Whole-Body MR Angiography: Assessing the Global Burden of Cardiovascular Disease[1]

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Cardiovascular disease remains the leading cause of morbidity and mortality worldwide, with an estimated 15 million deaths in 2015 (1). Prevention of cardiovascular disease requires timely identification of individuals at increased risk to target proven dietary, lifestyle, and drug interventions. For many decades, interventions to reduce the risk of cardiovascular disease among asymptomatic persons have been implemented largely by using a two-step process based on absolute risk. First, by using a global risk–estimating algorithm such as the Framingham risk score or the European Systematic Coronary Risk Evaluation (SCORE), physicians have stratified patients who are candidates for primary prevention into lower-, intermediate-, and higher-risk subgroups, typically calculated over a 10-year time frame. Then, guidelines based on such stratification have traditionally targeted lifestyle interventions to those persons at "lower" and "intermediate" risk while limiting more aggressive pharmacologic interventions (such as statin therapy) to those with "higher" risk profiles. Although this approach has led to a substantial reduction in cardiovascular disease burden, there is a bewildering array of models predicting incident cardiovascular disease in the general population. For instance, a recent systematic review of 212 articles describes 363 prediction models (2). Most of these models, however, have not been externally validated or directly compared on their relative predictive performance, making them currently of yet unknown value for practitioners, policy makers, and guideline developers. Furthermore, an important shortcoming of these risk prediction models is the lack of information about the presence and extent of atherosclerosis in individual patients.

To address this shortcoming, considerable efforts have been put into identification of noninvasive and cost-effective biomarkers, which can inform treating physicians about the presence and extent of atherosclerotic arterial disease. For instance, patients who are at intermediate risk for cardiovascular disease events may benefit from net reclassification of risk based on blood biomarkers linked to inflammation, oxidative stress, lipid metabolism, thrombosis, endothelial dysfunction, hemodynamic stress, and cardiomyocyte injury (3). In addition, multiple imaging biomarker modalities, including coronary artery calcification and carotid ultrasonography (US) may play an important role in further risk stratification for patients in the later stages of cardiovascular disease development. Apart from identifying individuals with subclinical atherosclerotic arterial disease, the data obtained from these markers could play an important role to monitor the effects of pharmacologic therapy (4).

In this issue of *Radiology*, Lambert and colleagues (5) found that nearly half of asymptomatic men and women over age 40 years at low to intermediate risk for cardiovascular disease have detectable arterial narrowing in at least one vessel at whole-body magnetic resonance (MR) angiography, and over a quarter of individuals had arterial narrowing in multiple vascular segments. These findings derive from the Tayside Screening for Cardiac Events (TASCFORCE) study, a prospective cardiovascular risk screening study in healthy volunteers over age 40 years living in Scotland who are free from cardiovascular disease and without an indication for preventive medication under current guidelines. Individuals at high risk (defined as a risk increase of greater than 20% for a cardiovascular event in 10 years), individuals with known atherosclerotic disease, and individuals with blood pressure of greater than 145/90 mm Hg were excluded from participating.

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See also the article by Lambert et al in this issue.

In total, 1528 participants underwent contrast material–enhanced whole-body MR angiography by using 25 mL of macrocyclic gadolinium-based contrast agent with a 3.0-T MR system. Per subject, 31 vascular segments from the carotid arteries down to the ankles were visually assessed for the presence of stenosis or aneurysmal disease. Diagnostic images were obtained in 1513 participants (44 435 vascular segments) and less than 1% of vascular segments were not interpretable. Arterial narrowing was found to be diffusely distributed throughout the vascular tree, without a clear anatomic predilection. These findings corroborate our understanding that atherosclerosis is a systemic disease, which starts to develop at an early age and gradually becomes more severe over time.

As expected, multivariable analysis of the relationship between findings at whole-body MR angiography and traditional cardiovascular risk factors such as age, sex, smoking status, blood pressure, and lipid levels revealed an association with the presence and extent of atherosclerosis (ie, participants with higher levels of risk factors more often had atherosclerotic arterial disease). Several interesting observations can be made about this study. First, no differences in global atheroma burden were found between men and women, which is in contrast to a recent study in which subclinical atherosclerosis burden was assessed by using a three-dimensional vascular US protocol for volumetric quantification of plaque burden (6). Furthermore, the authors also found an association between global atheroma burden and socioeconomic deprivation. Although this is not the first study to describe this association, the findings underscore the multifactorial and complex nature of cardiovascular disease and the challenges associated with preventive measures aimed at lifestyle modification.

It is also important to note that the known traditional cardiovascular risk factors, as well as demographic factors and blood markers, explained just a small proportion of the observed variability in atheroma between participants (adjusted R^2 value of 11.4%). In general, the higher the adjusted R^2 value, the better the measured variables as a whole explain the measured global atheroma burden. Several reasons may explain this finding. Most importantly, participants with high risk were excluded from participating in the study. In other words, individuals with the highest levels of risk factors were not imaged with whole-body MR angiography. It is likely that a stronger association would have been found if these participants had also been imaged. A second important explanation is random variability in the measured risk factors. It is well known that variables such as blood pressure, cholesterol, and heart rate can vary considerably over time (7) and a single measurement may not be representative. Finally, many other known but harder-to-measure risk factors—such as amount and intensity of physical activity, sleep duration, and exposure to stress and environmental pollution—as well as other unknown factors are likely to substantially contribute to the observed variation.

The ability to directly visualize arterial narrowing throughout the body without the need for radiation makes whole-body MR angiography a highly attractive modality to identify asymptomatic individuals at increased risk of experiencing a cardiovascular event. Contrast-enhanced MR angiography has been shown to be highly reliable in relation to the accepted standard of reference, intra-arterial digital subtraction angiography (8), and it can be assumed that the presence and extent of arterial narrowing visualized with the described imaging protocol are indeed an accurate reflection of the true global atheroma burden in the participants included in the study. Another advantage of whole-body MR angiography is the possibility to simultaneously depict the amount and distribution of body fat and muscle, which has been linked to coronary artery calcifications (9).

Nevertheless, an important drawback of the whole-body MR angiography used in the present study is the lack of visualization of atherosclerotic plaque burden because the vascular wall is not depicted; additional imaging time is required for this purpose. Another disadvantage is that the most widely used whole-body MR angiography techniques presently require injection of a gadolinium-based contrast agent, which is not without risk. However, good to excellent results have recently been described without the use of contrast agents (10). When such techniques become more widely available, whole-body MR angiography will become even more attractive as a tool used to obtain biomarkers of atherosclerotic arterial disease. Finally, the coronary arteries were not visualized and thus there is no direct information about coronary artery atheroma burden.

In conclusion, imaging biomarkers have been shown to significantly improve cardiovascular risk assessment by identifying individuals with subclinical atherosclerotic arterial disease. Whole-body MR angiography enables identification of arterial narrowing in all large and medium-sized arteries in the body in a single fast and easy to perform examination, without the need for ionizing radiation. It remains to be determined if and to what extent whole-body MR angiography is capable of reclassifying patients at low and intermediate risk to high risk, making them eligible for more intensive preventive treatment.

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