Utility of adenosine stress perfusion CMR to assess paediatric coronary artery disease

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Abstract

**Aims** Cardiovascular magnetic resonance (CMR), using adenosine stress perfusion and late-gadolinium enhancement (LGE), is becoming the ‘gold standard’ non-invasive imaging modality in the assessment of adults with coronary artery disease (CAD). However, despite its proved feasibility in paediatric patients, clinical utility has not been demonstrated. Therefore, this study aims to establish the role of adenosine stress perfusion CMR as a screening test in paediatric patients with acquired or congenital CAD.

**Methods and results** A total of 58 paediatric patients underwent 61 consecutive clinically indicated coronary artery assessments for diagnostic and clinical decision-making purposes. The diagnosis was based on X-ray or computed tomography coronary angiography for anatomy, adenosine stress CMR imaging for myocardial perfusion and LGE for tissue characterization. Two studies were aborted because of unwanted side effects of adenosine stress, thus 59 studies were completed in 56 patients [median age 14.1 years (interquartile range 10.9–16.2)]. When compared with coronary anatomical imaging, adenosine stress perfusion CMR performed as follows: sensitivity 100% (95% confidence interval, CI: 71.6–100%), specificity 98% (95% CI: 86.7–99.9%), positive predictive value (PPV) 92.9% (95% CI: 64.2–99.6%), and negative predictive value 100% (95% CI: 89.9–100%).

**Conclusion** In paediatric CAD, adenosine stress perfusion CMR imaging is adequate as an initial, non-invasive screening test for the identification of significant coronary artery lesions, with anatomical imaging used to confirm the extent of the culprit lesion.

**Keywords** Paediatrics, Coronary artery disease, Cardiovascular magnetic resonance imaging, Adenosine perfusion imaging
**Introduction**

Although rare, coronary artery disease (CAD) does occur in children, often requiring robust imaging techniques for diagnostic and management purposes. Known aetiologies in paediatrics include surgical re-implantation of the coronary arteries [e.g. following arterial switch operation (ASO) for transposition of great arteries (TGA)], repaired anomalous origin of the coronary artery (e.g. anomalous left coronary artery from right pulmonary artery, ALCAPA), and acquired coronary artery problems such as Kawasaki disease and other vasculitidis. In adults, coronary artery visualization is performed by invasive X-ray coronary angiography (XCA) and computerized tomographic coronary angiography (CTCA) as the current best available methods. In addition, assessment of the significance of any coronary lesions on myocardial perfusion can be performed using stress echocardiography and/or single photon emission computed tomography (SPECT). Increasingly however, adenosine stress perfusion cardiovascular magnetic resonance (CMR) imaging is emerging as the ‘gold standard’ for assessing reversible myocardial perfusion. In children, the assessment of CAD is less straightforward. Most tests are associated with ionizing radiation exposure and those that assess myocardial perfusion suffer from poor resolution in smaller subjects. Furthermore, only two studies have assessed the feasibility of adenosine stress perfusion CMR in children with congenital and acquired heart disease. Hence, in this current study, we aimed to assess the role of adenosine stress perfusion CMR as a screening test for significant coronary artery lesions in paediatric patients with acquired or congenital CAD.
Methods

Study population

Between August 2009 and May 2014, a total of 58 consecutive paediatric patients underwent 61 clinically indicated CMR scans for assessment of CAD at a single paediatric centre. This included 23 patients who were referred for clinical assessment by their responsible cardiologist and 35 TGA patients post ASO referred for routine coronary artery assessment. The study had Institutional ethical approval and all parents/guardians, and where appropriate patients, gave informed consent for the use of their clinical data. All subjects underwent a CMR to assess reversible myocardial perfusion using adenosine stress imaging and late gadolinium enhancement (LGE) to assess fibrosis. There were no contraindications to adenosine use in all subject enrolled in this study. Patients' coronary artery anatomy was evaluated using either invasive XCA or CTCA.

CMR imaging

All CMR images were acquired using a 1.5T magnet (Avanto; Siemens Medical Systems, Erlangen, Germany).

Stress perfusion CMR imaging

All patients were instructed not to consume caffeine-containing products for 24 h prior to adenosine stress testing. Following insertion of a wide bore cannula appropriate for patient age and size, preferable sited on the antecubital vein, myocardial perfusion was performed under pharmacological stress with intravenous adenosine—dose = 140 μg/kg/min. The targeted cardiovascular stress response was a 20% increase in heart rate and, in cases of no significant heart rate response; adenosine was infused continuously for 4 min while monitoring the patient for side effects. Myocardial signal increase during first-pass was visualized during a bolus injection of gadolinium (Dotarem®, gadoterate meglumine, Gd-DOTA, Guerbet, Paris, France) at 0.1 mmol/kg, at a flow rate of 2–5 mL/s, followed by a saline flush of 25 mL at the same flow rate. Short-axis images were acquired with a saturation-recovery, spoiled gradient echo sequence in at least 3 slices per heart beat (slice thickness 8 mm). Imaging parameters were as follows: TI 200 ms, TR 260 ms, TE 1.1 ms, flip angle 12°, matrix 192 × 144, rectangular field of view of 187 × 250 mm, number of excitations 1, and acquisition every RR interval. Data from 50 cardiac cycles were acquired. Patients were asked to hold their breath for as long as possible, then revert to shallow respiration during this acquisition, or, for those imaged under general anaesthesia, data were acquired during suspended mechanical ventilation. The perfusion sequence was repeated at rest with the same parameters and bolus injection of gadolinium 15 min after the heart rate had return to baseline following cessation of the adenosine stress perfusion scan.

Late gadolinium enhancement imaging

LGE was performed in the long- and short-axis planes, using an inversion recovery prepared gradient recalled echo sequence, 10–15 min after injection of gadolinium (Dotarem®, gadoterate meglumine, Gd-DOTA, Guerbet, Paris, France at 0.1 mmol/kg). The inversion time was adjusted (250–350 ms) in order to null the normal viable myocardium. Acquisition parameters were as follows: TR 2.9, TE 1.3, flip angle of 50°, slice thickness of 8–10 mm, matrix 256 × 192, and field of view of 350 mm. All LGE images were interpreted according to the AHA 17-segment model.12

Coronary angiography
Coronary artery anatomical imaging was performed either by invasive XCA or CTCA. Choice of anatomical imaging modality was driven by diagnosis, age of the patient and occasionally referring clinician.

**X-ray coronary angiography**

As per institutional policy all invasive coronary angiograms were carried out under general anaesthetic. Once in the catheterization laboratory (Artis biplane system Siemens Medical Solutions, Erlangen, Germany), vascular access was achieved through the femoral artery. Anangiographic catheter was then advanced into the aortic root, where selective coronary intubation was achieved and angiography was performed by hand injection of a non-ionic, iodinated contrast agent (Omnipaque 240–350 mg iodine/mL, Nycomed, Oslo, Norway) into the selected coronary artery. In small children, or in those in which anatomy precluded selective cannulation of the coronary arteries, an angiographic catheter was advanced into the aortic root where the contrast agent was injected into the aortic root at a dose of 1–1.5 mL/kg. Some patients \( n = 9 \) had a combined CMR and XCA using our combined X-ray/CMR hybrid lab. These subjects were initially placed in the scanner for the CMR study, and then transferred to the biplane catheter laboratory with the use of a mechanized sliding table (Miyabe, Siemens Medical Solutions) that allows bidirectional transfer between the CMR scanner and the catheterization laboratory.\(^{13}\)

**Computed tomography coronary angiography**

All computed tomography (CT) examinations were performed with a prospective, ECG-triggered protocol using a Dual-source 64-row CT (Somatom Definition, Siemens Medical Solution, Forchheim, Germany). The scanning direction was craniocaudal, and all studies were performed without sedation and without heart rate lowering medications. The CT scanning was performed with intravascular administration of non-ionic, iodinated contrast agent (Omnipaque 350 mg iodine/mL, Nycomed, Oslo, Norway) at 2 mL/kg (maximum dose 100 mL), delivered via a pressure injector followed by a chaser bolus of 10 mL saline into an antecubital vein.

**Diagnostic image quality for CMR and CTCA**

Diagnostic image quality was assessed by two cardiovascular imaging consultants independently and blinded to the imaging techniques used. Assessment was based on a four-point scoring system. The four-grade scoring system used for the evaluation of the images was as follows: 1 = excellent image quality and no artefacts, 2 = Good image quality, minor artefact and mild blurring, 3 = poor quality but diagnostic, 4 = non-diagnostic, 0 = absent structure. The scoring system was based in part on the American Heart Association (AHA) 17 segments and was adjusted for this study population of patients.\(^{14}\) Where applicable each consultant added a comment on the presence/absence and possible cause of any coronary artery stenoses. Limits of agreement on image quality score between the two independent consultants were assessed using Kappa analysis.

**Image post-processing and analysis**

Image analysis was performed using open-source software OsiriX (OsiriX Foundation, Geneva, Switzerland). Significant coronary artery stenosis was defined as a luminal narrowing of the coronary artery of ≥50%. Perfusion abnormalities were assessed qualitatively by visual comparison of the contrast enhancement in different myocardial regions and the final diagnosis was reached by consensus. First-pass and LGE images were reviewed as cine loops and standalone images, respectively. A significant perfusion deficit was present if gadolinium wash-in was delayed in the
subendocardial layer or transmurally, inducing a signal reduction in the myocardium that persisted throughout the entire first-pass of gadolinium.

**Statistical analysis**

Categorical variables are expressed as counts and percentages, and continuous variables as median and range, mean ± standard deviation (SD), accordingly. Where there were reference standards, using a two-way contingency table, diagnostic performance of adenosine vasodilator stress is assessed and percentages are presented with 95% CI.
Results

There were 18 females and 40 males, median age 14.1 years (IQR 10.9–16.2) (range 3.3–18.5 years), BSA 1.32 ± 0.5 m². Table 1 shows the cardiac diagnoses for these patients. Fifty-six of the 58 patients completed the protocol. Two studies were terminated due to unwanted adenosine-related side effects: one patient had extreme chest discomfort and nausea, and the other had atrial tachycardia during the adenosine infusion, with symptoms subsiding in both patients soon after stopping the infusion.

The remaining 56 patients completed 59 CMR perfusion and tissue characterization studies with anatomical imaging provided by XCA in 23 and CT in 36 studies. For the 36 patients imaged with CTCA, 34 were TGA post ASO, 1 was ALCAPA post repair and the other was being evaluated for Kawasaki disease. The remaining diagnoses were all imaged using XCA. Two patients had repeat perfusion and tissue characterization studies performed with concomitant X-ray angiography, and one of these two patients had a further repeat study after coronary intervention. CTCA images were of good to excellent diagnostic quality. There was good agreement between the two independent reviewers as demonstrated by Kappa analysis in Table 2. The resting (baseline) haemodynamic parameters were a heart rate (HR) = 94 ± 14/min, systolic blood pressure (SBP) = 108 ± 11 mmHg, and diastolic blood pressure (DBP) = 65 ± 12 mmHg. During the adenosine-induced hyperaemia HR = 118 ± 8/min, SBP = 93 ± 11 mmHg, and DBP = 58 ± 15 mmHg.

CMR perfusion and LGE

Of the 59 successful perfusion scans, 14 (24%) had inducible ischaemia on adenosine stress perfusion CMR mainly involving the subendocardial layer. All studies with inducible ischaemia are displayed in Table 3, together with associated coronary lesion as diagnosed on XCA or CTCA, the presence of LGE on tissue characterization and clinical decisions taken at a departmental joint cardiac meeting. One of the 14-perfusion studies with inducible ischaemia was found to be a false positive—patient 11 in Table 3 denoted by italics. This patient had a perfusion defect on stress perfusion CMR, but on XCA assessment, the coronary arteries were completely patent (Figure 1). Two of the 14 positive inducible ischaemic scans were for follow-up imaging of a known lesion in previously scanned patient. This patient was scanned three times, firstly, as a referral of known Kawasaki disease with chest pain on exertion and ECG changes; secondly, as a combined imaging and interventional procedure to confirm the extent of the lesion and perform percutaneous coronary intervention under the same general anaesthetic; and thirdly, to confirm resolution of reversible ischaemia a few months following the percutaneous intervention (Figure 2). This patient is denoted by (*) in Table 3. Of the remaining patients with inducible ischaemia, there were two patients with Kawasaki disease: one of these patients had multiple aneurysms of the right and left coronary arteries at XCA (Figure 3). This patient is under close follow-up on oral anticoagulation. Four patients with inducible ischaemia were repaired ALCAPA patients, all of whom had LGE. There were two positive perfusion studies in patients with ASO post TGA anatomical repair. Both patients had mild left main stem stenosis on anatomical imaging: one on XCA and one on CTCA. There was one positive study in a patient who had an atretic left main stem on XCA and has had the recommended surgical revascularization done with repeat perfusion scan showing complete resolution. Finally, there was one positive perfusion study due to exogenous homograft compression. This was a patient with Takayasu’s arteritis, and homograft repair that was compressing the previous LIMA graft, but on XCA the native left coronary artery had recanalized. On myocardial tissue characterization, LGE was detected in eight scans, all involving the subendocardium. Six of these are listed in Table 3 with concomitant inducible ischaemia. The two scans
with LGE and no inducible ischaemia were a previous ALCAPA with a classical distribution of LGE involving the basal, antero-lateral LV wall, and papillary muscles and a patient with previous left main stem atresia after surgical repair.

Left ventricular function was preserved in all but three patients (LVEF = 63.6 ± 7.8%). The three individuals with suppressed LV function on CMR were, one patient post cardiac transplant for cardiomyopathy assessment with EF = 52%, and two ALCAPA post repair patients, each with EF = 54%.

**Diagnostic accuracy**

The diagnostic performance of adenosine stress perfusion CMR in our patients was based on positive inducible ischaemia in the presence of a coronary artery lesion at XCA or CTCA. Positive adenosine stress perfusion CMR and anatomical coronary imaging were concordant in 13 studies and discordant in 1 (Figure 1 and Table 3), whereas 44 patients had true negative tests based on perfusion and anatomical imaging. Therefore, the effectiveness of adenosine stress perfusion CMR, compared with the detection of significant anatomical coronary artery disease by XCA or CTCA was as follows: sensitivity 100% (95% CI: 71.6–100%), specificity 98.0% (95% CI: 86.7–99.9%), positive predictive value (PPV) 92.9% (95% CI: 64.2–99.6%), and negative predictive value (NPV) 100% (95% CI: 89.9–100%).
Discussion

This study explores the applicability of adenosine stress perfusion CMR imaging in children with coronary artery disease, and follows on from two previously published paediatric feasibility studies. In this study, we used both XCA and CTCA for anatomical evaluation of the coronary artery tree. XCA has long been used as the conventional ‘gold standard’ in paediatric cardiology with plausible success, despite concerns of radiation exposure and risk of chromosomal damage leading to development of malignancies. Previously, the role of CT angiography in children was confined to detailing extravascular structures. However, the introduction of heart rate gated low dose CT scans has expanded the role of CT to the evaluation of the whole coronary tree for anomalous origins, course and termination with resounding success. Its feasibility has recently been tested by Ou and colleagues in a study examining coronary arteries of a group of ASO survivors with impressive results. They compared conventional CTCA with XCA, and showed CT to have sensitivity, specificity, and PPV of 100%. However, in small children with minute cardiac chambers and even smaller coronary arteries, compounded by very fast heart rate, XCA remains superior to CTCA, as it suffers fewer artefacts.

Our study demonstrates that adenosine stress perfusion CMR is a good test for identifying significant perfusion defects in children with coronary artery disease, with a 100% NPV. This suggests that it can be used as a screening imaging biomarker for paediatric patients referred with suspected coronary artery disease. The high accuracy we report with sensitivity of 100% and specificity of 98% is in keeping with that reported in a paediatric adenosine stress feasibility study by Beuchel and colleagues, and in adults with congenital heart disease stressed with either adenosine or dipyridamole. However, the high NPV demonstrated in our study is of clinical importance, as some of the paediatric patients referred might not present with classical symptoms of myocardial ischaemia.

There was one false-positive adenosine stress perfusion CMR in this study. In the adult literature, false-positive results have been attributed to a number of reasons such as delayed enhancement of a region of the heart. These occur in instances where microangiopathies or coronary grafts are present causing delayed passage of the contrast by a few heartbeats during stress. Interestingly, our false-positive case occurred in a patient with repaired double outlet right ventricle (DORV) and possible abnormal ventricular arterial (V-A) coupling affecting coronary artery perfusion despite the patency coronary artery tree at coronary angiography. DORV, like all other conotruncal anomalies suffers from poorly distensible aorta, which behaves like the aorta of hypertensive adults, hence the abnormal V-A coupling. Abnormal coronary artery flow in the face of abnormal coupling has been suggested in hypertensive adult patients, which may have accounted for the false-positive result in this repaired DORV patient.

The TGA post ASO group in this study constitutes an interesting cohort, with regard to understanding the fate of re-implanted coronary arteries late after ASO. A bimodal nature to developing coronary artery stenosis with an early peak related to initial learning curve on the surgeons hands and a second peak mostly due to growth-related stretch or progressive fibrocellular intimal thickening have been suggested. However, to date there are no follow-up guidelines for imaging and treating coronary arteries post ASO. Our findings of two patients having inducible ischaemia in this study demonstrate that even in asymptomatic patients adenosine stress perfusion CMR can detect significant coronary artery lesions. Lack of classical symptoms of myocardial ischaemia in these patients may be attributed to development of collaterals. In a study examining asymptomatic teenage ASO survivors with adenosine stress perfusion, no inducible ischaemia was
Suggesting that perhaps anatomical imaging of the coronary tree should be the first line of investigation before subjecting these patients to stress perfusion imaging. Another intriguing group of patients we evaluated in this study is the ALCAPA post re-implantation, which yielded classical findings of basal, antero-lateral late gadolinium enhancement pattern, including the papillary muscles is in keeping with the previously published literature.

In this study, the Kawasaki disease group of patients offers peculiar characteristics of coronary perfusion abnormalities that do not fit into the conventional interpretation of both anatomical and functional images. This in part is due to the diverse nature of coronary sequelae of this vasculitidis, presenting as stenotic, aneurysmal, ectasia, or even coronary microvascular dysfunction. The mechanism of action of adenosine in perfusion imaging is through its vasodilator effect on the coronary arteries. Previous nuclear imaging studies have showed decrease hyperaemia with impaired vasodilatory capacity in patients with Kawasaki disease even with normal coronary tree. In 14 patients with convalescent Kawasaki disease, Bratis and colleagues showed that first pass perfusion CMR had an impaired myocardial perfusion reserve resulting from coronary microvascular dysfunction. Our findings in Kawasaki disease show that adenosine stress perfusion CMR can be used to monitor the response to therapeutic interventions in these patients, suggesting that it might be added to the management guidelines for Kawasaki disease. We believe that it is not only the flow limiting stenoses and microvascular-related abnormal vasodilatory response that are responsible for perfusion defects in these patient, but also seeding of micro thrombi from these aneurysms complicating with microvascular obstructions.

Paediatric patients, and in particular those with congenital heart disease, are often subjected to serial imaging as part of their disease work-up. Therefore, an ideal screening imaging biomarker for them should be non-invasive, with no ionizing radiation exposure: adenosine stress perfusion CMR seems well suited for this role. Moreover, the multiparametric nature of CMR in these patients ensures completeness and quality of data. Apart from determining the presence or absence of a coronary lesion with associated ischaemia, global ventricular function, and the presence of a pre-existing infarct can be diagnosed.

Technical challenges

Although CMR adenosine stress perfusion can be performed routinely in adults with CAD, in many centres, young children present a number of technical challenges that can be resolved by appropriately adapting imaging parameters to the individual patient. It should be stressed that CMR stress perfusion can be used as both a diagnostic and prognostic tool in adult patients with known or suspected coronary disease as demonstrated by published large population studies. It is therefore no surprise that most of the imaging parameters and gadolinium contrast dose used in paediatric studies are adapted from adult studies. Of interest, the aetiology of CAD in adults is mainly due to atherosclerotic disease; as opposed to younger patients whose coronary artery insufficiency may be the result of different pathological processes, such as inflammatory, compressive, torsion, and postsurgical translocation. Therefore, it is difficult to extrapolate the vast experience of adenosine stress perfusion MRI in adult to children without technical adjustments.

Firstly, poor compliance and inability to breath-hold are among the well-known problems associated with imaging small children. To overcome this limitation we imaged all children younger than 8 years old and those requiring invasive catheterization under general anaesthesia with mechanical ventilation, and suspended breaths during image acquisition. Other main concerns, especially with very small children (youngest in our group being 3.3-years), are high baseline heart rate, heightened heart rate response to adenosine and small body size, and subsequently the heart size. Measures to
rectify these limitations include vendor-specific-automated R-wave detection allows for vector-cardiographic triggering, which in turn allows CMR imaging of fast heart rates without having to manipulate the scanner. In this study, a dummy sequence run was performed in all subjects without contrast and stressor in order to assess the vigour of ECG gating at high heart rate prior to the actual stress perfusion imaging. For adequate spatial resolution that is necessary for adequate transmural discrimination between subendocardial and subepicardial perfusion defects, field of view (FOV) was lowered to allow for wrap while sparring LV walls for analysis and slice thickness reduced to 8 mm. Furthermore, the presence of artefacts hampers interpretation and analysis of cardiac MR perfusion images, especially in children with small hearts. Larger susceptibility artefacts have been shown to cause trouble in low spatial resolution. Dark rim artefacts are known to be problematic due to high gadolinium contrast in the blood pool, and can be resolved by increasing spatial resolution in the phasing code direction.

With regard to future perspective, a number of multicentre studies have shown that perfusion CMR can be used as first-line modality to work up patients with known or suspected CAD in the adult population. Adult data on patients with abnormal autonomic regulation of coronary arteries secondary to diabetes mellitus, and those with microvascular insufficiency as a result of syndrome X suggest that this technique has a future in transplant arteriopathy patients and in patients with certain types of cardiomyopathy.

**Study limitations**

This is a small study compared with adult studies on the subject, but it must be remembered that paediatric CAD has a different aetiology and pathophysiology compared with adults, and thus we cannot directly infer findings in adult literature to this group of patients. The second limitation of this study is the heterogeneous nature of the aetiological substrates. Unlike in adult CAD, lesions in paediatric CAD may range from stenotic, to compressive, kinking, and aneurysmal in nature, suggesting a need for a diverse treatment strategy. Additionally, no single ‘gold standard’ coronary anatomy imaging modality was used, though both X-ray and CTCA have now been well validated in adults with CAD. After ethical considerations prior to the start of the study, it was not possible to offer all our patients X-ray angiography, and CT angiography was felt to be an acceptable alternative given the adult literature on its accuracy for detecting CAD. Additional limiting factor in imaging young children is very fast heart rate, which causes susceptibility to limited temporal resolution and need for high spatial resolution for optimal image quality. Therefore, imaging strategies applicable to bigger children cannot be directly extrapolated to younger children. Local expertise should help guide the imaging team as to which modalities to use for optimal image quality.
Conclusions

This study demonstrates the utility of adenosine stress perfusion CMR imaging as a screening tool in paediatric patients with acquired and congenital coronary artery disease. We have shown that adenosine stress perfusion is highly sensitive, and specific with a 100% NPV in this small group of patients. We have demonstrated that anatomical imaging of the coronary arteries can be used to confirm the location and extent of the culprit lesion. Overall, this approach was used to play a significant role in guiding the clinical decision making process in paediatric patients with suspected CAD.
Acknowledgements

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Conflict of interest: none declared.
References


Tables

Table 1
List of cardiac diagnosis for patients referred for adenosine stress perfusion CMR

<table>
<thead>
<tr>
<th>Cardiac diagnosis</th>
<th>( N = 58 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALCAPA post coronary re-implantation</td>
<td>5</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>8</td>
</tr>
<tr>
<td>TGA post ASO</td>
<td>35</td>
</tr>
<tr>
<td>DCM</td>
<td>3</td>
</tr>
<tr>
<td>DCM post cardiac transplant</td>
<td>1</td>
</tr>
<tr>
<td>Congenital atresia of LMS</td>
<td>2</td>
</tr>
<tr>
<td>Bicuspid aortic valve post CoA repair</td>
<td>1</td>
</tr>
<tr>
<td>Aortic stenosis post Ross procedure</td>
<td>1</td>
</tr>
<tr>
<td>DORV post repair</td>
<td>1</td>
</tr>
<tr>
<td>Takayasu's arteritis treated with Ross</td>
<td>1</td>
</tr>
</tbody>
</table>

- ALCAPA, anomalous left coronary artery from the right pulmonary artery; TGA, transposition of great arteries; ASO, arterial switch operation; DCM, dilated cardiomyopathy; LMS, left main stem; DORV, double outlet right ventricle; CoA, coarctation of the aorta.

Table 2
Image quality score and kappa analysis

<table>
<thead>
<tr>
<th>Segment</th>
<th>Average IQ</th>
<th>Kappa</th>
<th>( p )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal RCA</td>
<td>1.5 ± 0.7</td>
<td>0.835</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid RCA</td>
<td>1.9 ± 0.8</td>
<td>0.743</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LMS</td>
<td>1.3 ± 0.6</td>
<td>0.727</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proximal LAD</td>
<td>1.4 ± 0.7</td>
<td>0.825</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid LAD</td>
<td>1.8 ± 0.8</td>
<td>0.825</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proximal LCX</td>
<td>1.6 ± 0.7</td>
<td>0.858</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid LCX</td>
<td>2.0 ± 0.9</td>
<td>0.837</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- RCA, right coronary artery; LMS, left main stem; LAD, left anterior descending; LCX, left circumflex.
Table 3
Clinical decision made on each patient with reversible ischaemia and a corresponding anatomical lesion at the first examination

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (gender)</th>
<th>Cardiac diagnosis</th>
<th>Perfusion defect</th>
<th>LGE</th>
<th>Coronary anatomy and imaging</th>
<th>Clinical decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17.1 (m)</td>
<td>KD</td>
<td>Subendocardial: base, mid, inferior wall</td>
<td>None</td>
<td>XCA–LAD stenosis with good collateralizatio</td>
<td>Medical therapy and close FU</td>
</tr>
<tr>
<td>2</td>
<td>14.1 (f)</td>
<td>ALCAPA post repair</td>
<td>Subendocardial: base, mid, apical anterior and lateral</td>
<td>Subendocardial: mid, apical, anterior, lateral, papillary muscles</td>
<td>XCA–occlusion of re-implanted coronary</td>
<td>Surgical revascularizatio n</td>
</tr>
<tr>
<td>3</td>
<td>9.6 (f)</td>
<td>ALCAPA post repair</td>
<td>Subendocardial: base, papillary muscles, and anteroseptal wall</td>
<td>Subendocardial: circumferential, papillary muscles</td>
<td>XCA–occlusion of re-implanted coronary</td>
<td>Surgical revascularizatio n</td>
</tr>
<tr>
<td>4</td>
<td>10.0 (m)</td>
<td>KD</td>
<td>Subendocardial: base, mid, papillary muscles, and septal, infero-lateral</td>
<td>None</td>
<td>XCA–aneurysms of left and right coronary</td>
<td>Anticoagulation and close FU</td>
</tr>
<tr>
<td>5</td>
<td>17.5 (f)</td>
<td>ALCAPA post repair</td>
<td>Subendocardial: base, mid, papillary muscle, and anterior and lateral wall</td>
<td>Subendocardial: papillary muscles and lateral</td>
<td>XCA–occlusion of re-implanted coronary</td>
<td>Surgical revascularizatio n</td>
</tr>
<tr>
<td>6</td>
<td>12.6 (m)</td>
<td>LMS atresia</td>
<td>Subendocardial: basal, septum, anterior, and lateral</td>
<td>Subendocardial: papillary muscle, anterior</td>
<td>XCA–LMS atresia</td>
<td>Surgical revascularizatio n</td>
</tr>
<tr>
<td>7.1*</td>
<td>7.2 (m)</td>
<td>KD</td>
<td>Subendocardial: base, mid, apical, anteroseptal, infero-septal, and inferior</td>
<td>None</td>
<td>XCAsevere LAD and mild RCA stenosis</td>
<td>Percutaneous revascularizatio n</td>
</tr>
<tr>
<td>7.2*</td>
<td>8.5 (m)</td>
<td>KD</td>
<td>Subendocardial: base, mid, apical, anteroseptal, infero-septal, and inferior</td>
<td>None</td>
<td>XCA–severe LAD and mild RCA stenosis</td>
<td>PCI–LAD coronary stent offered</td>
</tr>
<tr>
<td>7.3*</td>
<td>9.0 (m)</td>
<td>KD</td>
<td>Subendocardial and inferior</td>
<td>None</td>
<td>XCA–mild RCA stenosis</td>
<td>Monitor closely</td>
</tr>
<tr>
<td>8</td>
<td>17.2 (f)</td>
<td>ALCAPA post repair</td>
<td>Subendocardial: base, mid, papillary muscle,</td>
<td>Subendocardial: papillary muscles, lateral wall</td>
<td>CTCA–occlusion of re-implanted coronary</td>
<td>Surgical revascularizatio n</td>
</tr>
<tr>
<td>Patient</td>
<td>Age (gender)</td>
<td>Cardiac diagnosis</td>
<td>Perfusion defect</td>
<td>LGE</td>
<td>Coronary anatomy and imaging</td>
<td>Clinical decision</td>
</tr>
<tr>
<td>---------</td>
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</tr>
<tr>
<td>9</td>
<td>4.2 (f)</td>
<td>Takayasu’s homograft LIMA</td>
<td>Subendocardial: mid, anteroseptal</td>
<td>Subendocardial: mid, anterior, anteroseptal</td>
<td>XCA–blocked LIMA graft, but native left coronary artery has self recanalized</td>
<td>Follow-up clinically and watch for symptoms</td>
</tr>
<tr>
<td>10</td>
<td>14.8 (f)</td>
<td>TGA post ASO</td>
<td>Subendocardial: mid, anterior, and lateral</td>
<td>None</td>
<td>XCA–mild LMS proximal stenosis</td>
<td>Close monitoring and reduce strenuous exercise</td>
</tr>
<tr>
<td>11</td>
<td>17.2 (f)</td>
<td>DORV post Repair</td>
<td>Subendocardial: mid, septal</td>
<td>None</td>
<td>XCA–normal coronary tree</td>
<td>Reassurance that coronary tree is normal</td>
</tr>
<tr>
<td>12</td>
<td>17.2 (f)</td>
<td>TGA post ASO</td>
<td>Subendocardial: mid, anterior, and lateral</td>
<td>None</td>
<td>CTCA–LMS stenosis</td>
<td>Close FU, reduce strenuous exercise, and repeat assessment in near-future</td>
</tr>
</tbody>
</table>

- KD, Kawasaki disease; ALCAPA, anomalous left coronary artery from the right pulmonary artery; TGA, transposition of great arteries; ASO, arterial switch operation; DORV, double outlet right ventricle; LIMA, left internal mammary artery; XCA, invasive X-ray coronary angiography; CMRA, cardiovascular magnetic resonance angiography; CTCA, computerized tomographic coronary angiography; RCA, right coronary artery; LMS, left main stem; LAD, left anterior descending artery; PCI, percutaneous coronary intervention.
Figures

Figure 1
Images from Patient 13 in Table 2 with false-positive perfusion defect. (A) Adenosine stress perfusion CMR imaging shows reversible subendocardial ischaemia involving the septum denoted by white arrows, (B) rest image. (C) X-ray coronary angiography images, left lateral projection showing unobstructed RCA, and (D) left anterior oblique projection (LOA 30°) showing unobstructed left coronary system. LMS, left main stem; LAD, left anterior descending; LCX, left circumflex.

Figure 2
X-ray angiographic and adenosine perfusion CMR images of patient represented with 7.1* 7.2* and 7.3* in Table 3 who had repeated imaging. LAD, left anterior descending; LCX, left circumflex artery. (A) Selective left coronary artery injection shows LAD stenosis (arrow). (B) Adenosine stress perfusion image showing a perfusion defect on the LAD territory. (C) PCI image with the coronary stent during deployment in the LAD. (D) Post intervention selective angiogram with no stenosis. (E) Repeat adenosine stress perfusion CMR image 8 weeks later, showing no perfusion defects on adenosine stress imaging.
Figure 3
X-ray angiographic and adenosine perfusion CMR images of Patient 4 in Table 3. (A) Selective injection of RCA showing aneurysmal dilatation. (B) Selective left main stem injection showing a large LAD aneurysm. (C) Adenosine stress CMR showing a perfusion defect (arrow) and (D) rest perfusion CMR at the same level as image (C) no perfusion defect seen denoting reversibility.