Reviews

Coronary Magnetic Resonance Angiography

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Cardiovascular diseases and particularly coronary artery disease (CAD) are the main cause of death in the western world, in both men and women. Though many noninvasive tests are commonly used for the diagnosis of CAD, invasive coronary angiography is still considered as the most reliable method for assessment of the coronary vessels. Noninvasive coronary angiography remains a challenge. Both transthoracic and transesophageal echocardiography have limited value, due to the distance of the transducer from the coronary vessels, which, in combination with their small size, results in inadequate resolution. Over the last few years, coronary magnetic resonance angiography (MRA), electron beam computed tomography and spiral computed tomography have been introduced as alternative methods for imaging of the coronary arteries[1].

Coronary MRA is particularly attractive because it does not expose the patient to ionizing radiation, nor does it require the use of radiopaque, osmotically active contrast media with potential nephrotoxicity. Furthermore, coronary MRA can be obtained in any direction and plane, without any restriction to the angulation of the images. Finally, coronary MRA can easily be combined with a comprehensive evaluation of the anatomy and function of the left ventricle and assessment of myocardial viability, thus covering all the requirements of a comprehensive cardiac examination. Over the last decade coronary MRA has significantly improved from a technological standpoint and has established clinical indications. This review will focus on the basic principles that are important for coronary MRA, and on the current and future clinical applications. There will be no extensive reference to the radiofrequency sequences that can be used, as the technical data are not of particular interest to the clinical practitioner.

Challenges

Coronary MRA faces several challenges. Firstly, the coronary arteries are a moving target, subject to continuous movement due to cardiac contraction and respiration. The coronary tree is a complicated, three-dimensional structure, which is displaced towards the cardiac apex during ventricular systole, while at the same time it is deformed and rotates counter-clockwise. During the diastolic period it follows an opposite trajectory. At the same time, during free breathing the heart (and the coronary arteries) follow the diaphragmatic displacement and move cranially during inspiration and caudally during expiration. The displacement of the heart due to respiration varies widely (chest wall versus diaphragmatic breathing), but also in the same subject depending on the depth of inspiration.

Other technical challenges include the small size of the coronary arteries (diameter 2-4 mm), the tortuous course and the surrounding epicardial fat, which emits a strong signal in the magnetic field. Even with the most sophisticated techniques, interpretation of the coronary MRA from individual slices may be difficult, due to deviation of the artery outside the imaging plane, which may present as discontinuity. These discontinuities may be erroneously interpreted as atheromatic lesions, although such lesions may not be present. Imaging of the coronary veins, which course parallel to the arteries, may be an additional impediment to the correct interpretation of coronary MRA.

Imaging of the normal coronary arteries

The first reports of coronary artery imaging were published in the late 1980s, and showed only limited success. Using conventional black blood techniques (spin echo) with electrocardiographic (ECG) gating, only the very proximal segments of the coronary arteries could be visualized in a small number of selected patients. The conventional approaches did not suffice to demonstrate coronary stenoses. Interest in coronary MRA revived after the introduction of a white blood sequence (gradient echo), which acquires the image data with ECG-gating in multiple segments (segmented k-space) in many cardiac cycles. For this sequence, a two-dimensional image with resolution 1.9×0.9 mm can be completed in 16 consecutive cardiac cycles, a period during which breath-holding may be used to minimize respiratory motion. In this initial sequence the time during which data are acquired was approximately 100 ms, so as to “freeze” cardiac motion. Typically the data acquisition occurs in mid-diastole, a period of relatively little motion (diastasis), and when there is relatively increased blood flow in the coronary arteries. In order to image the entire coronary tree, multiple sections are obtained with consecutive breath-holds. Although imaging of the coronaries can be completed within 10-15 breath-holds, the depth variability between serial breath-holds may result in discontinuities in the course of the coronary vessels that may be misinterpreted as stenoses. Three-dimensional techniques have been introduced to overcome the limitations of the two-dimensional approaches. Three-dimensional acquisitions have the advantage of providing a high signal, and can offer consecutive sections in the imaged volume.

In order to overcome problems related to breath-holding, free-breathing techniques were developed. The most reliable approach uses navigators that can monitor in real time the motion of any moving structure, such as the diaphragm. Assuming a constant relationship between the respiratory diaphragmatic motion and the motion of the coronary arteries, the information regarding the location of the position of the diaphragm can be used to predict the position of the coronaries, so that the data acquisition is performed only when the coronary arteries are at (approximately) the same position. Gating can be performed retrospectively or prospectively, or even be combined with active correction of the location of data acquisition, so that the information regarding the position of the coronary arteries can always be adjusted to the correct location.

A large variety of technical approaches has been described for coronary MRA, which includes virtually any imaging sequence. Despite recent progress, there is still not a uniform agreement on the optimal acquisition scheme for imaging of the coronary arteries. In general, the three-dimensional approaches seem to have gained broader acceptance, and most of the modern systems can achieve high spatial resolution (in-plane resolution <1 mm). The proximal segments of the native coronary arteries can be visualized in the majority of volunteers and patients. These include the entire left main, the proximal 5-6 cm of the left anterior descending and the right coronary, and 2-3 cm of the left circumflex coronary artery (Figure 1). Among the epicardial vessels, the left circumflex coronary artery is the hardest to visualize, mainly because of the distance of the vessel from the surface coils that are used for data collection.

Imaging of the take-off of the coronary arteries led to the first clinical application of coronary MRA, which is assessment of congenital anomalies of the coronary origin. Early literature reports included isolated cases where coronary MRA simply corroborated angiographic findings regarding the origin and proximal course of the coronary arteries. Later, data from series of patients with such anomalies were reported, and to date there are at least four such publications including patients who had both conventional angiography and coronary MRA, and in whom the results of the two tests were compared[2]. Coronary MRA in all studies was found to be equivalent, in certain cases superior to the conventional

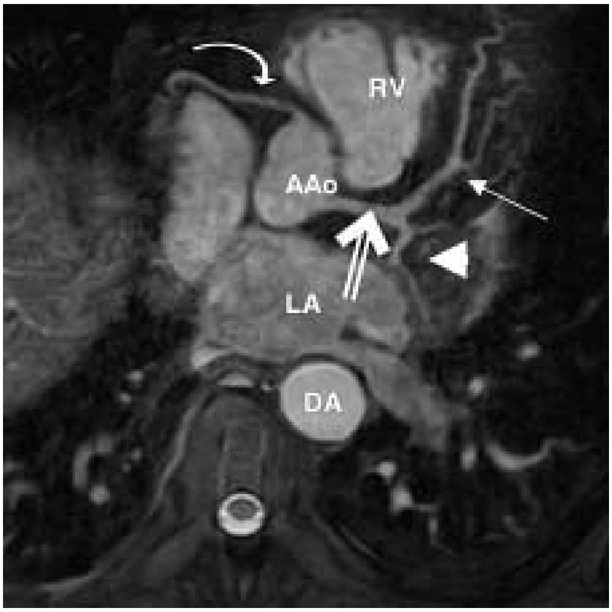

Figure 1. Imaging of the proximal coronary arteries with a three-dimensional high-resolution technique during free breathing, with monitoring of the motion of the right hemidiaphragm and prospective slice correction. In this reformatted image, the left main (double white arrow) and several centimeters of the left anterior descending (white arrow), the right (curved arrow) and the left circumflex coronary artery (arrowhead) can be visualized on a single plane. AAo=ascending aorta, LA=left atrium, RV=right ventricle, DA=descending aorta.

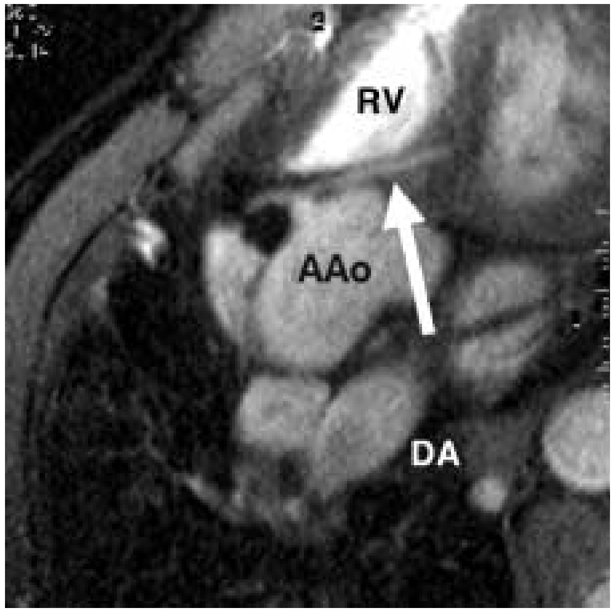

Figure 2. Anomalous origin of the left coronary artery from the right sinus of Valsalva. The anomalous vessel (arrow) courses between the ascending aorta (AAo) and the right ventricular outflow tract (RV). This anomaly has been associated with sudden death in young adults during strenuous exertion.

angiography, as it can better demonstrate the relationship of the vessels to surrounding anatomical structures, which may be difficult with conventional angiographic (projection) techniques (Figure 2).

Imaging of coronary artery aneurysms is another clinical application of coronary MRA. The majority of acquired coronary aneurysms are due to Mucocutaneous Lymph Node Syndrome (Kawasaki's disease), a generalized vasculitis of unknown etiology usually occurring in children less than 5 years of age. Cardiac involvement is common and coronary artery aneurysms develop in approximately one fifth of all cases. Although approximately half of the children with coronary aneurysms during the acute phase of the disease recover fully and have normal-appearing vessels by angiography one to two years later, coronary aneurysms are responsible for both short and long-term morbidity and mortality. Among children, transthoracic ultrasound is usually adequate for diagnosing and following aneurysms, but echocardiography is not reliable after adolescence, because of limited penetrance of the ultrasonic beam in the adult chest. As these patients require frequent evaluation, coronary MRA in specialized centers is a unique technique for this purpose as it is noninvasive and does not expose the patients to ionizing radiation.

The assessment of native coronary artery integrity continues to be the long sought application of coronary MRA. With the use of bright blood (gradient-echo) approaches the fast moving coronary blood provides high signal (bright), while slow or turbulent flow presents a signal void (dark)[3]. In areas with focal stenoses there is signal loss and the magnitude of signal loss correlates with the degree of angiographic stenosis. Nevertheless, with the bright blood angiographic approaches, false positive and false negative interpretations may be given. If, for example, there is slow flow distally to a significant stenosis, this may present as complete signal loss, although the vessel is patent. Similarly, as these techniques are not sensitive to the direction of blood flow, a total occlusion with adequate collateral circulation may present as adequate signal, even in the vessel lumen distal to the stenosis.

Data from more than 30 studies from single centers have been published to date regarding the ability of coronary MRA to identify atherosclerotic stenoses[4,5]. These reports describe the use of both two-dimensional and three-dimensional techniques, while for suppression of the respiratory motion breath-hold and free breathing approaches with navigator monitoring of the diaphragmatic motion have been employed. In general, there is considerable heterogeneity in the reported sensitivity and specificity, which largely depends on the different technical approaches, the evaluation of different patient groups, the different methods of data analysis and the different experience of the individual centers. Recently, most of the cardiac MR centers use three-dimensional coronary MRA techniques, as these approaches provide inherently higher signal (increased signal to noise ratio) and allow reconstruction in any orientation. Most of the contemporary approaches do not use exogenous contrast media, although the use of paramagnetic contrast media has also been described. With the technical advances and better patient selection, the accuracy of coronary MRA for the detection of significant coronary stenoses seems to be improving over the last few years.

An international multicenter study was recently reported and demonstrated very high sensitivity (>95%) for the identification of significant coronary artery disease (left main or three-vessel disease). Accordingly, for patients referred for their first diagnostic conventional angiography, a normal coronary MRA reliably excludes the presence of extensive coronary disease, while patients with left main or three-vessel coronary disease are correctly identified as having coronary artery disease. Thus, initial patient groups that may benefit from coronary MRA include those for whom the clinical question is whether they have multivessel disease or nonischemic cardiomyopathy.

One of the problems that have recently emerged and restrict the widespread clinical application of coronary MRA is the significant increase of percutaneous procedures with stent placement, as the long term patency is significantly better than in the conventional balloon angioplasty techniques. Imaging with MRI is safe in these patients, even immediately after the placement of the stent, but the material used for stents (stainless steel, alloy or tantalum) creates susceptibility artifacts from the metal-induced field inhomogeneity. These artifacts present as signal voids at the site of the stent, which prohibit evaluation of adjacent segments of the coronary arteries. The signal loss depends on the sequence used and is relatively larger for bright blood sequences. Evaluation of the blood flow and its direction proximally and distally to the stent may provide indirect information with reference to the stent patency and is an alternative method of assessing stents that has been tested successfully.

MRA of aortocoronary bypass grafts, including saphenous vein and internal mammary grafts, is technically less challenging than for the native coronary arteries, as the bypass grafts move relatively less, have a more straight and predictable course and larger diameter (Figure 3). Both black blood and bright blood techniques have been successfully used to assess bypass graft patency. Presence of blood flow is imaged as signal void (black blood techniques) or high signal (bright blood techniques) in a cross-section of the graft. Intravenous contrast administration may convey additional information and has also been used successfully. Nevertheless, for imaging of stenoses in bypass grafts coronary MRA has the same limitations and challenges as those previously described for imaging of the native vessels and is of limited clinical utility.

Figure 3. Patent venous bypass graft (arrow) to the left circumflex coronary artery, as visualized with coronary MRA. AAo=ascending aorta, PA=pulmonary artery.

Future directions

Substantial research is being performed into improvement of coronary MRA that will allow its wider use in clinical practice. There are multiple research directions, that are summarized in table 1.

Improvement of imaging sequences aims at faster data acquisition and better suppression of artifacts from motion, field inhomogeneity, etc., while at the same time utilizing the recorded signal in an optimal way. Steady state free precession and spiral sequences seem to hold promise for significant improvements in coronary MRA. Furthermore, parallel imaging approaches are already gaining widespread acceptance and decrease the imaging time several-fold.

Reconstruction techniques aim to improve the presentation of coronary MRA images so that the three-dimensional nature of the coronary arteries can be more easily comprehensible. Projection methods that visualize the entire coronary tree in a single plane, co-registration with data from other imaging modalities (e.g. myocardial perfusion studies) and virtual angioscopy are some of the possible future directions for development.

The use of contrast media has the theoretical advantage of offering higher signal and greater contrast between the vessels and the surrounding tissues. Intravascular contrast agents allow image acquisition during several minutes, so that the full advantage of free-breathing techniques can be utilized. Although there is no ideal contrast yet, several contrast media from various manufacturers are in phase II and III clinical trials.

Interventional coronary MRA is a revolutionary development that to date has only been described in experimental animals, but promises to be applied to humans in the near future. With this technique, the introduction and advancement of catheters and the selective engagement of the coronary ostium are performed under MRI guidance in real time. Subsequently, contrast is selectively infused in a single coronary artery and projections similar to conventional angiography can be obtained. Angioplasty with MRI guidance has also been reported in experimental animals, and with the continuous technical improvements it may be applied in humans in the not too distant future.

Lastly, an important direction of coronary MRA is for imaging of the atherosclerotic plaque. It is now well known that most of the acute coronary syndromes occur on hemodynamically "non-significant" lesions. The "soft" atheromatous plaque, with a large lipid core and thin fibrous cap, has been implicated as the vulnerable plaque that is rupture-prone and may cause complete vessel occlusion due to clot formation. Coronary MRA is one of the few non-invasive techniques that can image atherosclerotic plaque and evaluate its consistency. Although imaging of the wall of large vessels (aorta, carotids) is feasible with current technology, evaluation of atheromatous lesions of the coronary vessels will undoubtedly bring a revolution in the imaging and in clinical cardiology.

Table 1. Future directions for development of coronary MRA.

1. Improvement of imaging sequences
2. Improvement of reconstruction techniques and image presentation
3. Contrast media
4. Interventional coronary MRA
5. Imaging of the atherosclerotic plaque

Conclusions

Coronary MRA is a fast developing field. Today, the clinical applications of coronary MRA are mainly restricted to experienced centers and the main indications include evaluation of coronary artery anomalies, assessment of coronary aneurysms and patients with Kawasaki disease, evaluation of bypass graft patency and exclusion of significant proximal coronary artery disease in selected patients. Coronary MRA promises to be one of the main diagnostic imaging methods in the near future.

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