Cardiovascular Magnetic Resonance Imaging of Coronary Arteries

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Introduction

Over the last few decades, there has been an increased emphasis and focus on identification, prevention, and treatment of coronary artery disease (CAD) by both national and international societies and medical communities [1]. Despite this increased attention CAD remains globally the most common cause of death: an estimated 7.3 million people died from CAD in 2008, a number projected to double by 2030 [2, 3].

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Investigating patients with risk factors for CAD or any anginal symptoms remains challenging: The correct diagnosis needs to be established to allow modification of pharmacotherapy and guide intervention. However, the risk of harming the patients needs to be minimized. In the US alone, 16,300,000 patients have CAD, leading to approximately 715,000 heart attacks annually and an estimated CAD-related cost of $109 billion annually [4, 5]. There are more than 1,000,000 cardiac catheterizations performed in the US annually. Up to 40 % of them identify no significant CAD [6]. This implies that 400,000 patients are exposed unnecessarily to the risks of diagnostic coronary angiography. This results in an increase of morbidity and mortality for these patients, which includes vascular side effects, accumulation of radiation dose and, rarely, stroke, myocardial infarction (MI), or coronary artery dissection. An alternative approach that could minimize these risks, but at the same time provide equal sensitivity and specificity in identifying CAD, would be of high clinical value.

In this chapter the various imaging modalities for investigating patients with suspected CAD or other coronary anomalies are reviewed.

Imaging Modalities for Investigating Patients with Suspected Coronary Artery Disease

When reviewing patients with suspected CAD, clinicians must decide whether the combination of risk factors for an individual patient (such as hypertension, hypercholesterolemia, diabetes, smoking, obesity, and a family history of CAD) and a possible history of chest pain potentially indicating significant CAD would merit initiation of pharmacotherapy and further investigation. The benefits of any potential imaging tests must be balanced against the risks associated with each procedure, for that particular patient. In this section the commonly used imaging tests for investigating patients with suspected CAD are discussed.

Invasive Diagnostic Coronary Angiography

For more than 50 years diagnostic coronary angiography has remained the “gold standard” test for identifying significant epicardial CAD. As an invasive procedure it is still inconvenient for the patients, has the potential for morbidity and mortality, and involves significant costs and exposure to radiation (ranging from 2.3 to 22.7 mSv with a mean of 7 mSv) [7].

Rare risks include coronary artery dissection, stroke, myocardial infarction (MI), radial or femoral dissection, aorto-venous fistulae, retroperitoneal bleeding and significant bruising, and the potential need for blood transfusion. When diagnostic angiography identifies significant lumen narrowing of the coronary arteries

(>50 % of the vessel diameter) this can lead to significant change in pharmacotherapy and/or intervention both of which can improve symptoms and prognosis. In the 40 % of patients with no significant CAD using luminography with cardiac catheterization the therapeutic consequences remain unclear. Some of these patients have no CAD and have undergone an invasive test unnecessarily. However, it is increasingly understood that visualization of just the coronary lumen could underestimate the burden of atherosclerosis in the wall of the vessel. The absence of significant lumen narrowing based on the results of coronary angiogram and the resulting halt of medical therapy could have adverse implications in the long-term outcome of these patients. The ideal test would therefore be a low risk noninvasive radiation-free test, which will identify major epicardial vessel disease and early coronary vessel wall atherosclerosis.

Computed Tomography Coronary Angiography

Computed tomography coronary angiography (CTCA) is a noninvasive method currently used mainly for delineating coronary artery lumen in patients with known or suspected coronary artery disease. Patients require intravenous peripheral cannulation for contrast injection. A heart rate below 70 bpm is beneficial for image quality and reduction of radiation dose with current state of the art scanners. This is often achieved with intravenous administration of beta blockers. With new optimized protocols and prospective ECG triggering, a relatively lower dose of radiation of 3.4 ± 1.4 mSv [8] is required (equivalent to just under 2 years background radiation for a person living in the United Kingdom). However this still confers a risk of neoplasia of 0.13–0.16 % (i.e. approximately 1 in 650 patients will develop a cancer as a result of this test) [9], making this method less appropriate for screening and assessing patients at low cardiac risk. Finally, coronary calcification and arrhythmia can impair image quality, and arrhythmia is frequently found both in patients with suspected coronary artery disease but particularly in an aging population.

Cardiovascular Magnetic Resonance in the Assessment of Atherosclerosis

Cardiovascular magnetic resonance (CMR) enables a comprehensive evaluation of patients with suspected or known coronary artery disease. This method can provide information regarding cardiac anatomy as well as myocardial function, viability, and perfusion (Figs. 1–3). Non-significant CAD can be ruled out with a high level of security [10]. CMR can also visualize the coronary artery lumen and vessel wall. Coronary vessel wall imaging may also allow early detection of atherosclerosis, prior to acute myocardial infarction.

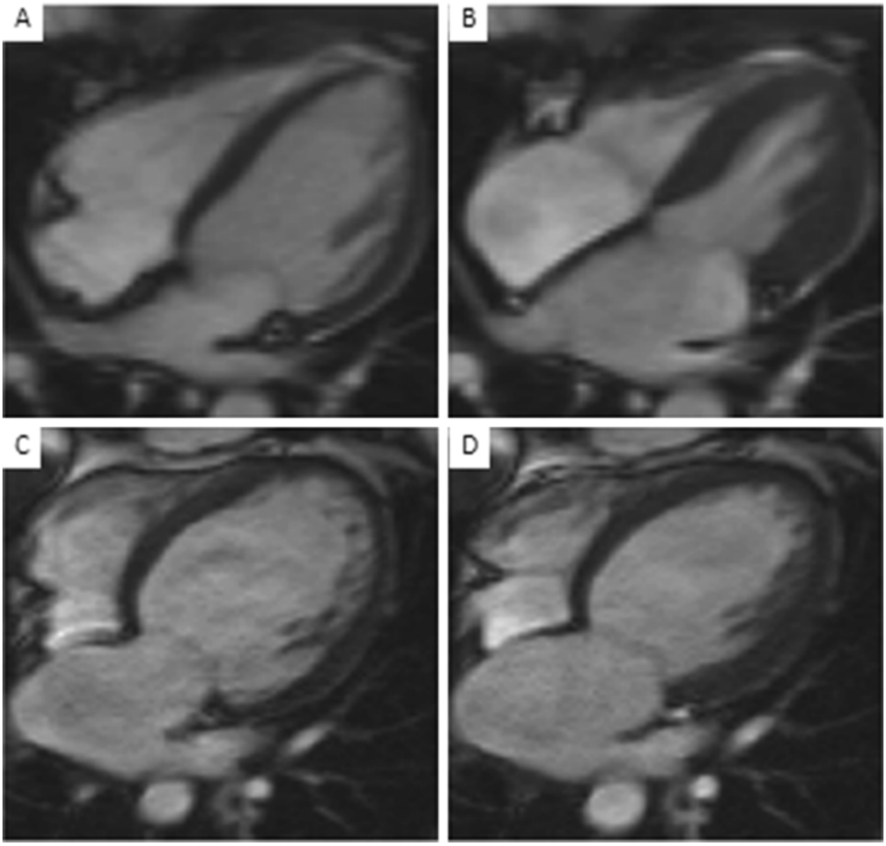

Fig. 1 CMR provides an excellent modality for delineating cardiac anatomy and function. (**a**) represents a four-chamber view of a normal heart in diastole and (**b**) in systole. (**c**, **d**) represent images in diastole and systole from a patient with ischemic cardiomyopathy and impaired ejection fraction

This early identification allows guiding of pharmacotherapy at a very early stage, offering the opportunity of halting the rate of progression of atherosclerosis and even potentially reversing its burden [11]. Hence, in addition to the relevant anatomical and functional information which can be acquired in a single, safe, noninvasive, and radiation-free examination, CMR has the potential of visualizing the coronary artery lumen and wall to identify early signs of atherosclerosis. However, there are challenges in imaging the coronary artery lumen and wall, limiting the use of CMR in clinical practice at present.

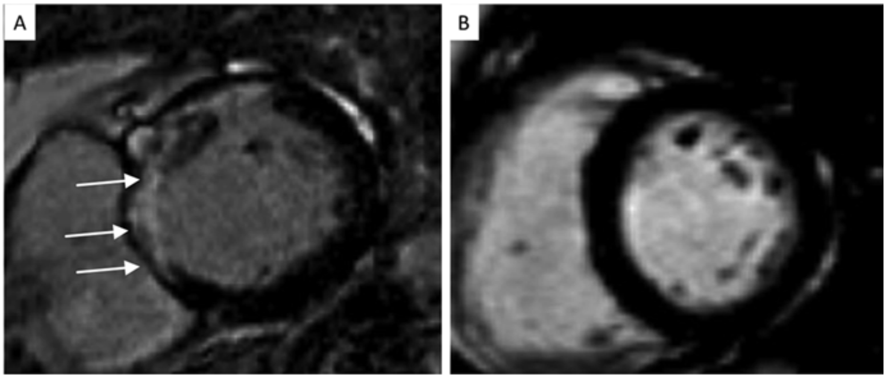

Fig. 2 Following administration of the paramagnetic contrast agent containing gadolinium, areas of myocardial enhancement (*white area* shown by *white arrows*) can be identified representing myocardial fibrosis (scarring). Such areas represent not viable myocardium, which will not benefit from revascularization of the coronary artery supplying blood to this area. Image (**a**) is from a patient with 3-vessel CAD. The area supplied by the left anterior descending (LAD) coronary artery is not viable (*white arrows*), therefore LAD revascularization will not be beneficial. Image (**b**) is from a patient with 3-vessel CAD as well where there is no late Gadolinium enhancement (LGE). The myocardium is viable and revascularization can be recommended

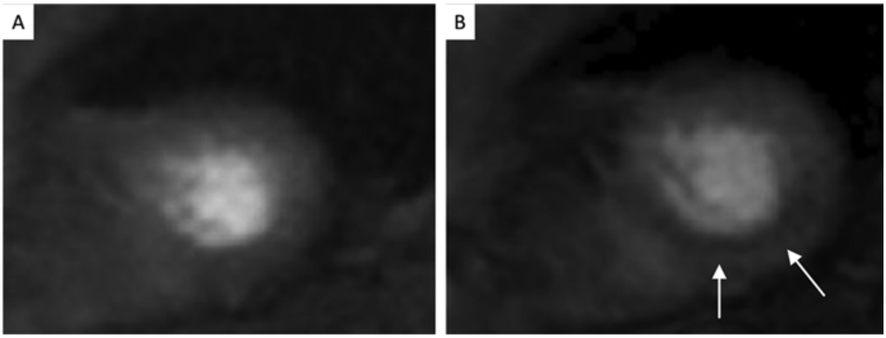

Fig. 3 Images taken from the same patient at rest (**a**, on the *left*) and following stress using adenosine (**b**, on the *right*). The *black area* on the *right* represents a perfusion abnormality indicating reversible ischemia in the right coronary artery (RCA) territory

Challenges in Undertaking Coronary Magnetic Resonance Angiography

Since the first studies on the use of coronary MRA (CMRA) [12–15] there have been significant technical advancements, leading to better imaging quality with reduced scanning time. However, movement of the coronary arteries due to cardiac and respiratory motion introduces motion artifacts. Reduction of these artifacts is crucial due to the small and tortuous caliber of the coronary vessels. The following section describes some of the challenges associated with coronary MRA.

Cardiac Motion: Coronary Movement in Systole and Diastole

An ideal subject for visualization using magnetic resonance is something that remains still during the entire acquisition time. In humans for example the upper and lower limbs can be very still and allow for good visualization. The coronary arteries are small, often tortuous, and they are displaced during the cardiac cycle. This leads to significant motion artifacts when trying to visualize the coronaries and the vessel wall. For optimal results, any CMR sequences aimed at visualizing the heart and the coronaries in particular need to take this into consideration. Synchronizing image acquisition to the ECG (R-wave) corresponding to the times of minimal displacement is therefore mandatory for successful coronary artery imaging with CMR. Coronary artery motion is minimal during end-systole and mid-diastole and previous research has shown the advantage of acquiring image data during both rest periods [16]. The specific advantages of both techniques are illustrated in Table 1.

The optimal trigger delay and the length of the acquisition window vary with the patient's heart rate. The rest period should be identified for each patient from a high-temporal resolution cine scan usually as a four chamber view performed shortly before the coronary scan [17]. Real time arrhythmia rejection algorithms that facilitate only the inclusion of regular heartbeats within certain limits might further improve image quality for MRA angiography [18, 19].

Table 1 Comparison of cardiac imaging in end-systole and mid-diastole in an attempt to image the heart in minimal displacement during the cardiac cycle

Comparison of cardiac imaging with cardiovascular magnetic resonance aiming for minimal displacement	
During end-systolic rest	*During mid-diastolic rest*
Advantages	*Advantages*
Heart rate variability less important	Longer acquisition window
Larger diameter of the venous vessels (if this information required)	Higher signal when gradient echo sequences used
Disadvantages	*Disadvantages*
Shorter acquisition window	Heart rate variability has higher potential to affect image quality

Respiratory Motion

Another major problem for cardiac imaging with CMR is the displacement of the heart during respiration. It can often reach a distance that can be ten-fold higher than the coronary artery diameter. Synchronization of the image acquisition with the respiratory cycle is therefore mandatory. Several methods have been used to minimize this respiratory motion. Initial approaches for visualizing the proximal native coronary arteries used two-dimensional breath-holding or averaging techniques and mid- or late-diastolic image acquisition with average 6–8 phase encoding lines acquired during each cardiac cycle. However, the main drawback of such techniques was that a long breath-hold of up to 20 s was required for each image slice, which is not easily achieved by every patient. Furthermore, even if patients can initially manage a 20 s breath-hold to complete the MRA an average of 25 slices are required per patient. This can be very tiring and it is therefore common to see the quality of breath-holding decreasing towards the end of the examination, leading to misregistration artifacts between successive breath-holds, degrading the overall image quality. Currently breath-holds for high-resolution three-dimensional datasets are too long and imaging results were rather disappointing. Currently a prospective real-time navigator of the diaphragm is most commonly used and successful technique for coronary lumen and vessel wall imaging.

To compensate in part for this problem, Ehman and Felmee [20] first proposed the use of respiratory MR navigators to remove the time constraint of a breath-hold. The MR navigator (typically an one-dimension pencil beam) is usually placed on the dome of the right hemidiaphragm [21] (Fig. 4). Data are only accepted if the diaphragm-lung interface is within a user-defined window (usually up to 8 mm), preferably positioned around the end-expiratory interface position. If the navigator signal falls outside this predefined window, data is rejected and needs to be reacquired in the following cycle. This results generally in a gating efficiency of around 40–60 %, which means that a large proportion of the scanning time is actually not used [22, 23]. To improve this shortcoming several new self gating navigator approaches have been developed to

1. Directly measure the motion of the heart.
2. Account for the 3D motion of the heart (food-head, left-right, and posterior-anterior).
3. Achieve 100 % scan efficiency by applying more sophisticated motion correction methods including 3D rigid body or 3D affine.

Other approaches included scanning the patient in prone position [24] and the use of thoracic or abdominal bandings [25].

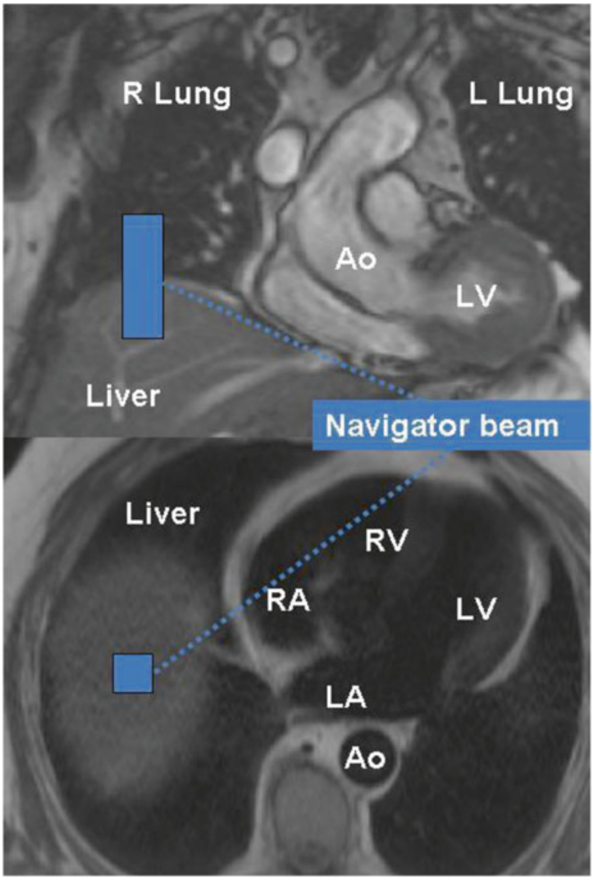

Fig. 4 Using scout images the position of the respiratory navigator can be planned. A pencil beam (one-dimensional navigator) is usually placed on the dome of the right hemi-diaphragm (heart in the left chest). Using the respiratory navigator a three-dimensional volume covering the whole heart can be acquired in a free breathing subject. *R Lung* right lung, *L Lung* left lung, *Ao* aorta, *LV* left ventricle, *RV* right ventricle, *LA* left atrium, *RA* right atrium

Cardiovascular Magnetic Resonance Sequences

Image quality for coronary MRA was significantly improved using two-dimensional gradient echo techniques (Edelman [26] and Manning [27]). Sixteen heartbeats were required initially in order to acquire one slice during a single breath-hold, which meant that most patients would tire towards the end of the test. Following the introduction of navigator techniques as described above, three-dimensional imaging covering the whole heart became feasible. Due to its ease to use, this is now the preferred approach in the clinical arena. Several modifications are currently available. The most widely accepted is a T2 preparation technique in combination with a three-dimensional gradient echo (at 3 T) or steady-state free-precession (SSFP) technique (at 1.5 T). Steady-state free-precession sequences are usually preferred at 1.5 T. Although possible at 3 T, the use of SSFP sequences is currently limited by the prolongation of repetition times, increased sensitivity of off-resonance and the

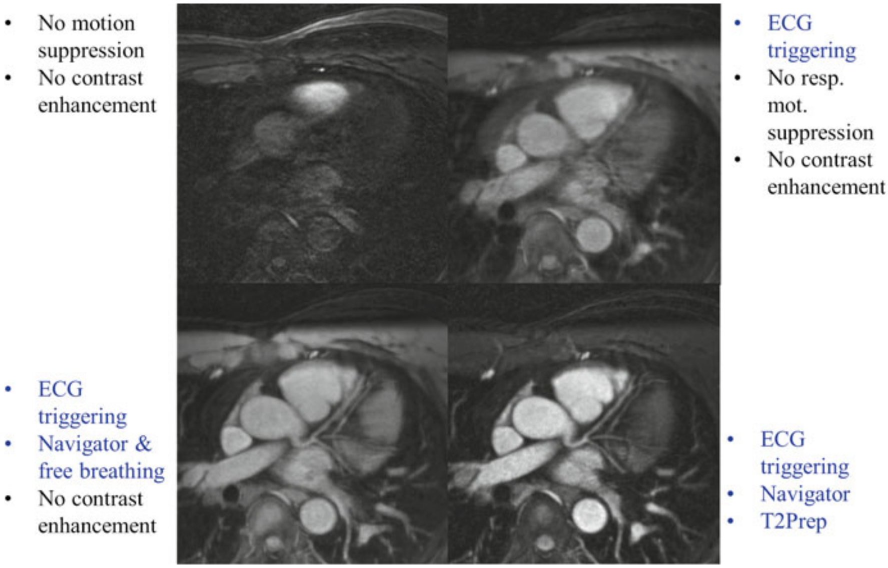

Fig. 5 Progressive improvement in the image quality can be noticed by adding ECG triggering, then a respiratory navigator followed by T2 preparation. (Image courtesy of Matthias Stuber, Professor and Director CVMR/CIBM/CHUV, University of Lausanne, Switzerland)

need for higher flip angles. T2-preparation and fat suppression techniques are now preferred for noncontrast-enhanced imaging of the coronary artery lumen. The epicardial fat can cause artifacts and fat suppression techniques reduce the signal generated by the epicardial fat tissue, making the lumen of the coronaries more visible [26, 28]. T2-preparation techniques improve the contrast between the coronary lumen and the underlying myocardium [29] as although blood and myocardium have similar T1, they have different T2. Additionally T2-preparation suppresses deoxygenated venous blood leading to better visualization of coronary arteries. An example of the currently most commonly used technique is shown in Fig. 5.

Contrast Agents for Coronary Angiography

The currently most commonly used type of contrast agents in CMR are nonspecific and distribute in the extracellular space. These are used for first pass contrast-enhanced angiography, perfusion imaging, and late gadolinium enhancement (LGE) imaging of the myocardium [30]. Other types of contrast agents include intravascular targeted [31] and blood pool iron contrast agents (fast and slow blood pool clearance). Each contrast agents has specific characteristics, which needs to be encountered for its clinical use. It is very important to choose the sequence design appropriately for the clinical question and the contrast agent used [31].

On a practical level the ultimate decision depends on the clinical question for the individual patient, balancing the luminographic information required against the vessel wall and myocardial information required. For example, extracellular contrast agents quickly extravasate into the interstitial space, and while they provide excellent detection of scar tissue by LGE (indicating previous myocardial infarction, Fig. 2a), diffuse fibrosis by T1 mapping and viability of the myocardium (suggesting that the muscle is still alive and that myocardial function is likely to improve following revascularization, Fig. 2b), they are suboptimal for coronary artery lumen imaging due to their rapid clearance. Blood-pool contrast agents on the other hand, offer the highest contrast between the vessel lumen and the surrounding tissues but might provide less information regarding late Gadolinium enhancement (LGE). Contrast agents with low albumin-binding properties have the potential for combined coronary artery and infarct imaging This is due to their prolonged retention time in blood and their higher relaxivities thereby improving coronary artery imaging while maintaining a good late enhancement for fibrosis and viability assessment [32]. Intravascular contrast agents are best used for coronary artery lumen imaging with an inversion prepulse instead of a T2-preparation prepulse [33, 34] The diagnostic value of this approach in patients with coronary artery disease still needs to be evaluated in larger clinical studies.

Are We Ready for Coronary Magnetic Resonance Angiography to Enter Routine Clinical Use?

The advances in coronary lumen and vessel wall imaging currently allow clinical applications in selected patient groups [35] (Figs. 6–8). This includes patients with Kawasaki disease [36–38] and imaging the origins and course of the coronary vessels in patients of different age groups for diagnosis and planning of interventional procedures.

Equally the origins of the coronary vessels can also be visualized in every patient, if needed [16]. When trying to visualize the mid- or the distal segment of a vessel, however, imaging quality is often less optimal. Images of the right and left coronary arteries are usually of better quality than those of the circumflex coronary artery as demonstrated in Fig. 6. This is because the circumflex artery tends to run in the direct vicinity of the myocardium and great cardiac vein and is further away from the CMR receiver coils. Previous studies have shown that the mean length of arteries that could be seen with coronary MRA is about 80 mm for the right coronary, 50 mm for the left anterior descending and 40 mm of the circumflex coronary artery [39] (Fig. 8).

However, coronary MRA is currently not a standard clinical tool in patients with coronary artery disease. This is due to relatively lengthy acquisition times, limited spatial resolution, and being dependent on a regular heart rate in a cooperative patient. Significant further improvements regarding faster acquisition times and more time efficient data acquisition techniques may bring coronary MRA into

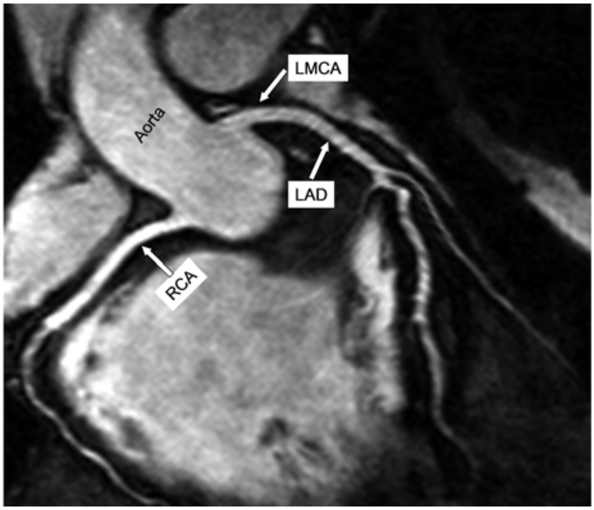

Fig. 6 In this healthy subject the proximal origin and course of the right coronary artery, left main coronary artery, and left anterior descending coronary artery are well visualized and seen to be free of any significant disease [6]. Please note that the vessel wall is imaged using the same CMR sequence (see Fig. 7). *RCA* right coronary artery, *LMCA* left main coronary artery, *LAD* left anterior descending coronary artery

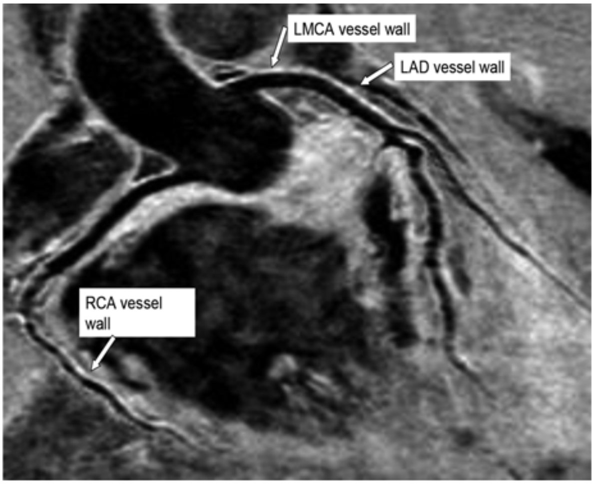

Fig. 7 CMR imaging from the same healthy subject as shown in Fig. 6, with emphasis on imaging of the coronary wall, confirming no significant atherosclerotic process in the wall of the vessel [6]. The same CMR sequence can be used to visualize both the coronary lumen (Fig. 6) and coronary wall (Fig. 7)

clinical practice together with myocardial perfusion imaging and LGE as a reliable and safe alternative for invasive and x-ray-dependent coronary artery angiography in the cardiac catheterization laboratory.

At present current clinical applications are listed below:

1. *Coronary artery origin anomalies*

Coronary MRA can provide excellent delineation of the origin and proximal course of both the right and the left coronary arteries including children and young adults [16]. This is particularly helpful in the evaluation of young patients with chest pain and/or syncope, where the anomalous coronary origin needs to be excluded as an

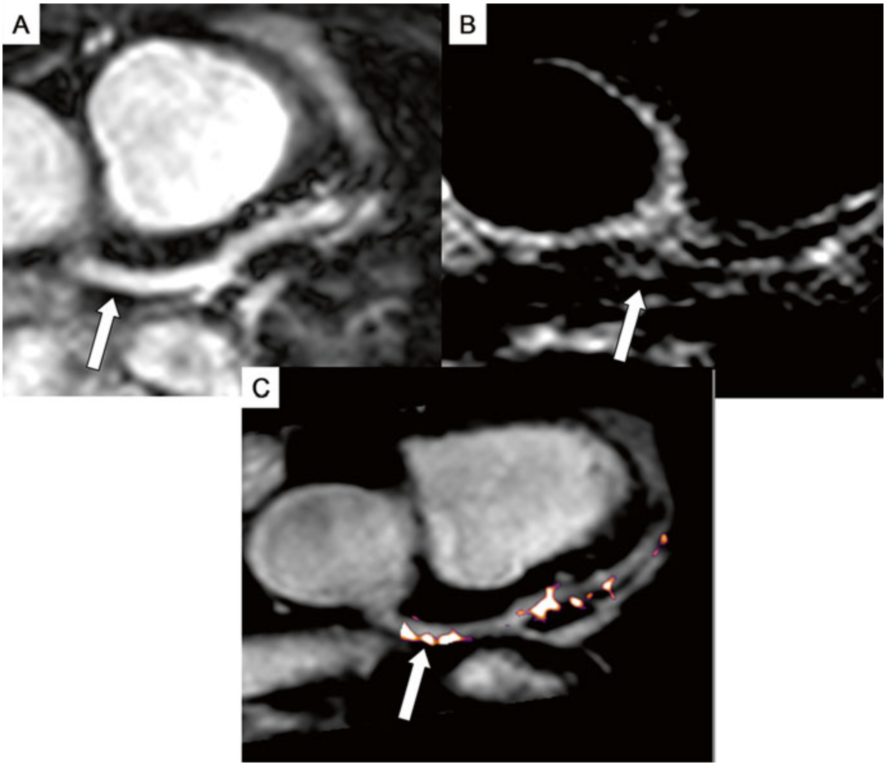

Fig. 8 CMRA shows the left main coronary artery (*arrow*) and the left anterior descending. (**b**) demonstrates late gadolinium enhancement (LGE) in the vessel wall (*arrow*) and (**c**) shows the result of superimposing image (**a**) and (**b**). This combines coronary artery anatomy as well as vessel wall imaging with LGE in one image. (Image adapted with permission from reference [35])

alternative to computed tomography and invasive coronary angiography [40] (Fig. 9).

2. *Coronary artery aneurysms*
   - Patients with vasculitis such as patients with Kawasaki disease need life-long follow-up and carry higher risk when investigated with invasive x-ray-dependent coronary angiography. Sometimes these patients develop extensive coronary artery aneurysms with the risk of coronary artery stenosis and thrombosis within the coronary artery aneurysm. Coronary MRA is accepted as a valuable alternative to follow-up coronary artery aneurysms location and extension noninvasively without the use of x-ray radiation [36–38] (Fig. 10).

3. *Coronary bypass graft assessment*

In patients following coronary artery bypass graft surgery (CABG) anginal chest pain is a common finding, both soon after CABG but more commonly a few years later. Frequently prior operation notes are not available and thus the luminal integ-

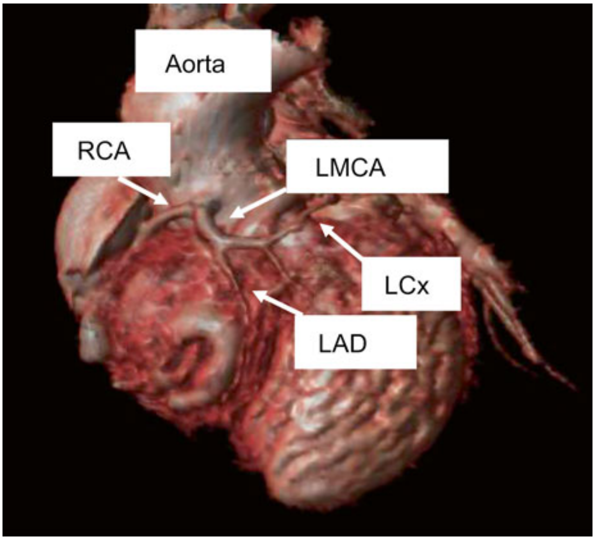

Fig. 9 This CMRA image shows a single coronary artery in a 3-year-old patient with a hypoplastic right ventricle. The left main coronary artery (LMT) arises from the right coronary artery (RCA). *Ao* aorta, *LAD* left anterior descending artery, *LCX* left circumflex coronary artery, *LV* left ventricle, *RV* right ventricle. (Image adapted with permission from reference [40])

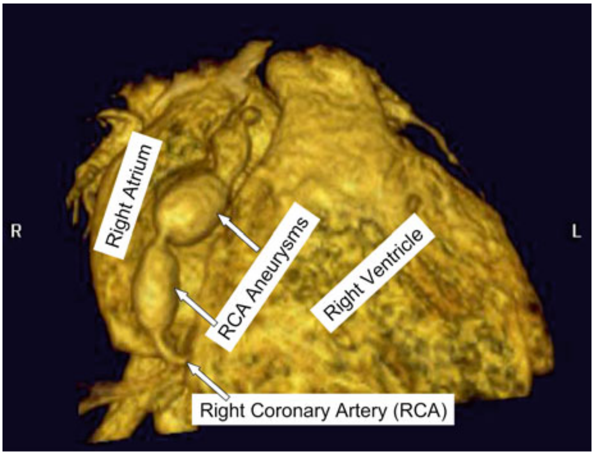

Fig. 10 Multiple aneurysms of the right coronary artery are shown in an 8-year-old patient with Kawasaki disease using volume rendering of a free breathing respiratory navigator-gated and ECG-triggered isotropic, whole-heart, 3D steady-state-free-precession magnetic resonance dataset. *RCA* right coronary artery. (Image adapted with permission from reference [36])

rity of the grafts needs to be assessed. Coronary MRA may provide a road map prior to cardiac catheterization angiography to describe the number and location of arterial and venous grafts used. Bypass grafts however have certain distinct characteristics differentiating them from the coronary arteries, actually making them ideal for visualization with CMR: they are usually much larger compared to native arteries and they typically have a rather straight and (sometimes) known course. Furthermore, they tend to remain in an almost stationary position with each successive cardiac cycle. With spin and gradient echo techniques and the use of contrast agents, the sensitivity in identifying a blood signal inside a graft approaches 95–100 % [41–43]. The major limitation in graft imaging with CMR lies in the metallic clips frequently used (particularly for left and right internal mammary grafts), which causes signal voids and susceptibility artifacts, sometimes preventing a full assessment of their anatomy. To fill this gap subsequent coronary angiography or aortography can be targeted to the remaining questions. This will reduce the time in the cardiac catheterization laboratory, radiation exposure, and risk associated with invasive angiography.

4. *Patients with a dilated heart*
   When faced with a patient with a dilated heart, it is not clear whether this phenotype relates to ischemic cardiomyopathy or dilated non-ischemic cardiomyopathy. Traditionally such patients undergo invasive angiography or Computed Tomography coronary angiography to exclude coronary artery disease. However, it has been recently proposed [44] that coronary MRA in conjunction with late gadolinium enhancement and perfusion imaging of the myocardium is sufficient to establish the diagnosis without the need of further anatomical coronary tests.

Conclusion

In clinical cardiology the role of cardiac magnetic resonance is a well established tool for diagnosis and monitoring of cardiac anatomy, function, viability, and perfusion. Even though coronary MRA technology has improved significantly in the last few years, it is not used routinely at present in clinical practice. However, coronary MRA plays an important role for diagnosis and follow-up of specific coronary lesions, such as patients with vasculitis e.g. patients after Kawasaki disease. Coronary artery aneurysm location and size can be assessed with this technology radiation free and noninvasively which is very important in pediatric patients. Coronary MRA also allows visualization of coronary artery origins and course, which allows clarification of unclear chest pain in children and young adults. It also provides additional support for planning complex congenital heart surgery. Further improvements in motion compensation and more time efficient acquisition and reconstruction techniques make it more likely that coronary MRA will play an increasingly important role in the clinical routine of cardiac disease in the future.

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