TITLE: Magnetic Resonance Imaging for Patients with Congenital Heart Disease: A Review of the Clinical-Effectiveness

DATE: 03 April 2009

CONTEXT AND POLICY ISSUES:

Cardiac magnetic resonance imaging (CMRI) uses high intensity magnetic fields and radiofrequency to generate 3-dimensional (3D) tomographic images with high resolution and excellent contrast. CMRI is gaining increasing importance in the diagnosis and management of pediatric and adult congenital heart disease (CHD), and other cardiac conditions. Advantages of CMRI are a wide field-of-view, absence of non-ionizing radiation, a variety of imaging sequences, and for some applications, avoidance of intravenous contrast material. Drawbacks are claustrophobia in about 2% of patients undergoing CMRI, the magnetic field applied during the scan, which may preclude use in patients with metallic implants or devices with magnetically or electronically-operated switches, and the risks associated with general anesthesia (if used). Other applications for MRI in CHD are an emerging role in fetal cardiac evaluation, imaging of the brain in newborns with CHD due to risks of brain injury and adverse neurodevelopmental outcomes, and to confirm diagnoses when other imaging methods have limitations or provide inconclusive results.

Alternative cardiac imaging techniques include cardiac catheterization angiography, echocardiography, radionuclide imaging, and cardiac computed tomography. Echocardiography is usually a first-line modality as it is portable, non-invasive, and provides immediate high resolution anatomical and physiologic information. The quality of echocardiography images can be compromised in uncooperative patients or if there are poor acoustic windows; in addition, it is limited in providing the position of extracardiac vascular structures, and in cases of complex intracardiac relationships, it may be difficult to synthesize a 3D image. Cardiac catheterization angiography has traditionally been used as a complementary procedure to echocardiography, as it provides hemodynamic information and enables visualization of the great vessels; however, it is invasive and associated with negative effects (e.g., arterial and venous injury, stroke, bleeding) and requires exposure to radiation.
comparison, CMRI provides both anatomic and hemodynamic information whereas echocardiography and angiography alone do not.

In Canada, CHD affects 1% to 1.2% of live births (i.e., approximately 3,300 to 4,600 new cases each year). Due to advances in pediatric cardiology and cardiac surgery, the number of adults living with CHD is increasing. Approximately 3,000 pediatric and 300 or more adult cardiac surgeries are performed each year in Canada for CHD and it is estimated that the number of adult Canadians living with CHD is between 70,000 and 105,000. Many types of cardiac defects fall under the auspices of CHD, including pulmonary and aortic stenosis, aortic coarctation, septal defects, patent ductus arteriosus, cyanotic defects, Tetralogy of Fallot, transposition of the great arteries, and Ebstein’s anomaly. Treatment of CHD may include medication, cardiac catheterization to repair simple holes in the heart, angioplasty to repair defective valves, surgery, and heart transplantation.

The purpose of this report is to review the evidence for clinical-effectiveness of CMRI compared to echocardiography and angiography for diagnostic evaluation of patients with CHD. This information will be used for future planning and investments with the diagnostic imaging provision in a provincial jurisdiction.

RESEARCH QUESTION:

What is the clinical-effectiveness of magnetic resonance imaging for the evaluation of patients with congenital heart disease?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 4, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology assessment agencies, and a focused Internet search. Results include articles published between 2004 and March 2009 and are limited to English language publications only. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), and controlled clinical trials.

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessments, systematic reviews, and meta-analyses are presented first. These are followed by RCTs and controlled clinical trials.

SUMMARY OF FINDINGS:

The literature search identified one systematic review, one RCT, and 32 controlled clinical trials. No health technology assessments or meta-analyses were identified.

Health technology assessments

No health technology assessments were identified.

Of note, a prioritizing summary produced by the Australia and New Zealand National Horizon Scanning Unit in 2004 on cardiac catheterization guided by MRI in children and adults with CHD was identified. It did not appear that a systematic review of the literature was conducted for the summary. It was noted that since MRI technology is established in Australian hospitals, the
use of MRI for this new indication is unlikely to impact significantly on costs, although there may be additional costs associated with training personnel to use MRI-guided cardiac catheterization, particularly with pediatric cases. It was concluded that there is a small evidence base to support the safety and effectiveness of the use of MRI-guided cardiac catheterization; however, it was recommended that this technology be archived.

Systematic reviews and meta-analyses

A 2007 systematic review by the Swedish Council on Technology Assessment in Health Care that examined various methods of early prenatal diagnosis was identified. The objective of the review was to examine the scientific and economic evidence for the methods currently used, or about to be adopted, for prenatal diagnosis to detect fetal chromosomal and structural abnormalities. Although the methodology description in the review indicated that the identified literature was systematically reviewed and study quality assessed, no specific information on study selection or the numbers and types of included studies was provided. With regard to MRI imaging, it was noted that, from the point of view of safety, MRI has been deemed suitable after the first trimester if other non-ionizing techniques are insufficient or if it can be expected to yield data that would otherwise require exposure to ionizing radiation. This statement is valid for MRI equipment with magnetic field strength up to 1.5 Tesla. It was concluded that MRI may serve as a supplement to ultrasonography for detecting fetal structural abnormalities, primarily in the central nervous system and thorax. The conclusion was assigned an ‘Evidence Grade 3’, which indicates it is supported by at least two studies with medium quality and relevance among the total scientific evidence.

Randomized controlled trials

One prospective, single-centre RCT by Brown et al. (2007) was identified that compared cardiac catheterization and CMRI (including both imaging and gadolinium-enhanced angiography) in 82 patients (2 months to 5 years of age) with CHD and a functional single ventricle. The patients were under consideration for anastomosis of the superior vena cava to the pulmonary artery, or the bidirectional Glenn operation. They were randomized to either cardiac catheterization (n=41) or CMRI (n=41). There were no baseline differences between groups. Outcomes were frequency of adverse events (AEs), hospital length of stay, total hospital charges, and a composite score of clinically successful surgery (i.e., successful bidirectional Glenn procedure comprising no unplanned postoperative interventions or procedures, oxygen saturation ≥75% at the time of hospital discharge, eligibility for discharge from the cardiac intensive care unit by postoperative day 4, and eligibility for hospital discharge by postoperative day 7; and clinical assessment at three months after surgery, including cutaneous oxygen saturation, clinical well-being, and frequency of new diagnoses or reintervention).

There were four treatment crossovers in order to ascertain additional information, three to catheterization and one to CMRI (P=0.62). Catheter interventions (e.g., balloon dilation, coil occlusion, stent) were performed in 17 patients (41%) in the catheterization group. Results demonstrated that catheterization resulted in more minor AEs (78% versus 5%; P<0.001), longer preoperative hospital stays (median 2 days versus 1 day; P<0.001), and higher hospital charges (US$34,477 versus US$14,921; P<0.001). There was one major AE in the CMRI group (a patient with pulmonary atresia palliated by a shunt developed shunt thrombosis during the CMRI scan and required resuscitation, movement to the catheterization laboratory, and stenting of the shunt, which was successful). The operative course and frequency of postoperative complications were similar between the two groups. The proportion of patients who had a
successful bidirectional Glenn operation was also similar (71% versus 83%; P=0.3) between groups. At the 3-month follow-up, there were no differences in clinical status, oxygen saturation, or frequency of reinterventions. This study is limited by being single-centre, which limits generalizability, and its small size and duration (i.e., only three months follow-up). It is possible that with a larger sample size or longer duration of follow-up, differences between treatment groups could be more apparent. The study was also not blinded, although it may be difficult to conduct a blinded trial comparing two different diagnostic methods (and types of image scans) in this patient population. Overall, it was concluded that CMRI is a safe and cost-effective alternative to catheterization in properly selected patients prior to the bidirectional Glenn procedure; however, further studies are needed to determine if there are long-term benefits from certain transcatheter interventions in these patients and the generalizability of the results to other centres.

**Controlled clinical trials**

A total of 32 controlled clinical trials were identified in which CMRI imaging and/or CMRI angiography was compared with cardiac catheterization angiography or echocardiography in patients with CHD. Details of these studies are provided in Appendix 1.

The identified studies compared the diagnostic accuracy of CMRI and/or CMRI angiography with that of conventional cardiac catheterization angiography or echocardiography to detect volume, functional, and anatomical defects in patients with CHD. Studies were small and included heterogeneous patient populations (i.e., wide age ranges of patients with a variety of congenital defects). None of the identified studies were randomized or reported the effect of the diagnostic method on patient outcomes (e.g., AEs, surgical success, length of hospital stay, or mortality). A variety of CMRI (e.g., spin echo, cine, steady state free precession, phase velocity mapping, phase contrast, gadolinium-enhanced) and echocardiography [e.g., 2-dimensional (2D), real-time, 3D (RT3DE), transesophageal, Doppler] imaging protocols were investigated in the studies; however, it is beyond the scope of this review to report results by the specific type of imaging modality used. Nonetheless, wherever possible, if contrast material was used with CMRI imaging or angiography, it is reported in the study details in Appendix 1.

**CMRI compared with angiography**

Nine studies were identified that compared cardiac catheterization angiography with CMRI imaging and/or angiography in patients with a variety of congenital cardiac defects (e.g., Tetralogy of Fallot, aortic coarctation, ventral septal defects, criss-cross heart). The studies included small numbers of patients (n=13 to n=53) across a wide range of ages (1 day to 79 years). Many included a wide patient age range in an individual study (e.g., 5 years to 63 years). All patients in the studies received both diagnostic procedures and the time interval between procedures varied from being done consecutively or on the same day, to up to 12 months apart, or the time interval was not specified. None of the studies were randomized or included healthy subjects as a control group. One study was conducted as a retrospective comparison. The studies were designed to evaluate the diagnostic accuracy of CMRI imaging or angiography compared to conventional cardiac catheterization angiography. Six of the studies reported the degree of correlation between methods to detect specific functional or anatomical abnormalities which ranged from r=0.756 to r=0.97 across studies. One study also reported the extent of agreement between methods for measurement of the pulmonary arteries by Kappa statistics (i.e., ranging from 0.853 to 1.00). Three studies reported the degree of diagnostic concordance between imaging methods (i.e., 77% to 94.4% across studies) and two studies reported the sensitivity (i.e., 93.9% and 97.9%, respectively) of CMRI and other
All studies concluded that CMRI was a non-invasive, feasible, comprehensive technique with diagnostic accuracy comparable to conventional cardiac catheterization angiography. In two studies, CMRI was superior to angiography in delineating small (minor) branches of collateral circulation and in revealing additional extracardiac thoracic vascular abnormalities. In one study, although there was high correlation between CMRI and angiography or all measured aortic diameters in patients with recoarctation of the aorta, there was only moderate correlation between measured pressure gradients and percent stenosis by either method or between methods.

**CMRI compared with echocardiography**

Twenty-three studies were identified that compared echocardiography with CMRI and/or angiography in patients with numerous congenital cardiac defects (e.g., aortic coarctation, aortic stenosis, hypoplastic left heart complex, septal defects, Tetralogy of Fallot, patent foramen ovale, functional single ventricle, persistent fifth aortic arch). The studies included small numbers of patients (n=4 to n=121) over a wide range of ages (i.e., 4 days to 65 years). Many included a wide patient age range in an individual study (e.g., 4 days to 50 years). All patients in the studies received both diagnostic procedures and the time interval between procedures varied from being done consecutively or on the same day, to up to six months apart, or the time interval was not specified. None of the studies were randomized. Three studies included healthy subjects. Four studies were conducted as retrospective comparisons and one study was a pilot study. Similar to the angiography studies, these studies evaluated the diagnostic accuracy of CMRI imaging or angiography compared with various types of echocardiography.

Sixteen of the studies reported the degree of correlation between methods to detect specific functional or anatomical abnormalities which ranged from \( r=0.15 \) to \( r=0.99 \) across studies. One study reported the extent of agreement between methods for the detection of right-to-left shunt by Kappa statistics [0.76; 95% confidence interval (CI): 0.58; 0.94]). Only one study reported the degree of diagnostic concordance between the imaging methods (i.e., concurrence of 100% for diagnosis and 60% for grading of patients). Six studies compared the diagnostic accuracy of real-time, 3D echocardiography (RT3DE) with CMRI and reported correlations of \( r>0.9 \). None of the studies reported on patient outcomes.

Overall, CMRI was found to be a feasible, accurate technique and it was concluded that diagnostic accuracy of CMRI was comparable to echocardiography in 14 studies and superior in eight studies. In one study, that compared CMRI and echocardiography in patients before and after closure of patent foramen ovale, it was concluded that CMRI (echo sequence) was inferior to transesophageal echocardiography in detecting contrast-enhanced right-to-left shunting and atrial septal aneurysm. In eight studies, CMRI was able to detect complex anatomical or functional anomalies that echocardiography could not. The correlation between RT3DE and CMRI for various volume and functional measurements appears to be stronger than for other types of echocardiography.

**Limitations**

No health technology assessments or meta-analyses were identified from the literature search. Only one systematic review was identified; however, its quality could not be assessed due to the
lack of information provided on the methodology used (i.e., no details on the study selection process, number, type, or quality of included studies were provided). The systematic review considered various diagnostic methods for detection of fetal chromosomal and structural abnormalities, one of which was routine ultrasound for detection of congenital heart defects in the fetus. Although the review concluded that MRI may serve as a supplement to ultrasonography for detecting fetal structural abnormalities, it did not appear that MRI was extensively reviewed.

Only one prospective RCT was identified. The trial is limited by being single centre, of small size and short duration, and it was not blinded (although it may be difficult to conduct a blinded study comparing two different imaging methods and types of scans in this patient population).

A large number of controlled clinical trials that compared CMRI imaging and/or angiography with conventional cardiac catheterization angiography and echocardiography were identified. These trials are limited by their small size, heterogeneous patient populations, and other methodological issues. By combining patients with different CHD etiology in these studies, it is possible that the diagnostic performance of CMRI could differ according to each condition because the size and orientation of vessels and structures vary. In some studies, the time interval between the diagnostic procedures compared was as long as six or 12 months. It is possible that the clinical condition of the patient may have changed during these long intervals which could confound interpretation of the diagnostic information. None of the studies were randomized or reported on relevant patient outcomes such as AEs or length of hospital stay or included long-term patient follow-up to determine if clinical outcomes differed between those receiving different diagnostic methodologies. Five studies were retrospective analyses, which make validation of the data and control of extraneous variables difficult. Only four studies that compared CMRI with echocardiography included a control group of patients with normal cardiac anatomy. It follows that the diagnostic performance of CMRI could be overestimated in those studies not including healthy controls because those interpreting the images know that all cases are positive, therefore there is no risk of falsely diagnosing a patient with normal vessels as having a defect. Lastly, the majority of studies were designed to evaluate the diagnostic accuracy of angiography or echocardiography versus CMRI as the ‘gold standard’, thus making it difficult to assess performance of CMRI relative to the other diagnostic modality.

The timeline for the literature search for this report encompassed only the last five years and retrieval was limited to English language studies only. As a result, there may be studies or systematic reviews published prior to this time or in other languages that were not included.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

The highest level of evidence identified to support the clinical-effectiveness of CMRI for diagnostic evaluation in patients with CHD is from one small, prospective, single-centre RCT that compared CMRI and cardiac catheterization angiography in infants undergoing a staged surgical procedure. In this study, CMRI was shown to be associated with fewer minor AEs, shorter preoperative hospital stays, and lower hospital charges than cardiac catheterization angiography. No RCTs comparing CMRI and echocardiography were identified. No health technology assessments or meta-analyses comparing CMRI with either angiography or echocardiography were identified. Although one systematic review was identified, its quality could not be assessed, and its main focus was on methods other than MRI for detecting fetal chromosomal and structural abnormalities.
The bulk of the evidence identified to support diagnostic effectiveness of CMRI imaging and angiography in patients with CHD comes from 32 controlled clinical trials designed to evaluate the diagnostic accuracy of CMRI compared to angiography or echocardiography. Taken as a whole, the studies found CMRI to be a feasible, accurate imaging technique with diagnostic accuracy that was comparable to, or superior to, conventional cardiac catheterization angiography or echocardiography. In many studies, CMRI was able to detect complex anomalies that the other methods could not. With regard to echocardiography, the correlation between RT3DE and CMRI for various volume and functional measurements appeared to be stronger than for other types of echocardiography. None of the identified studies reported on patient outcomes, therefore, it is not known if improved diagnostic accuracy translates into better patient outcomes such as fewer AEs, improved prognosis, reduced use of healthcare resources, or reduced mortality.

In comparison to other cardiac imaging techniques, CMRI is non-invasive and does not require serial exposure to ionizing radiation. This is of particular concern in children with CHD, due to the large number of imaging procedures that they will be required to undergo over their lifetime. Safety of healthcare workers performing imaging scans is perhaps also a consideration, and a technique such as CMRI that does not require radiation provides a definite advantage in this regard. The risks associated with CMRI are minimal although there is a possibility of an allergic reaction to contrast material or intolerance to general anesthesia (if used). Most risks are preventable by thorough patient prescreening (e.g., to identify possible sensitivities or presence of metallic implants or devices).

CMRI can be conducted in conjunction with conventional MRI procedures, and if MRI technology is already established in the healthcare setting, its use for cardiac imaging may not impact significantly on costs. There may be additional costs associated with training personnel to conduct CMRI, especially for CMRI-guided catheterization and/or in pediatric cases. If MRI technology is not already established, the cost of the instrumentation and the training of personnel may limit uptake of CMRI or necessitate that it be reserved for use when other cardiac imaging modalities such as echocardiography or angiography have diagnostic limitations or if their results are inconclusive.

The evidence identified to support clinical-effectiveness of CMRI for diagnostic evaluation of patients with CHD comes from a single RCT that reported patient outcomes. The evidence for diagnostic effectiveness of CMRI is provided by a large number of controlled clinical trials that evaluated the diagnostic accuracy of CMRI relative to conventional angiography or echocardiography. Overall, the results support that CMRI is an accurate, non-invasive, comprehensive cardiac imaging technique that is, at the least, comparable to other methods, although there is evidence that CMRI is superior to other methods for the diagnosis of complex cardiac anomalies. In order to better inform decision or policy makers, well-designed, prospective RCTs that focus on patient outcomes with long follow-up periods that compare CMRI with alternative imaging methods are required to provide strong evidence of the clinical effectiveness of CMRI in patients with CHD.

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REFERENCES:


## APPENDICES:

### Appendix 1: Details of controlled clinical trials

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<th>Publication</th>
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<th>Intervention and Comparator(s) (interval)*</th>
<th>Outcomes</th>
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<td><strong>CMRI compared with angiography</strong></td>
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| Bernardes et al. 2006<sup>31</sup> | Patients with TOF and pulmonary stenosis or atresia (n=30). Age range 1 - 18 years. | CMRI angiography  
Cardiac catheterization angiography (6 days to 12 months) | Assessment of the aorta, pulmonary trunk, patency of the arterial duct, aorto-pulmonary collateral arteries and surgically created shunts. | CMRI had >93% sensitivity, specificity and accuracy for defining presence or absence of, or detecting stenosis or hypoplasia of the pulmonary arteries. More (25 vs. 22) major aortopulmonary collateral arteries were detected with CMRI than conventional angiography. | CMRI is a useful tool in the evaluation of patients with TOF and can be considered a non-invasive alternative to cardiac catheterization in the evaluation of pulmonary vascular anatomy. |
| Durongpisitkul et al. 2008<sup>26</sup> | Patients with TOF including pulmonary atresia and ventricular septal defect (n=43). Age range 2-30 years. | CMRI (Gd-enhanced angiography)  
Cardiac catheterization angiography (within 2 months) | Pulmonary artery measurements | Correlation between methods for measurement of pulmonary arteries ranged from r=0.756 to r=0.844. Agreement between methods ranged from 0.853 to 1.00 by Kappa statistics. | Gd-enhanced CMRI angiography is a feasible, fast, and accurate technique to identify all sources of pulmonary blood supply in complex patients. It can better delineate small (minor) branches of collateral. |
| Eichorn et al. 2006<sup>27</sup> | Patients undergoing assessment for hemodynamically significant recoarctation of the aorta in which conventional cardiac angiography was also done (n=20). Age range 5-25 years. | CMRI (phase-contrast angiography)  
Cardiac catheterization angiography (interval not specified) | Flow measurements | High correlation between CMRI and cardiac catheterization for all measured aortic diameters (r=0.90; P<0.01). Moderate correlation between measured pressure gradients and percent stenosis by either method or between methods. | Measured pressure gradients using CMRI should be used cautiously when assessing patients for recoarctation of the aorta. |
| Esmaeili et al. 2006<sup>28</sup> | Patients with ventral septal defects (n=14). Age range 2 weeks - 15 years | CMRI  
Cardiac catheterization angiography (consecutively) | Flow measurements | Good correlation between methods (r²=0.8; P<0.0001, 95% CI: 0.62; 1.22). | CMRI based shunt measurements are a reliable alternative to the invasive shunt measurement by cardiac catheterization. |
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| Festa et al. 2006<sup>24</sup> | Patients with suspected partial anomalous pulmonary venous return (n=14) underwent both MRI and cardiac catheterization. Age range 5-63 years. | CMRI (Gd-enhanced and phase contrast angiography)  
Cardiac catheterization angiography (interval not specified) | Anatomy findings and quantitation of left to right shunt. | Anatomy findings were concordant in 12/14 (86%) of patients and in all operated patients, surgical findings were concordant with CMRI. Good correlation between methods for shunt evaluation (r=0.85). | CMRI provides a comprehensive evaluation of pulmonary venous return and amount of shunt and can be considered a non-invasive alternative to cardiac catheterization. |
| Ko et al. 2006<sup>32</sup> | Patients with CHD associated with ETVAs (n=53). Age range 1 day-40 months. | CMRI (Gd-enhanced angiography)  
Cardiac catheterization angiography (within 2 weeks) | Number of ETVAs and associated vascular lesions. | ETVAs findings were similar between methods for conotruncal, aortic, venous, or pulmonary vascular abnormalities. Overall sensitivity of CMRI was 97.9% and it revealed 11 additional ETVAs that were not found on cardiac catheterization. | Gd-enhanced CMRI angiography is clinically feasible for detailed anatomic delineation and treatment planning of various ETVAs in children with CHDs. |
| Ming and Yumin 2008<sup>30</sup> | Patients with criss-cross heart (n=18). Age range 5 months - 12 years. | CMRI (contrast-enhanced angiography)  
X-ray angiography (interval not specified) | Diagnosis of criss-cross heart (i.e., atrio-ventricular segmental situs and alignment) | CMRI resulted in the same diagnosis as x-ray angiography in 17/18 (94.4%) of patients. | CMRI was very helpful for the difficult diagnosis of criss-cross heart allowing clear visualization of various malformations. |
| Said et al. 2007<sup>29</sup> | Patients with previously diagnosed coronary artery fistulas (n=13). Age range 30-79 years. | CMRI  
Coronary angiography (interval not specified) | Correlation between diameters calculated by CMRI and coronary angiography. | Coronary fistulas were identified in 10/13 (77%) of patients by CMRI and retrospectively in two (92%) more. Good correlation (r=0.72) was found between methods for measuring fistulous diameters. | CMRI of congenital fistulas with clinically significant shunting is feasible and can provide additional physiologic data complementary to findings of conventional coronary angiography. |
| Valsangiacomo et al. 2005<sup>25</sup> | Patients with CHD (n=20). Age range 1 day-13 years. (21 datasets) | CMRI (contrast enhanced angiography)  
Cardiac catheterization angiography (0.3 to 5 months) | Measures of diameters of aorta and pulmonary arteries. | Correlation between methods was excellent (r=0.97 for both pulmonary arteries and aorta; P<0.0001). | Contrast enhanced CMRI angiography provides accurate quantitative anatomic information which highly agrees with conventional angiography data. |
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<td>Didier et al. 2006&lt;sup&gt;33&lt;/sup&gt;</td>
<td>Patients with native and postoperative aortic coarctation (n=121) divided into Group I (n=55 patients and 55 preoperative CMRI studies) and Group II (n=66 patients and 81 postoperative CMRI studies). Age range 4 days-50 years.</td>
<td>CMRI and CMRI angiography (Gd-enhanced) Echo (interval not specified)</td>
<td>Diagnosis of coarctation Cardiac anatomy</td>
<td>There was a close correlation (r=0.71) between CMRI and Echo pressure gradient estimates across the coarctation in preoperative patients, between CMRI aortic arch diameters and surgery, but poor correlation in isthmic measures. Postoperative anomalies (recoarctation, aortic arch hypoplasia, kinking, pseudoaneurysm) were not found with Echo in 50% of cases.</td>
<td>CMRI is superior to Echo for pre- and post-treatment evaluation of aortic coarctation.</td>
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<td>Grosse-Wortmann et al. 2008&lt;sup&gt;40&lt;/sup&gt;</td>
<td>Neonates (n=20) with borderline hypoplasia of the LV due to aortic stenosis, hypoplastic left heart complex, and unbalanced AVSD. Age range 2-37 days.</td>
<td>CMRI (phase contrast imaging) and CMRI angiography Echo (within 1-15 days of each other)</td>
<td>LVEDV AV annulus MV annulus TV annulus AAO Transverse arch Isthmus</td>
<td>Echo consistently underestimated LV volume and did not correlate with CMRI. Of all Echo measurements, MV z-score was the best predictor of LVEDV by CMRI (r=0.77; P=0.02)</td>
<td>CMRI is feasible in neonates with borderline LV hypoplasia. Echo does not accurately measure LV hypoplasia and may preclude some patients from BV repair identified by CMRI.</td>
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<td>Grothoff et al. 2008&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Patients with surgically-corrected TOF and PR (n=54). Age range 4-53 years.</td>
<td>CMRI (including flow velocity mapping) Echo (within 10 days)</td>
<td>Pulmonary valve insufficiency categorized as mild, moderate or severe.</td>
<td>Differentiation by Echo between the categories of mild, moderate and severe was confirmed by differences in PR fraction measured by CMRI.</td>
<td>Echo can estimate the severity of pulmonary insufficiency after repair of TOF with acceptable results compared to CMRI flow measurement.</td>
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<td>Hui et al. 2005&lt;sup&gt;54&lt;/sup&gt;</td>
<td>Patients with repaired TOF (n=30). Age range 6-45 years.</td>
<td>CMRI Echo (interval not specified)</td>
<td>RV function Echo comparison of modified short axis view and apical four chamber view</td>
<td>Both RV area fractions from the modified short axis view (r=0.674; P&lt;0.001) and apical four chamber view (r=0.512; P=0.025) by Echo correlated with the CMRI derived ejection fraction.</td>
<td>The novel modified short axis view from Echo may be superior to the apical four chamber view for routine follow-up of patients after TOF repair.</td>
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<td>Johnson et al. 2005</td>
<td>Patients with 22q11.2 deletion referred for cardiac evaluation (n=17). Age range 0.6 months -19 years.</td>
<td>CMRI Echo (interval not specified)</td>
<td>Cardiac anatomy</td>
<td>All CMRI findings were abnormal. In 16/17 (94%) patients, Echo was unable to define aortic arch anomalies correctly compared with CMRI.</td>
<td>A wide variety of complex aortic arch anomalies can be accurately defined by CMRI compared with Echo.</td>
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<td>Lai et al. 2008</td>
<td>Patients (n=87) with CHD and RV overload in three groups: Normal RV (Group I, n=31), Repaired TOF (Group II, n=33) and Unrepaired ASD and/or partially anomalous pulmonary venous connection group (Group III, n=23). Age range 14-21 years.</td>
<td>CMRI Echo (2D) (within 6 months)</td>
<td>2D RV linear and cross-sectional area measurements</td>
<td>Most 2D RV parameters were smaller by Echo than CMRI. Correlation was weak between methods for RV volumes (Group I: r=0.15-0.54, Group II: r=0.33-0.61, Group III: r=0.32-0.85). Difference was most pronounced in RV overload groups.</td>
<td>Correlation between 2D RV measurements by Echo and CMRI are weak. 2D Echo assessment of RV appears to be less accurate in patients with CHD and a dilated RV.</td>
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<td>Ley et al. 2007</td>
<td>Patients with mild to severe aortic insufficiency (n=30). Age range 3-27 years.</td>
<td>CMRI (phase contrast) Echo (2D and Doppler) (interval not specified)</td>
<td>LV indices: Clinical severity Valve morphology Regurgitation fraction</td>
<td>Good correlations between methods for ventricular mass, stroke volume and ejection fraction. Good correlation for regurgitation fraction (r=0.7). Different severity groups showed different regurgitation fractions and it was possible to discriminate between severity grades (P=0.01).</td>
<td>Echo and CMRI showed good agreement in evaluating morphology and function of the LV. The clinical severity of the disease can be evaluated correctly by CMRI.</td>
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<td>Lytrivi et al. 2005</td>
<td>Patients with CHD (n=35). Age range 6-42 years.</td>
<td>CMRI Echo (Color Doppler) (same day)</td>
<td>TV: Peak velocity contraction Myocardial acceleration (during isovolumic contraction) Peak systolic velocity Tei index RV ejection fraction by CMRI</td>
<td>Peak systolic velocity and myocardial acceleration during isovolumic contraction by Echo correlated well with RV ejection fraction by CMRI after adjusting for age, RV dilation and pressure overload (r=0.65 and r=0.73, respectively).</td>
<td>Color Doppler Echo imaging indices of TV annular motion are reproducible and provide a potentially useful complementary tool for assessment of RV systolic function in patients with CHD.</td>
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<td>Mohrs et al. 2007&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Patients suspected of having PFO (n=26) or undergoing routine assessment for residual shunt after transcatheter PFO occlusion. Age range 37-65 years.</td>
<td>CMRI (contrast-enhanced) Echo (1 week)</td>
<td>Measures of agreement for shunt by Kappa statistics</td>
<td>Kappa values for agreement of Echo and CMRI in detection of right-to-left shunt was 0.76 (95% CI: 0.58; 0.94) and was better in patients without PFO occlusion (0.91) than after occlusion (0.54)</td>
<td>CMRI cannot replace Echo for exclusion of potential embolic sources, such as thrombus in the left atrial appendage but it can be an attractive non-invasive technique if Echo is technically unfeasible or is declined by patients.</td>
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<td>Mohrs et al. 2005&lt;sup&gt;54&lt;/sup&gt; Pilot study for Mohrs et al. 2007&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Patients (n=15) with PFO and without PFO (n=5). Age range 35-63 years.</td>
<td>CMRI (contrast enhanced) Echo (1 week)</td>
<td>Diagnosis of PFO</td>
<td>Diagnosis of all patients was correct. Grading was identical in 60% of patients and differed by one score in 20%. Overall there was good correlation of grading scores (r=0.7; P&lt;0.05). Atrial septal aneurysm was found in 3/15 (20%) patients with PFO.</td>
<td>CMRI is a new non-invasive technique to detect PFO and atrial septal aneurysm. Grading is possible but warrants further investigation regarding its predictive value and impact on treatment strategies.</td>
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<td>Muthurangu et al. 2005&lt;sup&gt;53&lt;/sup&gt;</td>
<td>Patients with hypoplastic left heart syndrome after the Norwood operation and prior to bidirectional cavopulmonary connection surgery (n=37). Age range 120-242 days.</td>
<td>CMRI and CMRI angiography Echo (consecutively)</td>
<td>Ventricular function Valvar regurgitation</td>
<td>CMRI exhibited high sensitivity and specificity for identification of neoaortic (86% and 97%) and left pulmonary artery obstruction (100% and 94%). Echo exhibited poor sensitivity, but high specificity (i.e., 42% and 97% and 20% and 100% for neoaortic and left pulmonary artery stenosis). There was general agreement between methods for measures of ventricular function and valvar regurgitation although patients with good function on Echo displayed a wide range of ejection fractions.</td>
<td>CMRI can be used to define ventricular and valvar function and vascular anatomy in infants with hypoplastic left heart syndrome after the Norwood operation.</td>
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<td>Niemann et al. 2007</td>
<td>Patients with major CHD (n=16) and normal cardiac anatomy (n=14). Age range 4-52 years.</td>
<td>CMRI + Echo (RT3DE) (consecutively)</td>
<td>RV size and function</td>
<td>Both methods correlated closely for RV ejection fraction (r=0.91), RV end-diastolic volume (r=0.99) and end-diastolic volume (r=0.98).</td>
<td>RT3DE Echo is a robust, accurate, and reproducible modality for RV volume and function measurements.</td>
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<tr>
<td>Nusser et al. 2006</td>
<td>Patients undergoing transcatheter closure of PFO (n=75). Age range 36-61 years.</td>
<td>CMRI (contrast-enhanced) + Echo (interval not specified)</td>
<td>Atrial left to right shunting Detection of ASA</td>
<td>Prior to PFO closure, ASA was detected by CMRI in 37.3% of cases compared with 62.7% by Echo. Contrast-enhanced right to left shunting was detected by CMRI in 66.6% of cases with moderate to severe shunts seen with Echo, but only in 18.8% of mild shunts seen with Echo.</td>
<td>This CMRI technique (echo sequence) is inferior to Echo in detection of contrast-enhanced right to left shunting and identification of ASA.</td>
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<tr>
<td>Piaw et al. 2006</td>
<td>Patients scheduled for ASD closure (n=12). Age range 11-60 years.</td>
<td>CMRI (including phase contrast CMRI) + Echo (between 2-12 weeks)</td>
<td>ASD measurements</td>
<td>Echo significantly correlated with MRI (r=0.69 and r=0.59; P&lt;0.04). Bland-Altman analysis also determined general agreement between methods.</td>
<td>ASD sizing by CMRI correlated well with Echo estimations. Phase-contrast MRI provided additional information on ASD shapes and proximity to adjacent structures.</td>
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<td>Pemberton et al. 2008</td>
<td>Patients with aortic coarctation (n=2) and healthy volunteers (n=12). Age range 9-51 years.</td>
<td>CMRI (phase-encoded) + Echo (RT3DE) (consecutively)</td>
<td>Stroke volume</td>
<td>Correlation between two methods was $r^2=0.83$. Mean (SD) difference of 5.7 (8.75) mL with RT3DE underestimating stroke volume compared to CMRI.</td>
<td>RT3DE can be used to calculate stroke volumes but slightly underestimated the result compared with the ‘gold standard’ CMRI.</td>
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<td>Puchalski et al. 2008</td>
<td>Patients with CHD who underwent RV outflow tract reconstruction or pulmonary valve replacement (n=48). Age range 1.9-32.4 years.</td>
<td>CMRI (phase-contrast) + Echo (within 3 months)</td>
<td>PR fraction</td>
<td>Best correlations between methods were for PR jet width/annulus ratio (r=0.62) and diastolic flow reversal in pulmonary arteries (r=0.66); both P&lt;0.001.</td>
<td>As a surrogate, the most valuable Echo measure was PR jet width/annulus ratio combined with diastolic flow reversal for assessing PR severity following repair, but it does not replace the importance of CMRI evaluation.</td>
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<td>Puchalski et al. 2007</td>
<td>Patients with right-sided CHD (n=22). Age range 5-32 years.</td>
<td>CMRI Echo (eyeball method) (within 6 months)</td>
<td>RV size and systolic function</td>
<td>Reliability of Echo ‘eyeball method’ was ‘slight’ for identifying a severely dilated RV and for moderately to severe diminished RV systolic function was ‘fair’. Echo inter-rater agreement was poor for both outcomes.</td>
<td>Echo ‘eyeball method’ to estimate RV size and function has limitations when compared with CMRI, specifically due to variability between echocardiographers.</td>
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<td>Riehle et al. 2008</td>
<td>Patients with CHD (n=12). Age range 1-33 years.</td>
<td>CMRI Echo (RT3DE) (same day)</td>
<td>LV indicies: EDV ESV Stroke volume Ejection fraction Mass</td>
<td>All RT3DE volumes correlated strongly with CMRI (r=0.93 to 0.99); P&lt;0.001. Ejection fraction had a lower correlation (r=0.69); P=0.013.</td>
<td>Combined RT3DE acquisition and analysis machines can accurately assess the LV in patients with CHD, perhaps obviating the need for CMRI in some cases.</td>
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<td>Soriano et al. 2008</td>
<td>Patients with a functional single ventricle (n=29). Age range 0.1 - 98 months. (27 datasets were optimal for 3D Echo assessment)</td>
<td>CMRI Echo (RT3DE) (consecutively)</td>
<td>Single ventricle volumes, mass and ejection fraction.</td>
<td>3D Echo end diastolic volume correlated well (r=0.96) but was smaller than CMRI (9%; P&lt;0.01) as was ejection fraction (11%; P&lt;0.01). There were NS differences in measures of end-systolic volume and mass.</td>
<td>RT3DE measurements of mass and volumes compare well with those obtained by CMRI. 3D Echo will provide an important modality for serial analysis of ventricular size and performance in these patients.</td>
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<tr>
<td>Schwerzmann et al. 2007</td>
<td>Patients with repaired TOF (n=57). Age range 25-48 years.</td>
<td>CMRI Echo (within 6 months)</td>
<td>MPI to evaluate RV function.</td>
<td>Negative linear correlation between MPI and RV ejection fraction by CMRI (r=0.73; P&lt;0.001)</td>
<td>The Doppler-derived MPI is a simple and reliable method to evaluate RV systolic function in adults with repaired TOF.</td>
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<tr>
<td>Van den Bosch et al. 2006</td>
<td>Patients with CHD (n=32). Age range 19-51 years. (Data sets were feasible in 29/32 (91%) of patients)</td>
<td>CMRI Echo (RT3DE) (same day)</td>
<td>LV volumes and function</td>
<td>Good correlation between RT3DE with manual border detection and CMRI for LVEDV (r=0.97), LVEF (r=0.98) and LV ejection fraction (r=0.94)</td>
<td>RT3DE is feasible for volumetric analysis of the abnormal LV allowing accurate determination of LV volume and ejection fraction compared with CMRI.</td>
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<tr>
<td>Van den Bosch et al. 2006</td>
<td>Patients with CHD (n=20). Age range 19-49 years. (Data sets feasible in all patients)</td>
<td>CMRI Echo (RT3DE) (same day)</td>
<td>LV mass</td>
<td>Good correlation was observed between RT3DE data with sufficient image quality and CMRI (r=0.98).</td>
<td>Assessment of LV mass from RT3DE data is feasible in patients with CHD.</td>
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<td>Zhong et al. 2007</td>
<td>Patients with persistent fifth aortic arch (n=4). Age range 5 months -9 years</td>
<td>CMRI (contrast-enhanced angiography)</td>
<td>Diagnosis of persistent fifth aortic arch.</td>
<td>Echo detected an aberrant vessel with uncertain etiology in 2 patients and coarctation in the other 2 patients. Only 1 patient was diagnosed with aortic arch interruption. CMRI angiography clarified uncertain Echo findings enabling correct diagnosis.</td>
<td>Contrast-enhanced CMRI angiography is a safe, accurate and fast imaging technique for evaluation of persistent fifth aortic arch and may obviate the need for conventional cine angiography.</td>
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AAO=ascending aorta; ASA=atrial septal aneurysm; ASD=atrial septal defect; AV=aortic value; AVSD=atrioventricular septal defect; BV=biventricular; CHD=congenital heart disease; CMRI=cardiac magnetic resonance imaging; Echo=echocardiography; EDV=end diastolic volume; ESV=end systolic volume; ETVAs=extracardiac thoracic vascular abnormalities; Gd=Gadolinium; LV=left ventricle; LVEDV=left ventricular end diastolic volume; LVESV=left ventricular end systolic volume MPI=myocardial performance index; MV=mitral value; NS=not significant; PFO=patent foramen ovale; PR=pulmonary regurgitation; RT3DE=real-time, 3-dimensional, echocardiography; RV=right ventricle; TOF=Tetralogy of Fallot; TV=tricuspid valve; 2D=Two dimensional; 3D=Three dimensional

*Time interval between diagnostic procedures