Recent Advances in Cardiovascular Magnetic Resonance

Highlights From the 2011 Society for Cardiovascular Magnetic Resonance/Euro Cardiovascular Magnetic Resonance Joint Scientific Sessions, February 3-6, 2011, Nice, France

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The 2011 annual Scientific Sessions of the Society for Cardiovascular Magnetic Resonance (SCMR) was a joint meeting with the European CMR Working Group for the European Society of Cardiology. Attended by 1117 clinicians and scientists, this year's meeting introduced new enhancements with a greater number of poster abstracts as well as case review sessions. Along with the traditional basic science and physics, pediatric, and general cardiovascular magnetic resonance (CMR) tracks, this new format provided a more enriching discussion environment.

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During the 4-day program, 516 abstracts were presented (112 oral, 11 moderated posters, and 393 posters), highlighting new advances in the field and critically addressing some concepts that were introduced last year.[1] As discussed in the two plenary sessions, the main topics of the meeting involved the application of CMR to outcomes studies and randomized trials, its cost effectiveness, an increase in the studies of diffuse fibrosis, and a review of the application of T2 imaging techniques to assess myocardial edema. In this review we cover the full scope of these highlights and present some of the key themes of the meeting.

Technology Advances

CMR is a technology that continues to make substantial strides, and this year's meeting has again demonstrated that the field is rapidly evolving. High-field imaging (progressing from a magnetic field of 1.5T to 3.0T) continued to gain momentum, and many clinical and academic institutions have added 3.0T scanners to their installed base, making this magnetic field strength a substantial percentage of the platforms applied to CMR in cardiology.[2] Some of the problems inherent with high-field imaging were addressed by Rehwald and colleagues,[3] who showed that new T2 preparation techniques based on adiabatic refocusing pulses significantly reduced inhomogeneities and increased quality scores while maintaining specific

absorption rate limits within acceptable values. Techniques such as the one presented will certainly need to come into play as stronger magnets may be used in the future, as was shown by Suttie and colleagues,[4] who studied 10 human volunteers with cine sequences under 1.5T, 3.0T, and 7.0T. The authors demonstrated a significant increase in signal to noise (SNR) and contrast to noise (CNR) ratios with 7.0T, proving that CMR at ultrahigh fields is feasible and may have advantages over routine lower fields that are in use today.

Another area for improvement in CMR is the use of noncontrast methods to assess flow and perfusion in this era of increased surveillance of gadolinium-based contrasts.[5] In that regard, arterial spin labeling (ASL) has gained more attention, as was presented by Zun and associates,[6] who compared an ASL method using flow-sensitive alternating inversion recovery and steady-state free precession (SSFP) at 3.0T to standard first-pass perfusion in 29 patients. ASL was able to identify patients with reduced perfusion reserve and myocardial blood flow with a potential to diagnose significant coronary artery disease in the absence of a contrast agent. In the same way, application of diffusion-weighted imaging—a method widely used in other parts of the body—may also prove useful in the heart, as shown by Laissy and associates,[7] who used the technique to differentiate recent and chronic myocardial infarction (MI) with a high sensitivity of 97% and a significant apparent diffusion coefficient ratio among the groups. Taken together, these new methods, plus other noncontrast techniques for MR angiography,[8] allow for the possibility of studying patients in whom gadolinium use is considered unsafe.

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MR coronary angiography, one of the cornerstones for wider CMR use, was also a topic that generated great attention, meriting a dedicated case review session on optimizing protocols for image acquisition both at 1.5T and 3.0T. In the technical forefront, Agarwal and colleagues[9] presented a new method that might substitute the commonly used T2-prepared scans to suppress background myocardial signal. The authors performed local reinversion labeling of blood from the aorta and left ventricle (LV), resulting in almost double CNR as compared with the T2-prepared method resulting in the same SNR of blood. Despite that, for the right coronary artery the visible vessel length was smaller, indicating a tradeoff that might have to be further developed to increase the accuracy of the technique. As with the previous examples, all images were obtained without contrast agents maintaining an isotropic resolution of 1.3 mm at 3.0T. Another technical advance highlighted in the meeting was the use of multiradiofrequency transmission coils versus single transmission at high fields when studying the coronary arteries. Especially true for SSFP sequences, the use of multichannel transmission reduces inhomogeneity and may allow for shorter repetition times.[10] Ishida and colleagues[11] applied these concepts for studying whole heart coronary MR angiography at 3.0T using an SSFP sequence, comparing it with single transmission as well as a fast-gradient echocardiography method. Although image quality was rated higher for all SSFP images, there were still banding artifacts present despite the use of multichannel transmission, indicating some room for improvement.

Finally, CMR-guided intervention also drew much attention, with a specific lecture session and many abstracts presenting novel work. Quick and coworkers[12] demonstrated a pioneering work in the use of CMR to guide the emerging application of transarterial aortic valve implantation. Using a modified MR-compatible delivery device and a nitinol stent frame aortic bioprosthesis, the authors successfully implanted six valves in eight pigs with real-time guidance and postinterventional MR evaluation. Tzifa and coworkers[13] went even further and presented data on seven human patients in the first-in-human clinical trial of CMR-guided intervention. The preliminary results demonstrated successful interventions in pulmonary valve stenosis as well as aortic coarctation using real-time monitoring with a temporal resolution of 11 to 12 frames/sec. These two studies demonstrate the feasibility of CMR to guide such interventions with no exposure to ionizing radiation and with greater anatomic colocalization. With new sequence developments, such as the one presented by George and colleagues[14] (the Basic Science Early Career Award winner) that allow for real-time visualization of blood flow and no contrast, CMR can become the imaging modality of choice for percutaneous vascular interventions. Future comparative studies, as well as an increase in the number of centers that perform and patients who undergo such interventions, should be carried out to assess if this novel use of CMR will gain clinical applicability.

T1 Mapping, and Regional and Diffuse Fibrosis

The large amount of data available on late gadolinium enhancement (LGE) and regional fibrosis continued to grow, effectively earmarking this finding as a powerful diagnostic and prognostic tool in CMR.[15] However, more than a simple binary classification of black and white, LGE analysis has evolved into a more complex and profound evaluation, especially in the border zones of myocardial lesions. Heydari and associates[16] explored this concept by looking at LGE heterogeneity in patients with acute MI at baseline and at 6-month follow-up, demonstrating that the peri-infarct zone, characterized by heterogeneous LGE, may help predict adverse left ventricular remodeling. Previous characterization of this area as a substrate for arrhythmias and its association with higher mortality[17] suggests that the pure classification of LGE as present or absent might have to be reviewed as higher resolution and clearer definitions of heterogeneity are established.

Despite the proven clinical utility and potential of LGE, the evaluation of diffuse fibrosis and T1 mapping of the myocardium have gained increased interest because many diseases affecting the heart are more prone to diffuse rather than localized myocardial structural changes.[18] Mongeon and colleagues[19] used this concept to demonstrate that myocardial extracellular volume fraction defined by CMR is already increased in hypertensive patients compared with controls despite similar ventricular mass or changes in diastolic function by echocardiogram. In the same way, Thibault and associates[20] quantified T1 in 24 patients with asymptomatic type 2 diabetes, normal ejection fraction, and no LGE, comparing them with matched control subjects. The authors showed that diabetic patients already demonstrate shorter T1 times before and after contrast; this finding was associated with impairment of mitral inflow pattern by echocardiography. Taken together, these two studies demonstrate that T1 assessment and diffuse fibrosis by CMR may prove useful in subclinical heart changes that occur in chronic diseases associated with long-term myocardial consequences. The studies suggest that monitoring those changes might be beneficial to assess drug effects or rapid progression of disease.

Aside from its use in subclinical diseases linked to ischemic cardiomyopathies, diffuse fibrosis was also shown to provide for diagnostic and prognostic data in many other nonischemic cardiomyopathies. Campbell and coworkers[21] (winners of the Basic Translational Early Career Award) used the new technique of equilibrium contrast CMR[22] to study the extracellular volume of distribution of gadolinium in the hearts of amyloidotic mice, showing that the technique can detect minimum amyloid deposits as confirmed by histology. The same method was used to evaluate patients with severe aortic stenosis with planned intervention at baseline and 6 months postoperatively by Flett and associates.[23] They demonstrated that diffuse myocardial fibrosis was higher in patients with more severe LV impairment and aortic stenosis, and that this variable was the best predictor of postoperative improvement in exercise capacity. In the setting of systemic sclerosis, the search for diffuse fibrosis was also possible, this time using a modified Look-Locker inversion recovery (MOLLI) sequence and T1 mapping, as shown by Thuny and colleagues[24]; 37 systemic sclerosis patients with normal volumes and ejection fraction by echocardiography and no LGE were investigated. The study showed reduced T1 times after gadolinium contrast injection in patients with diastolic function as compared with controls, despite no overall changes in T1 among the entire group.

Although the best method to evaluate diffuse myocardial fibrosis and/or T1 is not yet established, to make this evaluation clinically useful it would certainly be desirable that the technique be simple and applicable to most patients. In that regard, Breton and associates[25] proposed a T1 mapping acquisition sequence that requires only two heartbeats. The new rapid method uses a proton density-weighted image in the first heartbeat and a saturation recovery T1-weighted acquisition for the second beat with a significant correlation (r = 0.99) to the routine MOLLI sequence. The rapid method would allow for definition of T1 maps despite cardiac motion or arrhythmias, thereby increasing the number of patients who could be studied.

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T2 and Edema Imaging

Edema imaging and the assessment of myocardial area at risk using T2-weighted (T2W) imaging was among the most discussed topics at the meeting. In 2010, after very early

enthusiasm with the presentation of new methods, controversy arose as to whether technical issues involving T2W imaging were in fact resolved—specifically, poor image quality, effects from stagnant blood, choice of threshold for definition of edema, and different coil sensitivities around the heart.[26] To support part of the skepticism surrounding T2W imaging, two papers, presented by Kim and colleagues[27] and Smulders and colleagues,[28] from Duke University (Durham, NC), compared T2W imaging with infarct area by standard LGE. The first abstract directly compared T2W and LGE transmurality in 34 dogs 3 days after the occlusion of the left anterior descending and left circumflex arteries, demonstrating that T2 hyperintensity and LGE were similar in the same proportion of cases. The authors concluded that T2W images are frequently not transmural and follow the course associated with infarct transmurality, therefore not representing in whole the real area at risk. The second paper assessed whether T2W imaging could differentiate acute versus chronic infarcts in 117 patients with a first acute MI. Results showed that for infarcts that are 1 to 6 months old, T2W imaging is less specific, maintaining a sensitivity of 88% and specificity of 66% for the cutoff of 1 month-old infarcts. The authors did emphasize that over one-third of the T2W images were graded poor, a finding that renders the technique not easily reproducible. Ugander and coworkers[29] also presented new data suggesting that noncontrast T1 mapping might also reproduce the same area at risk as T2W imaging. The study involved 12 dogs that underwent 2-hour coronary occlusions with microsphere assessment, and T1 and T2 SSFP mapping, with a threshold of 2 standard deviations for determining the area at risk. Both methods significantly corresponded to microsphere analysis, suggesting that not only T2 but also T1 could change with myocardial edema following ischemia/reperfusion injury. Data from the same group also showed that myocardial T1 increases with coronary occlusion; in tissues that eventually become infarcted this increase is higher and continues after reperfusion when compared with salvaged myocardium in which T1 stabilizes.

Despite these controversies, new data using T2W imaging also provided further evidence of the possible utility of this technique as it currently stands. Usman and colleagues[30] compared the T2 myocardial values of different patient groups, showing a significant increase in T2 values in patients with confirmed myocarditis (viral, sarcoid, and giant cell) in infarcted segments and in the apex of a patient with Takotsubo as compared with ruled-out myocarditis cases, noninfarcted segments, and the basal slices of the same patient with reversible apical dysfunction. The authors concluded that T2 mapping is a useful tool in evaluating patients with acute cellular response and edema in the clinical setting.

Two studies also demonstrated the use of T2W imaging after bouts of exercise as well as alcohol intake. The first study presented by Cocker and associates[31] showed an increase in the ratio of global myocardial to skeletal muscle signal after both incremental exertion to exhaustion and high-intensity interval training compared with pretraining values. The extent of increase in T2 values significantly correlated to LV ejection fraction. A second study of 31 healthy volunteers evaluated the effect of binge drinking at 12 hours and 1 week after alcohol intake. The authors found a significant increase in signal intensity with T2W images as well as with early T1-weighted global relative enhancement at 12 hours that subsided at 7 days, suggesting that even a single episode of heavy drinking leads to cardiac inflammation that could be detected by CMR.

Multicenter Trials, Outcome Studies, and Cost Effectiveness

In two of the most important sessions of the meeting, including the opening plenary, great attention was called to the use of CMR in studies devoted to outcome and cost effectiveness. The future of the modality lies within its ability to prove useful in altering patient treatment and overall survival.[32] This requires great attention to the use of CMR in multicenter trials and large global registries where its application can be fully exploited.

Carpenter and associates[33] showed the results of their worldwide survey in 34 centers involving 3376 patients with β thalassemia major, demonstrating that despite significant efforts a large proportion of these patients still present with moderate to severe iron overload as shown by CMR. This was the first registry of its kind with data from all geographical regions of the world. Regarding cost effectiveness, Hegde and colleagues[34] retrospectively reviewed 361 patient charts in two different centers to assess whether CMR use resulted in overall savings based on the benefits obtained by the examination. The authors showed that in 71% of patients a significant impact was observed by the use of CMR with avoidance of further invasive testing in 10.5%, resulting in a net savings of $833,037 for the group that was driven by patients with a new diagnosis.

Of course saving money does not justify the existence of any imaging modality if it does not change the

way patients are managed. In accordance with the recently published manuscript by Iles and colleagues,[18] Klem and associates[35] also demonstrated that using a scar threshold of 5% in patients undergoing evaluation for implantable cardioverter defibrillators (ICDs), one could identify those at increased risk for death or appropriate discharge (even in patients with preserved left ventricular ejection fraction). Gao and coworkers[36] complemented these findings by demonstrating, through multivariate analysis, that scar mass was the major predictor of adverse outcomes in both ischemic and nonischemic patients who underwent primary implantation of ICDs. Taken together, these new data suggest that CMR may become one of the gatekeepers for the indication of ICD implantation, with the absence or small amounts of LGE, indicating patients at low risk in whom the implant might provide no benefit. This also seems to be the case with regard to cardiac resynchronization therapy. Wong and coworkers[37] developed a three-point prediction rule using CMR showing response rates of 100%, 92%, 58%, and 40% for 3- to 0-point scores, respectively, using dyssynchronous segments defined as time to maximal radial strain $>$ 130 ms. They concluded that both dyssynchrony and scar, as indicated by CMR, can be highly predictive of the response to cardiac resynchronization therapy.

Metabolism and Spectroscopy

The assessment beyond anatomy and function has always been a significant advantage of CMR not yet fully explored. Metabolism assessment, especially with spectroscopy techniques at high fields,[38] is continually evolving, as shown by the new research presented at the meeting. Weiss and coworkers[39] used a navigated, local-look echo-planar spectroscopic imaging sequence that allowed for the in vivo assessment, during free breathing, of triglyceride and creatine spectra at different regions of the myocardium at 1.5T with an average 2.5-minute duration. Suttie and coworkers[40] used ^{31}P spectroscopy at 3.0T to show that patients with dystrophinopathies presented with significantly abnormal phosphocreatine to adenosine triphosphate ratios in segments with impaired regional contractility when compared with normal segments.

Although phosphorus has been the dominant nucleus for CMR spectroscopy, the use of ^{13}C-labeled metabolites was also highlighted because hyperpolarized ^{13}C can be used both for spectroscopy and CMR imaging.[41] Schroeder and colleagues[42] used ^{13}C spectroscopy to show very early metabolic changes in the heart in a pig model of dilated cardiomyopathy. With the same nucleus, using a pyruvate substrate, Frijia and coworkers[43] obtained three-dimensional metabolic images at 3.0T of the hearts from three pigs using a spiral sequence, suggesting that this new technique may allow for the investigation of the metabolism of the whole heart at once in different scenarios.

Conclusions

The program and abstract committees have managed to yield a very effective and integral meeting that was reflected in the quality of the scientific evidence highlighted above. SCMR has reached its initial vision and mission statements and is now widening its goals by becoming a truly international society for CMR. The recognition of new geographical areas to explore has brought participants from India and China into the program, along with new challenges and opportunities to be undertaken vigorously in the next few years. The use of this noninvasive, nonionizing green radiologic method in an era in which radiation is a grave concern will no doubt increase, with widespread availability and scientific breakthroughs paving the way. ■

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Main Points

- Technical advances such as high-field imaging, noncontrast sequences, and cardiac magnetic resonance (CMR)-guided interventions were reported in the meeting.
- Tissue characterization with T1 mapping and T2 edema imaging were largely discussed, and pointed to future clinical exploitation of both techniques.
- Outcome studies, multicenter trials, and cost-effectiveness evaluations were identified as key to the future of CMR.

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