictive muscular VSD, one had atresia of the right pulmonary artery (Swyer-James syndrome) with a secundum ASD and one had a secundum ASD only.

Seventeen of 20 patients were demonstrated by MRI to have ASDs, six classified as secundum type and 11 as SVASDs. All patients (100%) with SVASD had partial APVD; five of these also had abnormal systemic venous connections, including a persistent left SVC draining into a dilated coronary sinus. By contrast, only two of the six patients with secundum ASDs had APVD; in one patient, the left upper and middle lobes of the lung drained into the left brachiocephalic vein (Fig. 4), and in the other patient, the right upper and right middle lobes drained into the right SVC.

Cardiac catheterization. Nineteen patients underwent cardiac catheterization, and there were two complications: an allergic reaction to the contrast agent consisting of severe bronchospasm and rash, and development of congestive heart failure. Six patients had severe pulmonary hypertension (pulmonary artery systolic pressure >50 mm Hg). Pulmonary-to-systemic blood flow ratio (Qp/Qs) varied from 0.75 to 3.4 (mean 2.1 ± 0.8) (Table 2). Right atrial pressure ranged from 2 to 22, with a mean of 6 mm Hg.

Anomalous pulmonary venous drainage was diagnosed at cardiac catheterization in 12 of the 16 patients by selective hand injection of contrast; APVD was excluded in two patients (Table 2).

Atrial septal defect was diagnosed by oximetry and/or selective contrast angiography in six patients (43%), and was “suspected” in two additional patients, although the location and type of defect could not be determined.

Transesophageal echocardiography. Twelve patients underwent TEE, and APVD was diagnosed in seven patients,
although the specific lung segments drained could not always be determined.

An ASD was definitively identified in eight (67%), and in another patient, the presence of a SVASD was “suspected” but not confirmed. Transesophageal echocardiography excluded ASD in one patient, but misclassified two SVASDs as normal. This figure demonstrates the utility of the reformattig technique, which permits reorientation of the data set from a coronal (original) to an oblique parasagittal view and delineation of the course of nearly the entire BcphV. APV = anomalous pulmonary vein.

Surgical intraoperative findings. Ten patients underwent surgical correction of APVs and/or closure of the ASDs, and the intraoperative findings are outlined in Table 1. The anatomic findings at surgery confirmed those obtained by MRI and MRA in all cases (100%), including ASD size. In this subgroup of patients with surgical correlation (Table 2), the predictive diagnostic accuracy of TEE for APV was 80%, and 78% for cardiac catheterization. For detection of ASDs, the predictive diagnostic accuracy of TEE was 80%, and 44% for catheterization. Ten patients did not undergo surgical repair: four because of severe pulmonary hypertension (one of whom died suddenly without autopsy, three are currently listed for lung transplantation), one was not a surgical candidate due to severe chronic obstructive pulmonary disease and five did not undergo surgical closure because the intracardiac shunt was small (Qp:Qs < 1.5:1) with only minimal elevation of PA pressures.

Agreement analysis. Table 4 summarizes the agreement analysis. Specific comments for each anomaly follow.

APV. There were two false positive and three false negative errors by catheterization. In the false positive patients, one (Patient 1) had right PA atresia and an ectatic course of the left upper pulmonary vein, which when crossed via the
unsuspected ASD appeared to be an APV. Another (Patient 11) had angiography of a suspected right upper lobe (RUL) APV, but the catheter had crossed the ASD and entered the normally draining RUL pulmonary vein, which entered the left atrium at a more superior location than typical. The false negative patients all had high SVASDs (two of three were significant in size), that were oriented such that they could not be negotiated or crossed by catheter, and whose shunts were ascribed to APVs.

There were three false negatives by TEE, two due to high insertion of the APV (2.0 cm above the right atrium) into the SVC, and the third a left upper and middle lobe APV draining to the brachiocephalic vein (Fig. 4).

**DISCUSSION**

The major finding in this prospective study is that our modified imaging methods using fast segmented k-space imaging and contrast-enhanced ultrafast 3D MRA allowed unequivocal detection of APVs and ASDs in a population of
patients in whom diagnosis was inconclusive by cardiac catheterization and TEE. The advantages of this technique include imaging of a larger anatomic area than possible by TEE or catheterization and rapid data acquisition in a single breath-hold, which are important for imaging vascular structures within the thorax. Magnetic resonance angiography enables PAs and pulmonary veins to be differentiated and provides visualization of even the small pulmonary venous radicles, permitting determination of the number of anomalously draining pulmonary lobes. Furthermore, the entire course of the APV can be followed from the periphery through the hilum and mediastinum to their drainage sites. Accurate identification of APVD patterns is important since the surgical correction of APVs from the right upper and middle pulmonary lobes is different from that for infracardiac drainage or left-sided APVs (20). Noninvasive definition of retrocardiac or infracardiac pulmonary venous drainage and the anatomy of the lung from which the anomalous drainage derives is possible only with MRA (29).

Difficulties in diagnosing APVs may occur with TTE or TEE and cardiac catheterization. Restricted acoustic windows limit the use of TTE, and dilution of hand-injected angiographic contrast or levophase angiography at cardiac catheterization limits visualization of the pulmonary veins. Catheterization is also limited by the inability to distinguish an ASD from an APV when oximetry indicates an intracardiac shunt at atrial level if the ASD cannot be crossed with a catheter. Crescent-shaped SVASDs or those high in the atrial septum may be difficult to cross and thereby escape detection by catheterization, and in this study accounted for most of the eight false negatives at catheterization, despite a significant shunt fraction (mean Qp:Qs = 2.5:1). Although TEE enables inspection of the entire interatrial septum, the predictive accuracy of TEE for detection of normal and anomalous pulmonary veins has varied widely from 60% to 93% (3), and in our study was 75% (Fig. 5). Anomalous pulmonary veins that insert >2 cm above the right atrium or left-sided APVs were particularly difficult to detect in our study. Furthermore, the presence of four pulmonary veins does not exclude the presence of additional APVs (2), and recognition of multiple branching APVs or atypical drainage patterns are difficult to achieve by TEE (8). Also, TEE provides only limited information regarding the extent or region of the lung that has abnormal drainage (2,8).

Two previous small studies have demonstrated the utility of MRI in identifying the presence of APVs (9,10), and another suggested that the technique was limited in adults with congenital heart disease (20); however, these studies used older and less sensitive methods. A recent article compared spin echo to gradient echo MRI acquisition in detection of APVs, but was limited to axial or coronal orientations (12). We developed a modified MRI pulse sequence to permit high-resolution 3D imaging of nearly the entire thorax in one breath-hold, which is especially useful for detecting abnormal vascular communications outside the usual echocardiographic windows (8), and used an image workstation that allowed improved 3D reconstruction and visualization of the vasculature.

In this study, we made the initial tacit assumption that

Table 4. Agreement Analysis

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<tr>
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<th>Agree</th>
<th>Disagree</th>
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<tr>
<td><strong>APV</strong></td>
<td>Cath (n = 19)</td>
<td>TEE (n = 12)</td>
</tr>
<tr>
<td>MRI</td>
<td>14 (74%)</td>
<td>9 (75%)</td>
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<td>Sensitivity (vs. MRI)</td>
<td>80%</td>
<td>70%</td>
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<tr>
<td>Specificity (vs. MRI)</td>
<td>50%</td>
<td>100%</td>
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<tr>
<td><strong>ASD</strong></td>
<td>Cath (n = 19)</td>
<td>TEE (n = 12)</td>
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<tr>
<td>MRI</td>
<td>10 (53%)</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>50%</td>
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<td>Specificity</td>
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APV = anomalous pulmonary vein; ASD = atrial septal defect; Cath = cardiac catheterization; FN = false negative; FP = false positive; MRI = magnetic resonance imaging; TEE = transesophageal echocardiography. Sensitivity and specificity measurements calculated vs. MRI as reference standard.

Figure 5. Axial spin echo MRI demonstrating a sinus venosus defect (arrow) just caudal to the insertion of the superior vena cava and between the right atrium (RA) and left atrium (LA). Due to its location high in the atrium, it is sometimes difficult to cross with a catheter or to visualize with transesophageal echocardiography (TEE). This defect was misidentified on both catheterization and TEE examinations.
MRA was the reference standard before we analyzed the data obtained at cardiac catheterization, TTE and TEE or reviewed the intraoperative findings. The intraoperative findings in all 10 surgical patients were completely concordant with the MRA findings. The definitive diagnosis of ASD and APVD was established by cardiac catheterization in 53% and 74% of patients, respectively, compared to MRI and by echocardiography (TTE and/or TEE) in 83% and 75%, respectively. Both techniques had false positive and false negative diagnoses. Magnetic resonance angiography demonstrated that most patients (94%) had right-sided APVs, 75% of the APVs involved two or more lobes and 25% were from single lobes. Transesophageal echocardiography was not helpful in making a definitive diagnosis of infracardiac pulmonary venous drainage to the IVC, although this was suspected in two cases. Both cardiac catheterization and echocardiography identified the five patients with severe pulmonary hypertension, one of whom died from end-stage right heart failure (Patient 1) and two of whom are currently listed for lung transplantation (Patients 4 and 13). Quantitative assessment of PA pressures and direction of intracardiac shunt flow by cardiac catheterization plays an important role in determining the need for surgical correction, and our MRI and MRA methods in this study were used as an adjunct to catheterization in this decision process.

Newer methods have demonstrated that MRI techniques can accurately quantify the size and degree of shunting of ASDs, and may soon permit a completely noninvasive preoperative assessment (18,30,31).

**Study limitations.** The small sample size limits the more general applicability of our findings; however, despite this fact, important concepts and pitfalls of conventional imaging techniques were revealed. The dramatic difference in performance between MRI and standard methods may be due to selection of patients in whom conventional detection strategies failed; however, the surgical confirmation of the results lends support to the overall accuracy of the method. The MRA technique is not cardiac-gated, which may obscure small areas of interest, and therefore requires the use of additional gated sequences for accurate quantitation of ASD size and visualization of flow direction.

**CONCLUSIONS**

We have demonstrated that our new MRA imaging strategy, which is performed in a single breath-hold, can resolve the residual diagnostic problems in adult patients with ASDs and APVD. This challenging subgroup of patients requires highly accurate diagnostic testing to provide appropriate therapeutic guidance. These data underscore the importance of accurate identification of the pulmonary veins, especially in patients identified as having secundum ASDs and believed to be candidates for minimally invasive surgical or catheter-based closure procedures. We recommend the use of new ultrafast MRA and MRI techniques for patients in whom diagnosis remains inconclusive after cardiac catheterization, TEE or both.

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**Reprint requests and correspondence:** Dr. Victor A. Ferrari, Cardiovascular Division, University of Pennsylvania Medical Center, 3400 Spruce Street, Philadelphia, Pennsylvania 19104. E-mail: ferrariv@mail.med.upenn.edu.

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