Editorial

Understanding the Risk to Develop Atrial Fibrillation
And What Cardiac Magnetic Resonance Can Add

Juerg Schwitter, MD

MESA (Multi-Ethnic Study of Atherosclerosis) is an observational cohort study to determine the prevalence, correlates, and progression of subclinical cardiovascular disease. MESA participants were 45 to 84 years of age and were asymptomatic of clinical cardiovascular disease in 2000 to 2002 at recruitment and were studied in 6 centers in the United States. This ambitious setting offered the unique opportunity to monitor an asymptomatic cohort of subjects over a long time period, and the investigators decided in 2000 to evaluate cardiac structure and function by cardiac magnetic resonance (CMR) to obtain most accurate measurements.

See Article by Habibi et al

In this issue of Circulation: Cardiovascular Imaging, Habibi et al1 report on the predictive value of left atrial (LA) volumes as well as functional LA parameters for incident atrial fibrillation (AF). Out of the 5004 participants, 597 patients (197 cases developed AF during follow-up and 400 patients were randomly selected from the MESA cohort irrespective of their case status) were selected for this study and followed over a mean of 7.6 years. In addition to LA volumes and functional parameters, left ventricular (LV) mass, N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, arterial hypertension, and antihypertensive treatment were also identified as strong predictors of AF development. Body mass index, diabetes mellitus, smoking, total and high-density lipoprotein, and LV ejection fraction (EF) were not associated with incident AF.

Several of these findings are new and of major importance because AF is the most common cardiac arrhythmia, and it is associated with a substantial burden of cardiac and cerebrovascular morbidity and mortality. Over 2 million adults were diagnosed with AF in 2000 in the United States, and this number is expected to reach almost 6 million subjects in 2050.2 Among 66,357 patients admitted to 283 hospitals with acute decompensated heart failure, AF was present in 44% of patients with reduced EF versus 48% with preserved EF (HFpEF), and 30-day mortality in patients with AF and HFpEF was even higher than in heart failure with reduced EF patients.3 Accordingly, treatment strategies to prevent AF are of outmost importance. Diagnostic work-up and drug treatment seem most efficient economically when targeted to a high-risk population. The results presented by Habibi et al1 are, therefore, of major significance because they allow to identify individuals at high risk to develop AF based on models integrating demographic information, LA volume, and functional information, as well as circulating biomarkers. In future studies evaluating novel drug treatment strategies, patient selection could be enriched based on such model estimates of risk to include patients who will benefit most from treatment. This approach would permit to run trials for clinical outcomes at smaller sample size, which can produce results faster and at lower costs. CMR is a rapidly evolving technique that is becoming more widely available,4,5 and with appropriate standardization and harmonization, excellent image quality can be achievable in multicenter trials even in patients with implanted pacemakers6 and defibrillators.7

The present study is the first demonstrating the relative prognostic value of LA volumes and reduced LA reservoir (ie, total LA ejection fraction [LAEF]), reduced conduit (ie, passive LAEF), and reduced booster pump function (ie, reduced active LAEF) to predict incident AF. These CMR-based parameters all remained significant after adjusting for age, sex, ethnicity, hypertensive medication, and systolic blood pressure. However, when also adjusting for NT-proBNP and LV mass, active LAEF was no longer a predictor. In fact, active LAEF but not passive LAEF was inversely associated with NT-proBNP (r=-0.19; P=0.027), probably explaining why active LAEF did not remain in model 2, that is, after correction for NT-proBNP. Interestingly, NT-proBNP is well known as a predictor of incident AF,8,9 and in light of the present results, NT-proBNP seems to relate to active LAEF, whereas passive and total LAEF determined by CMR yield additional prognostic information. Of note, passive LAEF was a stronger predictor of incident AF (hazard ratio 0.68; P=0.003) than active LAEF (hazard ratio 0.74; P=0.014) in model 1 (which is not corrected for NT-proBNP). The occurrence of AF in HFpEF patients is heralding a worse outcome,3 and HFpEF is associated with a higher incidence of AF. Nevertheless, some typical characteristics of the HFpEF population, such as female sex, arterial hypertension, obesity, and diabetes mellitus, were not found to be prevalent in the HFpEF population of this study. Compared with the control group without incident AF, the AF population had a higher incidence of hypertension and antihypertensive treatment, but there was no preponderance of females and no preponderance of diabetes.
mellitus nor increased body mass index. This indicates that the population at risk to develop AF as presented in this study is not coherently matching key features of HFpEF populations. Mechanistic and pathophysiological insights provided by CMR as presented in this study may be helpful to better characterize the populations at risk to develop AF and HFpEF in future studies.

CMR is an extraordinarily versatile technique, which yields information on cardiac structure, function, tissue composition, and blood flow, with excellent spatial resolution. As a consequence, increasing amounts of data are produced during each CMR examination, and image data analysis can become a limiting factor. In this study, Habibi et al convincingly demonstrate the power of feature tracking to analyze large numbers of LA data. Feature tracking can accurately follow contours like the endo- or epicardium of the ventricles or atria, but it does not yield tissue deformation information as CMR tagging does. The authors used the area–length method to calculate LA volumes. This approach can underestimate true volumes by 10% to 20% depending on the shape of the LA. Also, to use a fast gradient echo readout is a limitation because nowadays steady state–free precession is applied generally, and it produces images of considerably higher quality. This readout can also be combined with the so-called compressed sensing technique, which can accelerate conventional cine acquisitions by ≤11-fold: steady state–free precession with compressed sensing affords acquisition of multiple slices of the LV or LA within a single breath-hold and 3-dimensional reconstructions with high temporal and spatial resolution. Thus, combining all these emerging novel features of CMR will allow to detect even more subtle alterations in LA structure and function, which will improve our understanding of the pathophysiology while sample sizes to detect differences can be reduced. Of course, LA volumes and phasic function parameters are not all that CMR can provide. Late gadolinium enhancement is able to quantify scar tissue, more easily in ventricular but increasingly feasible in atrial myocardium. Fibrosis in the LA was quantifiable in 85% of patients and was shown to be a strong predictor of AF recurrence after AF ablation in a multicenter trial. Although feasibility in humans remains unknown, preclinical studies suggest that atrial myocardial edema, potentially reversible damage, is detectable by T2 imaging. Atrial inflammation is also considered a pathophysiological mechanism leading to AF and has been demonstrated in patients with LV myocarditis. In this context, 19F-fluorine CMR might open new perspectives because it was shown to visualize macrophages in myocarditis. Interestingly, CMR is able not only to assess the LA in isolation, but it also offers the possibility to investigate the LA together with changes in the LV and the RV or by looking at the LV–aortic coupling. With this approach, CMR should allow us to better understand the pathophysiological processes that change tissue composition and function in the entire atrial–ventricular–vascular axis, leading finally to LA overload and AF. Also from MESA data, we know that reduced LA regional and global functions are related to both replacement and diffuse myocardial fibrosis of the LV myocardium. In addition, such changes can be monitored longitudinally because CMR is not handicapped by exposing patients to ionizing radiation. Finally, interventional magnetic resonance imaging guiding LA ablation in humans provides an intriguing window to the personalized medicine end of the atrial imaging spectrum to complement this work’s population focus.

Disclosures
Dr Schwitter serves as consultant to Medtronic and is primary investigator for several multicenter trials of Medtronic.

References


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