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ORIGINAL ARTICLE

Atypical atrial septal defects in children: noninvasive evaluation by cardiac MRI

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Abstract
Background Atypical left-to-right shunts at the level of the atrium in children such as sinus venosus atrial septal defects (ASDs) and partial anomalous pulmonary venous return (PAPVR) may be difficult to assess by transthoracic or transoesophageal echocardiography. Free-breathing cardiac MRI may be a powerful alternative.
Objective To assess the value of free-breathing cardiac MRI in the delineation of atypical ASDs in children.
Materials and methods A total of 82 children (mean age 5.9 years, range 1.1–15.7 years) with suspected ASD and inconclusive transthoracic echocardiography underwent cardiac MRI under free-breathing, mostly sedated conditions. Phase-contrast MRI was used for defect visualization and shunt quantification, and multiphase inflow MR angiography for delineation of pulmonary/systemic venous connections.
Results Of the 82 patients, 34 (41%) were diagnosed with atypical shunt lesions at the level of the atrium and 48 (59%) with simple secundum ASDs. No false-negative or false-positive findings were reported by MRI compared to cardiac catheterization and intraoperative findings. Superior sinus venosus ASD with partial anomalous PAPVR was present in 10 of the 82 children (12.2%), whereas 2 (2.4%) had a large posterior-inferior defect, 5 (6.1%) had isolated PAPVR, and 17 (20.7%) had multiple ASDs and/or associated vascular anomalies. Q_p/Q_s by phase-contrast MRI agreed well with oximetry values (mean difference 3%, limits of agreement ±21–25%; Bland/Altman analysis).
Conclusion Free-breathing cardiac MRI under sedation allows reliable identification of atypical left-to-right shunt defects at the level of the atrium in children in whom transcatheter ASD closure is unsuitable, including delineation of pulmonary or systemic venous anomalies and shunt quantification.

Keywords Heart · Congenital · Shunt · Atrial septal defect · MRI · Children

Introduction

Over the past decade novel interventional techniques for the treatment of atrial septal defects (ASDs) have become increasingly successful. This has increased the need for reliable identification of patients with left-to-right shunts at the level of the atrium in whom transcatheter defect closure is unsuitable [1]. Examples include superior sinus venosus ASDs (SVDs), which are usually associated with significant partial anomalous pulmonary venous return (PAPVR) from the right lung to the superior vena cava (SVC). PAPVR may also occur as an isolated lesion imposing volume load on the right heart, or PAPVR may be associated with secundum ASD. In these clinical situations surgery may be the preferred option. Moreover, any ASD

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may also be combined with systemic venous anomalies that need to be depicted prior to surgical intervention.

In such patients with atypical left-to-right shunt lesions at the level of the atrium, current imaging modalities have important limitations. Transthoracic echocardiography (TTE) may be inconclusive, and patients are therefore frequently referred for transoesophageal echocardiography (TEE) and/or cardiac catheterization for further diagnostic work-up. Cardiac catheterization carries well-known risks associated with invasiveness and exposure to ionizing radiation. TEE is semi-invasive in children and general anaesthesia may be required for the procedure, and although high diagnostic accuracy is achievable, it may sometimes be difficult to diagnose remote PAPVR [2, 3]. This would be easily possible using contrast-enhanced 3-D MR angiography (MRA), but general anaesthesia is also necessary in children unable to cooperate with breath-holding to achieve optimal diagnostic results [4]. Cardiac MRI (CMR), however, provides a variety of pulse sequences such as inflow MRA and cine phase-contrast MRI (PC-MRI) that may allow high-quality diagnostic imaging under free-breathing conditions, thus avoiding unnecessary general anaesthesia to achieve breath-holds in uncooperative younger children [5, 6]. PC-MRI has been shown to be valuable for sizing of simple secundum ASDs, both in children and adults [7, 8]. Moreover, the use of PC-MRI for quantification of left-to-right shunting is well established in these patients [9, 10]. Little is known, however, about the diagnostic accuracy of such free-breathing CMR techniques in the evaluation of atypical left-to-right shunt congenital heart defects at the level of the atrium. We therefore prospectively assessed the clinical value of free-breathing CMR in sedated children with atypical shunts at the level of the atrium and inconclusive TTE.

The hypotheses behind this study were that free-breathing CMR may be able to depict (1) the presence and type of all kinds of ASDs, and (2) the presence and type of isolated or associated systemic venous or pulmonary venous anomalies with higher sensitivity and specificity than cardiac catheterization, TEE or surgery.

Materials and methods

Study population

Over a period of 22 months we prospectively enrolled 82 children (mean age 5.9 years, range 1.1–15.7 years) with clinically suspected atrial left-to-right shunt and inconclusive TTE, which included those with (a) a defect not clearly visualized (including suspicion of multiple fossa ovalis defects), (b) different reports from different observers, or (c) suspected but not proved systemic or pulmonary venous anomalies. All patients were in sinus rhythm and had evidence of significant pretricuspid left-to-right shunting (i.e. an enlarged right heart by TTE). The study was approved by the institutional review committee in Bad Oeynhausen and written informed consent was obtained from parents or carers.

Study design

Each patient underwent CMR to determine defect size and location, left-to-right shunt, and pulmonary/systemic venous connections. Children considered suitable for transcatheter ASD closure were subsequently referred to the catheterization laboratory, and the MRI sizing results were compared with TEE measurements, as reported elsewhere [7]. In the remainder, the MRI results were compared with the surgical diagnosis. Prior to surgery, according to hospital practice at the time, cardiac catheterization was routinely performed to assess pulmonary and systemic venous return, to quantify left-to-right shunt, and to exclude pulmonary hypertension. Catheterization staff, the TEE operator and the cardiac surgeon were blinded to the MRI results. The MR operator was blinded to the echocardiography results. General anaesthesia was performed during transcatheter defect closure and/or TEE. Sedation for MRI and diagnostic catheterization was performed by a paediatric cardiologist trained in paediatric intensive care medicine using midazolam (0.2–0.3 mg/kg i.v. as a slow bolus; maximum total dose 3 mg) and thiopental (0.5–1 mg/kg i.v. as a repetitive slow bolus injection until effective sedation was achieved; maximum total dose 6 mg/kg). Blood pressure, transcutaneous oxygen saturation, heart rate and respiratory rate were monitored continuously by an experienced nurse in the scanner room for additional visual patient surveillance.

MR imaging technique

All examinations were performed on a 1.5-T whole-body MR scanner (ACS-NT; Philips, Best, The Netherlands; maximum gradient performance 21 mT/m amplitude, slew rate 105 T m^{-1} s^{-1}). A five-element cardiac phased-array coil was used for signal acquisition, and the body coil for signal transmission. Details of the MRI protocols are listed in Table 1. Turbo field-echo survey images in the coronal and sagittal planes were obtained, followed by diastolic gated, T1-weighted (T1-W) multislice spin-echo echoplanar images with transverse slices from the diaphragm to the upper mediastinum. ASD size and position were delineated by retrospectively gated 2-D PC-MRI. From sagittal surveys and transverse spin-echo echoplanar images at the level of the ASD, one to three contiguous cine PC-MRI

Table 1 MRI protocols

Parameter	Localizer	In-flow MRA	Phase-contrast MRI
Sequence type	Turbo field echo	Turbo field echo	Fast field echo
TFE factor	40	4–7	N/A
Field of view (mm)	250	330	260
Matrix size	128×256	256×204	228–256×256–304
Slice thickness (mm)	6	4.5–5.0 (gap −0.5 mm)	5–6
No. of slices	15 coronal, 15 sagittal	35–40	3 (each at different angles)
Echo time (ms)	2.3	4.7	About 6
Repetition time (ms)	9.5	11.0	15–20
Flip angle (°)	20	50	30
Trigger delay (ms)	240	270 (or multiphase)	N/A
No. of phases	1	If multiphase, 4–5	20
Velocity encoding (cm/s)	N/A	N/A	40–70
No. of signals acquired	2	1	1–2
Scan time (min:s, at heart rate 110/min)	1:30–2:40	About 5:30–6:00	2:50–3:40 (each slice)

slices were obtained in the atrial septal plane to provide an en-face view of the spatial position of the ASD (Fig. 1). For atypical ASDs, such as SVD, additional PC-MRI slices were acquired in the four-chamber view (Fig. 2) and sagittal plane. Flow was encoded in-plane, except for the en-face image (through-plane = slice-selection direction), and about 20 phase images per cardiac cycle were reconstructed. Pulmonary and systemic venous return was assessed by multiphase (i.e. four or five heart phases) or single-phase (triggered to early diastole) 2-D segmented k-space field-echo MR angiography (time-of-flight principle, see Table 1) with transverse plane acquisition. To quantify the left-to-right shunt (Q_p/Q_s), flow in the pulmonary artery (Q_p) and the ascending aorta (Q_s) was measured using a standard retrospectively gated through-plane PC-MRI protocol, as evaluated in children with a left-to-right shunt [10].

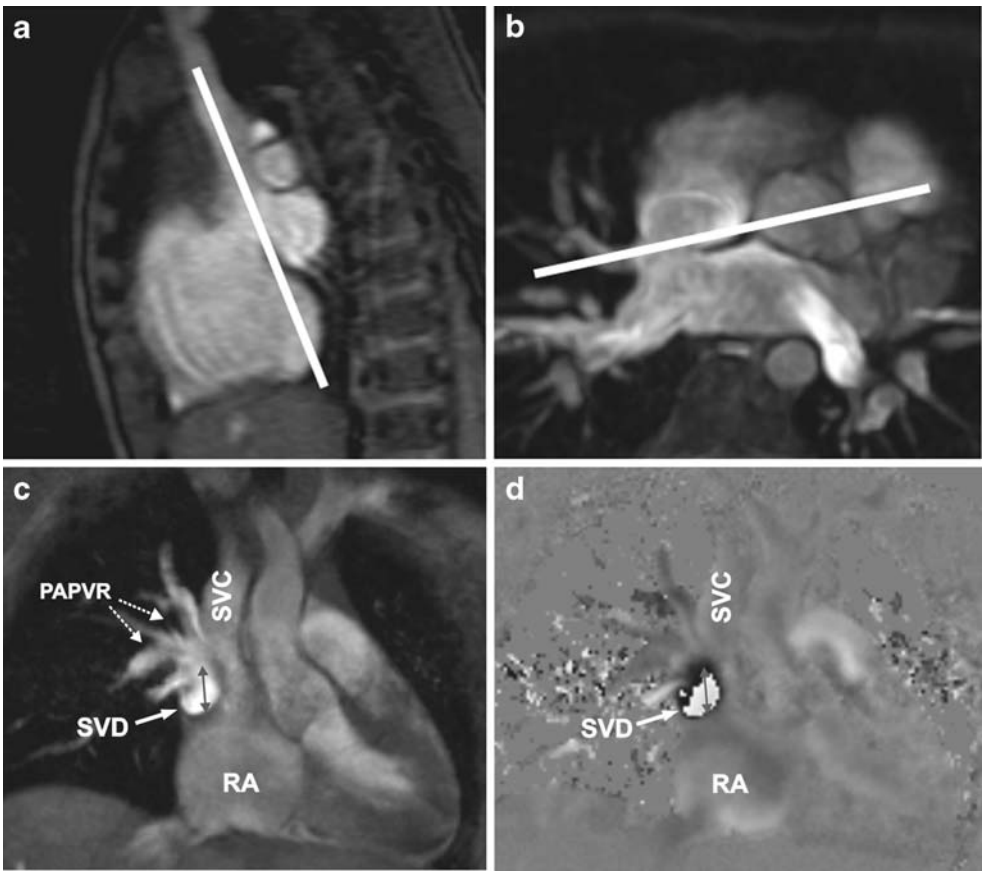

Fig. 1 En-face PC-MRI section of a superior SVD in the plane of the atrial septum, as planned from (**a**) a sagittal survey scan and (**b**) a transverse in-flow MRA slice at the level of the defect. PC-MR images in the coronal plane (**c**, **d**) show the size of the defect (*double-headed arrows*) and anatomical information in the magnitude image (**c**), whereas the shape can be estimated on the coronal phase image (**d**), which displays maximum flow. Note the anomalous pulmonary venous drainage from the right-upper lobe and middle lobe to the SVC (**c**) (*SVD* sinus venosus defect, *PAPVR* partial anomalous pulmonary venous return, *SVC* superior vena cava, *RA* right atrium)

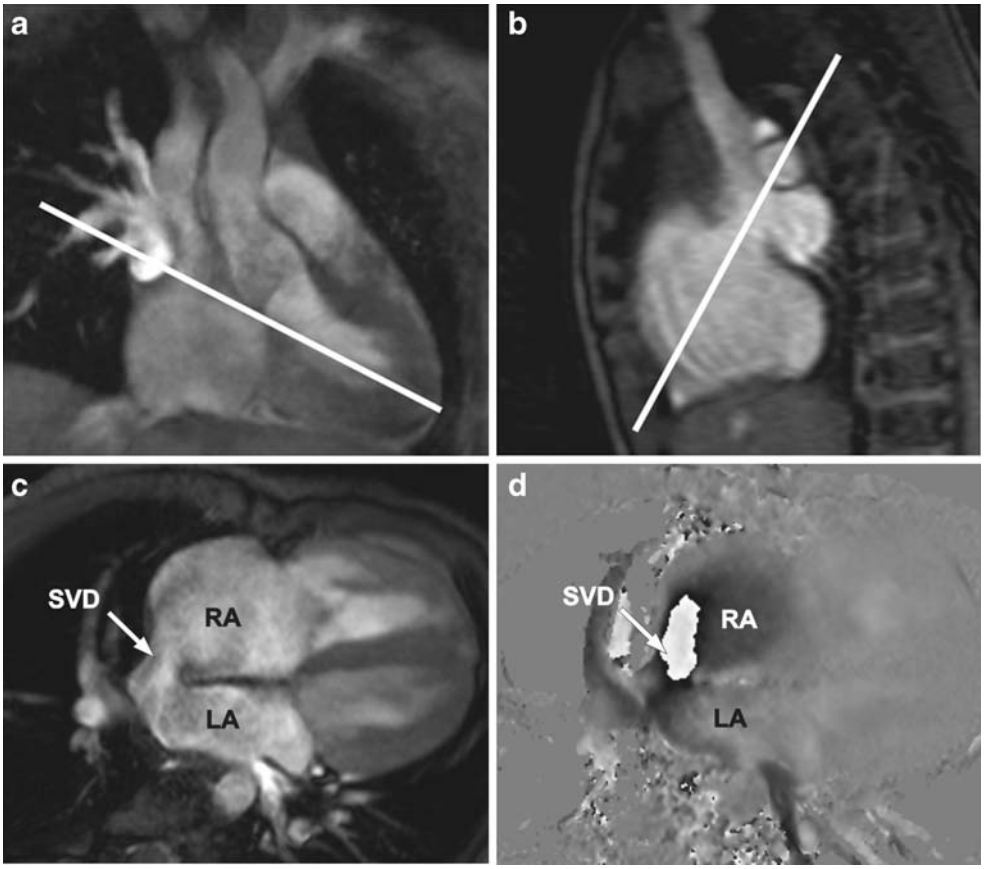

Fig. 2 Projection in a four-chamber view. PC-MRI of a superior SVD in the four-chamber projection, as planned from the coronal en-face projection (**a**, see also Fig. 1) and a sagittal survey scan (**b**) at the level of the defect. The size of the defect can be estimated on the phase image (**d**), which displays maximum flow, whereas anatomical information (e.g. adjacent structures) can be obtained from the corresponding magnitude image (**c**) (*SVD* sinus venosus defect, *RA* right atrium, *LA* left atrium)

MR image analysis

Atypical ASDs, such as superior or inferior SVDs were qualitatively described (Figs. 1 and 2). Quantitative PC-MRI flow data were analyzed off-line as previously described [10]. Multiplanar reformations in any desired image plane to delineate pulmonary and systemic venous connections could be reconstructed from the 2-D in-flow MRA stack yielding a '3-D' dataset due to the thin overlapping slices (Fig. 3).

Cardiac catheterization and intervention

All 82 children had routine diagnostic cardiac catheterization including oximetry to calculate Q_p/Q_s (Fick formula), as was hospital policy at the time, and 22 of these children who had a secundum ASD of adequate size and position underwent transcatheter defect closure using Amplatzer septal occluder systems [11].

Measurements during surgery

Surgery was performed through a midline sternotomy using induced ventricular fibrillation and intermittent cross-clamping of the aorta. Atypical atrial defects and the presence of anomalous pulmonary venous return were qualitatively described and compared to the MRI findings.

Statistical analysis

Data are given as mean values ± standard deviation (SD), or as percentages where appropriate. Bland-Altman analysis was used for comparison of PC-MRI and oximetry data for determination of the Q_p/Q_s ratio. Data were log-transformed, because differences increased linearly with mean Q_p/Q_s values [12].

Results

MRI studies were well tolerated and completed within 25–50 min (all patients). The mean heart rate was 98±15/min on MRI and 102±15/min on catheterization. In patients with an atypical ASD, scan time was usually much shorter (25–30 min) because detailed defect sizing was unnecessary. Atypical shunt lesions at the level of the atrium were present in 34 of 82 patients (41%), whereas isolated secundum ASD was diagnosed in 48 patients (59%). There were no false-negative or false-positive diagnoses by MRI, compared with cardiac catheterization and/or TEE and/or surgery.

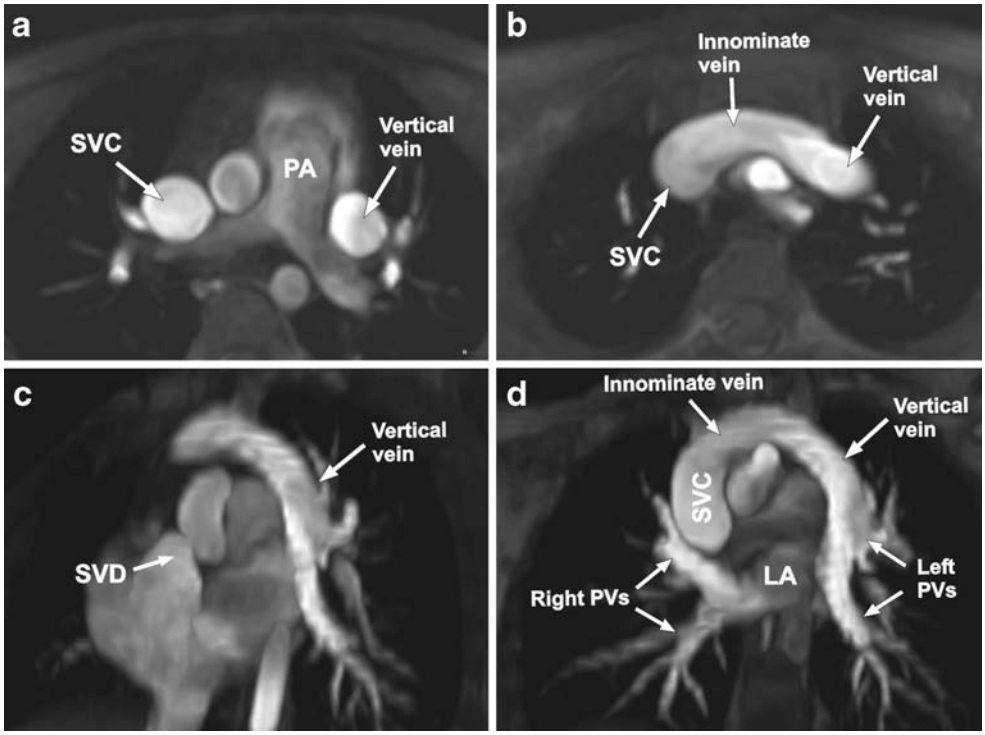

Fig. 3 In this 5-year-old girl there was anomalous pulmonary venous drainage from the left lung to the left innominate vein, not associated with an ASD. **a**, **b** Axial 10-mm slabs (reformatted from the 2-D inflow MRA slices) at the level of the pulmonary artery (**a**) demonstrate a large vertical vein collecting all pulmonary venous blood from the left lung and draining to the left innominate vein (**b**). **c** Paracoronal, reformatted 6-mm slab demonstrates the left pulmonary veins (in-plane) and their drainage into the ascending vertical vein. **d** Paracoronal, reformatted 20-mm slab demonstrates drainage of the vertical vein into the enlarged left innominate vein as well as correct drainage of all right-sided pulmonary veins to the left atrium (*PV* pulmonary vein, *PA* pulmonary artery, *SVC* superior vena cava, *LA* left atrium)

Atypical ASD and associated cardiovascular anomalies

Superior SVD was diagnosed in ten patients (12.2%) (Figs. 1 and 2). In all 10 children, right-sided PAPVR was present with the right upper lobe pulmonary veins draining to the SVC and the right middle lobe pulmonary vein overriding the defect, whereas the pulmonary veins from the right lower lobe and from the left lung drained into the left atrium. There was complete concordance between the MRI and cardiac catheterization findings regarding the number of anomalous pulmonary veins, their origin and site of anomalous drainage, and their relative sizes. In two patients (2.4%) a large inferior caval defect located posterior-inferiorly to the fossa ovalis was found. In both patients, the inferior vena cava drained predominantly to the right atrium and there was no PAPVR. In five patients (6.1%) there was isolated right-sided (two patients) or left-sided (three patients, Fig. 3) PAPVR. Moreover, four patients (4.9%) had a secundum ASD with associated PAPVR (one left-sided, three right-sided). Multiple ASDs were present in 9 patients (11%), one had multiple peripheral pulmonary arterial stenoses, one had left-sided persistent SVC drainage to the coronary sinus, one had a retro-oesophageal right subclavian artery, and one had an associated large net of Chiari. In all nine patients with multiple (haemodynamically relevant) ASDs, the ASDs were detected by PC-MRI in the en-face projection and confirmed by the additional slices. Two of these also had a multifenestrated septal aneurysm extending inferiorly to the oval fossa.

All 34 patients described above with an atypical ASD and associated anomalies had surgical correction of the lesion. There was complete concordance between the MRI with surgical diagnoses of type and estimated size of ASD, number and site of drainage of anomalous pulmonary veins, and any systemic venous anomalies.

Shunt quantification by PC-MRI: comparison with oximetry

The Bland-Altman analysis was applied to the log-transformed data [12], since differences increased linearly with mean Qp/Qs values. Estimation of the precision of the limits of agreement (defined as mean ± 2 × SD) was based on calculation of 95% confidence intervals (CI). A mean value of 1.0 after antilog transformation (dimensionless ratio) would be expected in the case of no difference between two tested methods. In 72 of the 82 patients in

whom PC-MRI was performed for shunt quantification, acceptable agreement with a small difference of 3% (mean 0.97 after antilog transformation) between the two methods was observed. Upper and lower limits of agreement were 1.21 (95% CI 1.15–1.27) and 0.75 (CI 0.71–0.78). Mean Qp/Qs was 1.87±0.68 from PC-MRI and 1.93±0.77 from oximetry, respectively.

Discussion

ASD occurs in about 1.5 per 1,000 newborns [13]. Large defects with relevant left-to-right shunting will present in infancy or childhood with failure to thrive, recurrent respiratory infection or murmurs caused by the relative pulmonary stenosis. Medium size ASDs may be symptom-free in childhood although shunting will cause right atrial and right ventricular dilatation. Arrhythmia, reduced exercise capacity, right heart failure and pulmonary hypertension can develop over decades when adequate treatment is delayed [14]. Nowadays, percutaneous device closure of a secundum ASD is the standard to prevent these sequelae after TTE diagnosis and transoesophageal guidance of the procedure.

In this study of children with left-to-right shunts at the level of the atrium and inconclusive TTE, we found free-breathing CMR performed under sedation to be an excellent method for both morphological and haemodynamic assessment, allowing selection of patients in whom transcatheter defect closure was unsuitable. The relatively large study population allowed the inclusion of a number of different kinds of atypical ASD such as inferior caval defects and superior sinus venosus defects in a prospective manner. Cine PC-MRI was found to be a powerful sequence to define the presence, size and position of an atypical ASD. This extends published data using PC-MRI for imaging and sizing of simple secundum ASDs to paediatric patients with atypical ASD [15–18]. Without the use of MR contrast agents, which is even more important because of new data regarding gadolinium-triggered systemic fibrosis [19], there were no false-positive or false-negative diagnoses using inflow MRA for the delineation of normal and abnormal pulmonary and systemic venous connections. Hence, sensitivity and specificity in this respect were 100% as compared with intraoperative findings.

As a result of this study, our hospital practice has changed, such that suspected atypical ASD and PAPVR are routinely evaluated by free-breathing CMR in the setting of a nondiagnostic TTE study. We no longer perform cardiac catheterization or TEE in these patients, unless transcatheter treatment seems a feasible option. Our free-breathing CMR protocol was straightforward with a scan time of usually less than 30 min, including shunt quantification, because in patients with atypical ASD detailed defect sizing was unnecessary and additional sequences could be omitted.

Conclusion

Free-breathing CMR under sedation allows reliable identification of children with atypical atrial-level left-to-right shunt defects in whom transcatheter ASD closure is unsuitable. ASD localization and diagnosis of pulmonary or systemic venous anomalies, including shunt quantification, are possible in less than 30 min.

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