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evascularization is not without risk to the patient, and the decision to proceed to percutaneous coronary intervention begins with comparing the patient’s individual risk of undergoing the procedure with the risk of conservative management without it. Despite improved understanding, predicting the risk for stable coronary artery disease is fraught with many unknowns, especially pertaining to the relative contributions of ischemia and plaque burden or their combination. Patients without ischemia do not undergo revascularization (1,2), and those with milder degrees of ischemia may not benefit from revascularization (3). In contrast, a greater ischemic burden is associated with a higher event rate, and these patients benefit from revascularization. However, how much ischemia is needed before such a benefit is seen remains a matter of debate. Much of our thinking is based on observational data, and it is only now being addressed in prospective and randomized trials such as ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches). Further investigation is needed to harmonize the definition of moderate to severe ischemia with various tests, because each modality uses its own definition, and positive results on different tests may represent different levels of ischemic burden.

There is also controversy regarding what constitutes ischemia: is the requirement an anatomic stenosis (lumenography), a physiologic stenosis with a critical threshold of flow limitation (fractional flow reserve assessment), or an index documenting limited perfusion (as with perfusion imaging)? Future studies might even image tissue oxygenation deficit, as in blood oxygen level-dependent imaging with cardiac magnetic resonance (CMR). The recently published PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial demonstrates that in patients with low pre-test likelihood for coronary artery disease, management guidance by computed tomographic angiography provides similar outcomes compared with management guidance by functional testing. This question will be further addressed by the MR-INFORM (MR Perfusion Imaging to Guide Management of Patients With Stable Coronary Artery Disease) study. This trial will assess whether clinical management in patients with high pretest probability can be guided noninvasively by perfusion CMR compared with invasive assessment by coronary angiography and fractional flow reserve measurement (4).

Most trials have focused on imaging flow-limiting stenosis (a focus on ischemia), with negligible emphasis on plaque burden. Plaque burden is a marker of disease severity and has strong prognostic value. Recent data based on computed tomographic angiography have confirmed the prognostic importance of plaque burden in a large cohort (5). Stenosis and plaque burden may even reflect different outcomes, such as the angina- or ischemia-related left ventricular dysfunction with stenosis versus acute events such as acute coronary syndromes or sudden cardiac death with plaque burden or plaque characteristics. What is missing is a pathogenetic link between ischemia and plaque burden: which is more important, and how do these markers relate to each other? An even more intriguing question is whether the type of plaque or degree of plaque burden can mediate or influence ischemia in non-flow-limiting stenosis. Recent studies seem to suggest that different types...
of plaque components can modulate ischemia to different degrees, probably via endothelial dysfunction, even in the presence of non-flow-limiting stenosis (6).

Guiding a patient and making a rational therapeutic decision also require appropriate markers of the risk of the procedure. However, the ability to predict post-procedural outcomes is even more limited than that to predict disease risk. Methods to predict a priori which patients will likely leak troponin post-intervention will thus be of clinical importance in estimating risk and benefit, but this is one of the holy grails in cardiology. Although vessel and lesion anatomy is an important determinant, early data seem to suggest that plaque burden and plaque characteristics can also predict post-procedural outcomes. Currently, risk assessment for individual patients is dictated mainly by their clinical presentation and the specific morphologic factors of lesions themselves observed during invasive studies. Several scores are available to predict procedural risk, including the well-known SYNTAX score. This score is based heavily on lesion location and complexity, with the presence of thrombus as visualized by invasive angiography conferring additional risk. Periprocedural myocardial injury (PMI) is observed in 5% to 30% of percutaneous coronary intervention procedures, and in the more severe cases, it is related to worse outcomes after otherwise successful revascularization. Even small troponin leaks have adverse long-term consequences (7). The risk markers of lesions themselves have been established with intravascular ultrasound, optical coherence tomography, and near-infrared spectroscopy and include the presence and pattern of calcium, the eccentricity of the stenosis, vessel remodeling, the presence of thrombus, and the presence of a vulnerable plaque characterized by a thin cap of the plaque or high intraplaque lipid burden. Noninvasive markers are evolving (e.g. napkin ring lesions, a high degree of soft plaque or extensive calcification at the lesion site) but these are still too few, are mostly generic, have very low positive predictive value, and may inadequately explain underlying mechanisms.

In this issue of JACC, Asaumi et al. (8) demonstrate a relationship between high-intensity coronary plaques on noncontrast T1-weighted CMR imaging and PMI during elective coronary intervention. This observation expands on several previous reports. A high T1 signal on noncontrast CMR images was observed in carotid plaques with high lipid or thrombus burden and was related to a greater likelihood of adverse events and worse outcomes (9). A similar imaging approach has been developed for the coronary arteries and has demonstrated high signal in the presence of coronary thrombus (10). High T1 signal in the coronary arteries also portends adverse event rates (11). The present paper relates this observation in coronary arteries to the occurrence of PMI. Although this does not yet allow the prediction of outcomes, the ability to noninvasively detect an active inflamed plaque, thrombus, or intraplaque lipids, and its relationship with PMI, opens up an avenue for improved individualized risk assessment on the basis of noninvasive imaging.

All our efforts so far have been concentrated into silos and dugouts—individually imaging stenosis or ischemia or function—as opposed to one comprehensive package—imaging the vessel wall, plaque, and lumen at the same time. Similarly, we have focused much on anatomy rather than biology, with only modest success in reducing hard events. The imaging of the future will have to integrate anatomy, physiology, and vascular pathology into the decision-making process, and studies such as this one show the way. A potential assessment of patients with stable coronary artery disease in the future might integrate information from various sources, possibly multimodal, hopefully noninvasive. Such a pathway could integrate the presence, severity, and significance of myocardial ischemia, the extent and location of coronary plaque, lesion morphology and complexity, and plaque stability and risk for embolization. This knowledge would then be used to determine an individual patient’s risk for cardiac events as well as the risk and benefit of a revascularization procedure. Personalized imaging and therapeutics for minimizing individual risk with specific therapies, including anti-ischemic drugs to reduce ischemic burden, heavier antiplatelet coverage, and targeted-intensity statins to minimize plaque instability, could logically follow.

Noninvasive plaque imaging and plaque characterization add another parameter to the already complex field of optimizing outcomes in patients with coronary artery disease. We need more information on the quantification of these parameters and their relative importance, as well as ways to minimize their risk, to guide patient management. Thoughtful imaging might show the way.

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