Volume : 5 | Issue : 5 | May 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

The Trend of Cardiovascular Imaging Like, CMRI (Cardiovascular Magnetic Resonance Imaging) & CCTA (Coronary Computer Tomography Angiography) and Future Aspect.

Medical Science

KEYWORDS : Cardiac Magnetic resonance imaging, Coronary CT angiography.

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ABSTRACT

Cardiac Magnetic resonance imaging (CMRI) sequences give complementary information on LV function, regional perfusion, angiogenesis, myocardial viability and orientations of myocytes. CMRI is useful for diffuse myocardial fibrosis associated with myocarditis, amyloidosis, sarcoidosis heart failure, aortic hypertrophic cardiomyopathy, congenital heart disease, restrictive cardiomyopathy, arrhythmogenic right ventricular dysplasia and hypertension. Coronary CT angiography has been increasingly used in the diagnosis of coronary artery disease owing to rapid technological developments, which are reflected in the improved spatial and temporal resolution of the images. High diagnostic accuracy has been achieved with multislice CT scanners (64 slice and higher), and in selected patients coronary CT angiography is regarded as a reliable alternative to invasive coronary angiography.3D and 4D Cardiac MRI and CT FFR are key role for future aspect in cardiology practice.

1. Introduction

Coronary artery disease is currently a worldwide epidemic with increasing impact on healthcare systems and major cause of mortality. Coronary angiography is gold standard to diagnose coronary artery diseases but it is invasive procedure. Due to this problem some patients are not agreed or unabailibity of interventional cardiologist in developing countries specially at district level, Non invasive diagnostic tools like cardiovascular magnetic resonance imaging (CMRI) and coronary computer tomography angiography (CCTA) are best options. Cardiac magnetic resonance imaging (CMRI) has moved from a research tool to a widely used diagnostic method in clinical practice last 10 to 15 years. While other imaging modalities like echocardiography and cardiac computed tomography depend solely on tissue density, the most important feature that CMR affords to the diagnostic toolset of the clinic cardiologist, is its ability to provide with a very-high spatial resolution, up to 0.5 mm × 0.5 mm in plane, a large array of different imaging sequences in order to assess *in-vivo* tissue characterization, in addition to radiation-free imaging. These imaging sequences investigate the presence of protons in different chemical environments, thereby allowing conclusions on the presence of fat, water (edema), blood or myocardium among other tissues. The addition of a contrast agent enhances the diagnostic capabilities to assess perfusion, fibrosis and necrosis as well as identify thrombus. Exploiting these different imaging sequences, in addition to the capability of performing high spatial resolution imaging in any desired imaging plane in 3-dimention (3D) space, CMR provides what could be also called "*in-vivo* pathology". Therefore, this has led to substantial progress in the assessment of patients with ischemic and non-ischemic heart disease.

Cardiac computed tomography (CT), and in particular coronary computed tomographic angiography (CCTA), stand poised to revolutionize the way in which cardiac pathology is diagnosed, and change the way in which decisions are made with regards to invasive treatment of cardiac disease. In particular, the diagnosis of coronary disease (the number one killer of patients in modern societies) will be strongly influenced in the coming years by this type of technology. However, there are many areas in cardiology and cardiovascular disease that will be influenced by this new technology.For most cardiac patients, the central question relates to the presence or absence of coronary artery disease (CAD) (i.e. coronary atherosclerosis).

2. The trend and future of cardiovascular magnetic resonance imaging (CMRI)

Cardiac Magnetic resonance imaging (CMRI) sequences give complementary information on LV function, regional perfusion, angiogenesis, myocardial viability and orientations of myocytes. T2-weighted short-tau inversion recovery (T2-STIR), fat suppression and black blood sequences have been frequently used for detecting edematous area at risk (AAR) of infarction. T2 mapping, however, indicated that the edematous reaction in acute myocardial infarct (AMI) is not stable and warranted the use of edematous area in evaluating therapies. On the other hand, cine MRI demonstrated reproducible data on LV function in healthy volunteers and LV remodeling in patients. Noninvasive first pass perfusion, using exogenous tracer (gadolinium-based contrast media) and arterial spin labeling MRI, using endogenous tracer (water), are sensitive and useful techniques for evaluating myocardial perfusion and angiogenesis. Recently, new strategies have been developed to quantify myocardial viability using T1-mapping and equilibrium contrast enhanced MR techniques because existing delayed contrast enhancement MRI (DE-MRI) sequences are limited in detecting patchy microinfarct and diffuse fibrosis. These new techniques were successfully used for characterizing diffuse myocardial fibrosis associated with myocarditis, amyloidosis, sarcoidosis heart failure, aortic hypertrophic cardiomyopathy, congenital heart disease, restrictive cardiomyopathy, arrhythmogenic right ventricular dysplasia and hypertension). Diffusion MRI provides information regarding microscopic tissue structure, while diffusion tensor imaging (DTI) helps to characterize the myocardium and monitor the process of LV remodeling after AMI. Novel trends in hybrid imaging, such as cardiac positron emission tomography (PET)/MRI and optical imaging/MRI, are recently under intensive investigation. With the promise of higher spatial-temporal resolution and 3D coverage in the near future, cardiac MRI will be an indispensible tool in the diagnosis of cardiac diseases, coronary intervention and myocardial therapeutic delivery.

In cardiomyopathy, CMR is becoming established as the endpoint of choice in clinical trials such as the recent INHERIT (Efficacy and safety of the angiotensin II receptor blocker losartan for hypertrophic cardiomyopathy (see figure-1 A) and the REGENERATE-DCM (Randomized trial of combination cytokine and adult autologous bone marrow progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy) trials, which capitalize on the low variability of quantitative CMR measurements. In parallel, the role of CMR in risk stratification is destined to expand further, following the results of a recent prospective study that showed the transmural extent of late gadolinium enhancement (LGE) by CMR is an independent marker of adverse prognosis in patients with amyloidosis(see figure-1 B). Meanwhile, the HCMR (Novel Predictors of Prognosis in Hypertrophic Cardiomyopathy) study, which aims to establish the prognostic value of CMR in hypertrophic cardiomyopathy, has recruited over 1/3 of its projected 2750 patients, promising to be another landmark study in establishing the future role of CMR tissue characterization in cardiomyopathy patients.

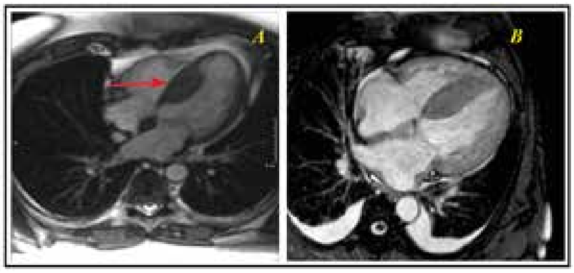

Figure-1 Cardiac MRI showed (A. Asymmetrical Hypertrophy, B. Amyloidosis)

In ischaemic heart disease, CMR is now firmly established as an alternative investigation to stress echocardiography and nuclear perfusion imaging in suspected stable angina and has a Class I recommendation in the current European Society of Cardiology guidelines in patients with stable CAD and intermediate pre-test probability. Two major outcome trials have completed recruitment in 2015 and are likely to shape the future use of CMR in this context.The CE-MARC 2 (Clinical Evaluation of Magnetic Resonance Imaging in Coronary heart disease) study was a prospective, multicentre, randomized, controlled trial comparing the efficacy and safety of CMR vs. conventional investigation in 1200 patients with suspected CHD (see figure-2 A, B) and is expected to report next year.The primary endpoint of the study is the avoidance of 'unnecessary' invasive coronary angiography, but cost effectiveness and clinical outcome will also be assessed.

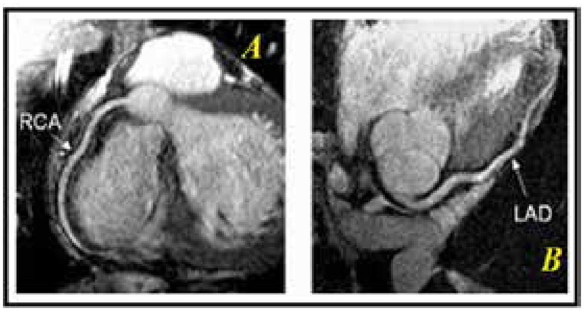

Figure-2 Cardiac MRI showed (A. Right coronary artery, B. Left Anterior Dissending artery)

The MR-INFORM (MR Perfusion Imaging to Guide Management of Patients With Stable Coronary Artery Disease) study directly compared an initial strategy of CMR perfusion with invasive angiography supplemented by fractional flow reserve (FFR) measurements in 918 patients with stable angina and an intermediate to high likelihood of CAD. This study, also expected to report in 2016, is the first multi-centre trial that directly compares modern non-invasive imaging with invasive FFR and may lead to future indications of CMR in higher risk populations.The results of these large prospective studies will determine the future role of CMR vs. other imaging modalities and other management strategies in patients with stable CAD. Meanwhile, CMR continues to be the endpoint of choice in clinical trials of acute myocardial infarction, because of its unique ability to precisely quantify infarct size and estimate myocardial salvage *in vivo*.Alongside the expanding clinical use of established CMR methods such as cine, perfusion, and LGE imaging, new methods that are considered to be the 'future of CMR' are developing at a rapid pace.Other methods with clear 'future potential' are multi-dimensional/ multi-directional flow (usually referred to as '4D flow'), which promises to have clinical applications in valvular heart disease, diseases of the aorta and also in myocardial disease (via derived parameters of wall shear stress), complementing existing CMR methods.

3. The trend and future of coronary computer tomography angiography (CCTA)

Coronary CT angiography has been increasingly used in the diagnosis of coronary artery disease owing to rapid technological developments, which are reflected in the improved spatial and temporal resolution of the images. High diagnostic accuracy has been achieved with multislice CT scanners (64 slice and higher), and in selected patients coronary CT angiography is regarded as a reliable alternative to invasive coronary angiography. With high-quality coronary CT imaging increasingly being performed, patients can benefit from an imaging modality that provides a rapid and accurate diagnosis while avoiding an invasive procedure. Despite the tremendous contributions of coronary CT angiography to cardiac imaging, study results reported in the literature should be interpreted with caution as there are some limitations existing within the study design or related to patient risk factors. In addition, some attention must be given to the potential health risks associated with the ionising radiation received during cardiac CT examinations. Radiation dose associated with coronary CT angiography has raised serious concerns in the literature, as the risk of developing malignancy is not negligible. Various dose-saving strategies have been implemented, with some of the strategies resulting in significant dose reduction.

As an alternative to invasive coronary angiography, coronary CT angiography (CCTA) has been increasingly used for the investigation of suspected CAD, and rapid technological developments have led to improved spatial and temporal resolution(see figure-3 A,B). The early generations of 4- and 16-slice CT scanners represented a technological revolution in cardiac imaging , although the diagnostic accuracy in terms of sensitivity was low for grading native coronary disease. Specificity for exclusion of CAD (negative predictive value) was good, and this generation of technology also proved useful for the evaluation of coronary anomalies and bypass graft patency. Improved spatial resolution with 16-slice CT plays an important role in the reliable detection and characterisation of coronary plaques and cardiac wall changes (such as remodelling of the coronary wall due to atherosclerotic plaques). However, the image quality is compromised in patients with a high heart rate, stents or severely calcified arteries . In 2004, all major CT manufacturers introduced the next generation of CT scanners with 32, 40 and 64 simultaneously acquired slices, which brought about a further leap in volume coverage speed. With gantry rotation times down to 330 ms for 64-slice CT, temporal resolution for cardiac electrocardiography (ECG)-gated imaging was again markedly improved. Improvement of image quality has also been reported in the visualisation of all coronary artery branches, with high sensitivity and specificity achieved . In patients with high heart rates, multisegment reconstruction algorithms were reported to provide diagnostic images by offering optimal temporal resolution, thus mitigating motion artefacts .

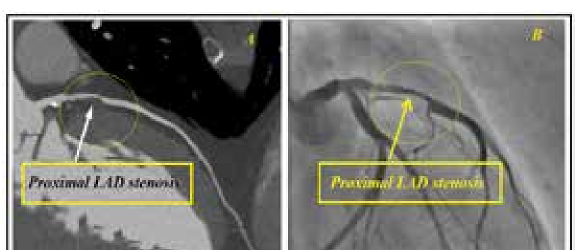

Figure 3 (A. CCTA showed High-grade proximal stenosis of the left anterior descending coronary artery (arrow), B. The insert shows the corresponding invasive coronary angiogram.)

Volume : 5 | Issue : 5 | May 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

The accuracy of coronary CTA for the detection of coronary artery stenosis is generally high . Problematic is a somewhat lower specificity. All published trials and meta-analyses that summarize these trials consistently indicate sensitivity values of more than 90% when compared with specificity values in the lower 80% range. Obviously, this will have consequences regarding clinical applications since the high sensitivity and consequently the high negative predictive value makes coronary CTA particularly suited to rule out coronary stenosis. However, in instances with unfavourable conditions for image quality, accuracy, and, in particular, the specificity of coronary CT angiography can be reduced. As stated above, this can for example be the case in the presence of pronounced coronary calcification and with an elevated or irregular heart rate. Also, patients who have a high pre-test likelihood of coronary artery disease show reduced accuracy.Hence, coronary CTA has very high sensitivity to identify coronary stenoses if image quality is good and the pre-test likelihood of the patients is in the lower range. This translates into a very high negative predictive value, which means to reliably rule out stenosis, and exactly that is the most frequent and prominent clinical application .

Large-scale registries and prospective trials have consistently shown an excellent prognosis and no need for further testing if CT demonstrates the absence of obstructive coronary lesions, both in acute and stable chest pain. This includes, for example, the CONFIRM registry with more than 25 000 patients and the randomized PROMISE trial with 10 000 patients, in which CT angiography as an initial test, performed just as well for suspected coronary disease as stress testing, with equal event rates during follow-up (3.3 vs. 3.0% in 2 years). Rates of invasive catheterization were higher in the CTA-based group (12.2 vs. 8.3%) but the rate of invasive angiograms that failed to show coronary stenosis were significantly lower (28 vs. 53%, $P = 0.02$). Interestingly, the randomized SCOT-HEART trial, published in 2015, evaluated 4146 patients with suspected coronary disease who received either standard workup for coronary disease or the same standard workup plus coronary CTA. After 1.7 years of follow-up, patients randomly assigned to also receiving coronary CTA displayed a 38% reduction in fatal and non-fatal myocardial infarction (which, however, barely missed significance at $P = 0.0527$).

Guidelines of national and international cardiac societies are starting to incorporate coronary CTA into their recommendations for the management of patients with stable and acute chest pain.European Society of Cardiology assign a 'Class IIa' recommendation ('should be considered') in patients with acute chest pain but absence of ECG changes and enzyme elevation as well as in patients with suspected stable coronary artery disease and a low-to-intermediate pre-test likelihood of coronary artery disease (roughly 15–50% pre-test likelihood). Very reasonably, the guidelines add that the respective centre must have adequate equipment as well as experience in coronary CTA and that patient characteristics are suitable for coronary CTA, with good image quality expected, which includes absence of pronounced coronary calcification.

The fact that coronary CTA is a purely anatomic test and *per se*, does not permit evaluation of the hemodynamic relevance of coronary artery stenosis, is a downside that it shares with invasive angiography. In fact, the development of coronary CTA during the past 15 years coincided with a period in which purely anatomic testing fell somewhat into disgrace, given the fact that the extent of ischemia, rather than the presence of stenosis alone, was repeatedly shown to predict a possible benefit of revascularization (for example, the FAME trials). For most 'candidates' for a coronary CTA examination, this is not relevant. They have a relatively low pre-test likelihood of disease, coronary CTA is performed to rule out stenoses, and if coronary CTA is 'negative'; no further testing is necessary. If stenosis are found and ischemia testing were desired, referral to another test for ischemia is a possibility [including coronary angiography with fractional flow reserve (FFR)], but CT itself also offers opportunities. The addition of CT myocardial perfusion imaging is one option. In the Core 320 trial, a combination of coronary CTA plus CT myocardial perfusion was tested against a combined gold standard of SPECT imaging plus invasive angiography and showed a high accuracy to predict hemodynamically relevant coronary artery stenosis. As an alternative, fluid dynamic modelling permits to simulate the effect of coronary artery stenoses on downstream myocardial perfusion under stress, based on the anatomy that is obtained by coronary CTA data sets obtained under resting conditions ('FFR-CT', see *Figure 4*). According to published data, such simulated FFR-CT results correlate quite closely with invasively measured FFR values. In the 'NXT Trial', published in 2013, the sensitivity of FFR-CT to identify coronary lesions with an invasively measured FFR ≤ 0.80 was 86%, specificity was 79% and overall accuracy was 81%.

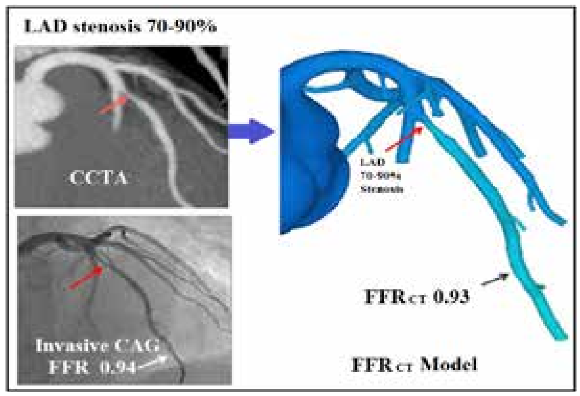

Figure- 4.(Simulated fractional flow reserve computed tomography based on fluid dynamic modeling with comparison to invasive coronary angiography.)

Coronary CT angiography allows the visualization of not only stenosis, but also non-stenotic coronary atherosclerotic plaque if image quality is good . Given the fact that the vast majority of cardiac events are caused by plaque rupture, the detection and characterization of plaque components is an interesting approach to improved risk stratification. To some extent, plaque characterization is possible since some parameters that are detectable by CT indicate the 'vulnerability' of coronary atherosclerotic lesions.They include a 'spotty' pattern of calcification, low CT attenuation (less than 30 HU), and a large degree of positive remodelling. In prospective trials, the overall extent of plaque in CT and the above-named features were shown to be associated with future coronary atherosclerotic events. However, the event rates in all of these trials were very low and even when plaque with 'advanced' features is present, overall prognosis is still rather good, which precludes the use of coronary CTA as a screening method in unselected populations.

Further developments of CT technology can be expected, but they will not be as fast or ground-breaking as some of the technical quantum leaps that have occurred in the past 10 to 15 years. The extent to which FFR-CT and CT myocardial perfusion imaging will turn into clinically robust diagnostic tools is somewhat uncertain at the moment, but will, in fact, not be so very relevant for the vast majority of patients at the lower end of the spectrum of pre-test probability, in which coronary CTA is a superb test, and in whom a 'negative' coronary CT angiogram allows to forgo any further testing. The major future development will therefore probably be, the wider availability, dissemination, and use of coronary CTA as a diagnostic test to rule out coronary disease, rather than its proliferation towards patients with higher pre-test likelihood or those with known disease.

4. Conclusion

Cardiac magnetic resonance imaging (CMRI) has become a basic diagnostic tool in cardiovascular medicine. The next decade will be marked by clinical trials investigating the prognostic value of the detailed imaging findings that can be obtained today, and may guide therapy and improve patient prognosis. coronary CT angiography (CCTA) and cardiac CT is a promising new technology that is already having an impact on the way in which coronary disease is discovered and followed. There is sufficient evidence to confirm that coronary CT angiography represents the most rapidly developed imaging modality in cardiac imaging, with satisfactory results having been achieved. Multislice CT scanning protocols in cardiac imaging should be standardised across institutions with the aim of reducing dose variation across patients and facilities. 3D and 4D Cardiac MRI and CT FFR are key role for future aspect in cardiology practice.

5. Acknowledgements

Author would like to thanks to Dr. Sonal Tanwar and Dr. Mayank Bansal . They provide lot of support to get learnings and related articles.

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