For more than 2 decades, myocardial perfusion imaging (MPI) has been one of the best clinical tools for guiding clinicians in the management of patients with suspected or known coronary artery disease (CAD). MPI has been considered the best noninvasive imaging modality for measuring myocardial blood flow. The presence of significant ischemia on MPI usually necessitates further evaluation with coronary angiography (CAG), whereas a normal or mildly abnormal finding is not followed by further evaluation, because the outcome is usually benign. Thus, the MPI-guided strategy has an established role in the screening, diagnosis, risk stratification and prognosis of patients with stable chronic chest pain syndrome. However, because MPI is a modality that demonstrates ischemia, but not the true extent of coronary atherosclerosis, it is limited to some extent in predicting future events. Approximately half of the patients with normal MPI have subclinical CAD on CAG, which explains why despite the evidence of normal myocardial perfusion patients with subclinical CAD are at relatively high risk of coronary events. Even though a normal MPI result generally indicates a benign prognosis, the warranty period of such a result could be substantially shorter in patients with high coronary risk factors.

Meanwhile, multislice computed tomography (CT) angiography and magnetic resonance imaging have been introduced into the field of cardiology, with tremendous technological advances in multislice CT CAG (CTCA). Given its high spatial resolution, non-invasive nature, and relative ease of use, CTCA has evolved rapidly over the past decade to be an excellent imaging modality for direct non-invasive anatomical assessment of coronary arteries, which enables early detection of CAD. However, although CTCA has excellent diagnostic sensitivity for identifying coronary lesions, it cannot as accurately delineate the hemodynamic significance of coronary stenoses as does CAG. Studies have indicated that an anatomically significant lesion does not always equate with functional significance. Nearly 50% of the significant lesions found on CAG or CTCA are not functionally relevant.

Cardiac magnetic resonance imaging (CMR) is an attractive alternative for achieving the same purpose as MPI without the radiation hazard to the patient. With a higher spatial resolution, CMR is more sensitive for detecting subendocardial ischemia, small myocardial infarction and/or fibrosis, which cannot be achieved with MPI. Magnetic resonance perfusion (MRP) with pharmacological stress provides a more accurate assessment of myocardial ischemia when compared with MPI.

Given these recent changes, there have been some paradigm shifts in the diagnostic strategy for patients with suspected or known CAD when using CTCA and/or CMR. A combined approach based on anatomy (CTCA) and function (CMR) may quickly and effectively identify those who will most likely benefit from further invasive CAG from among patients with chest pain suspected to be CAD.

The prospective study by Kirschbaum et al in the current issue of the Journal addressed the question of whether MRP can identify which patients with an abnormal CTCA require further invasive investigation. They investigated the additive value of MRP in symptomatic patients where CTCA was used as the first-line diagnostic tool and additional testing was indicated, using invasive coronary flow reserve (CFR) as the standard of reference. In their study, 230 symptomatic patients with suspected stable angina underwent CTCA. In patients with a visually assessed stenosis >50%, MRP was performed and the quantitative myocardial perfusion reserve index (MPRI) was calculated. CTCA showed non-significant CAD in 151/230 (66%) patients and significant CAD in 79/230 patients (34%), of whom 50 subsequently underwent MRP and CFR. MRP showed reduced perfusion in 32 patients (64%), which was confirmed by CFR in 27 (84%). All of the 18 cases of normal MRP (36%) were confirmed by CFR. The positive likelihood ratio of MRP for the presence of functional significant disease in patients with a lesion on CTCA was 4.49. The negative likelihood ratio was 0.05. Thus, the authors conclude that CTCA as a first-line diagnostic modality excludes CAD in a high percentage of patients referred for diagnostic workup of suspected stable angina. MRP made a significant contribution to detecting functionally significant lesions in patients with a positive CTCA result.

This important study highlights that the combined use of CTCA and CMR may lead to responsible diagnostic decision-making about which patients need invasive CAG. Using the combined approach, 84% of patients with positive CTCA and MRP results were confirmed by the reference standard, which has a post-test probability sufficient to warrant CAG. A negative rule out could be obtained in two-thirds of patients with one test and 10% underwent both tests without having...
functional CAD. This strategy is relevant to the recent agreement that revascularization decisions have to be based on both anatomical and functional information.

Another important point is that CTCa with CMR can classify patients into 3 categories: normal coronary artery, non-significant CAD, or significant CAD. This classification may allow straightforward and reliable risk stratification beyond ordinary risk evaluation such as the Framingham risk score or NCEP-ATPIII. CTCa can further differentiate patients as having non-significant CAD or completely normal coronary arteries, which is important because the presence of non-significant CAD may not be considered benign. The presence of atherosclerotic plaque on CTCa, even if not significantly stenotic, is different from being free from CAD. The presence of non-significant CAD on CTA has been associated with increased annualized event rates up to 1.5%, compared with very low annualized event rates of 0.7% in patients with completely normal coronary anatomy.4,5 Characterization of atherosclerotic plaque may lead to more patient-tailored approaches, such as optimal medical therapy, as well as vigorous lifestyle modification, which may lead better outcomes in the future. Therefore, CTCa is a good modality to use for patient with relatively low risk or low likelihood of CAD but who need evaluation of the presence of CAD because of chest pain or clinical suspicion.

Another important issue limiting the clinical use of diagnostic imaging is the radiation dose. Modern CT acquisition protocols, such as prospective ECG-gating and body mass adapted tube voltage and current modulation, can reduce the radiation dose from CTCa by 60–80%, so there is a negligible risk of cancer. However, if MPI is used for the evaluation of myocardial ischemia found on CTCa, the radiation dose becomes significant when it exceeds 20 mSv. On the other hand, MR is free from radiation exposure.

Multimodality cardiac imaging is a highly dynamic field because the technological advances and/or progression of non-invasive imaging are remarkable, in line with the increasing clinical interest. Its impact extends beyond clinical utility for the diagnosis of CAD to the organization of healthcare structures. Appropriate use of alternative and complementary tests will require their integration into the collaboration of clinical diagnostic services. As proposed in a joint statement from European medical societies including the European Association of Echocardiography, the Working Groups on CMR, Computers in Cardiology, and Nuclear Cardiology, of the European Society of Cardiology,9 colleagues with clinical and technical expertise together can exploit the potential of new techniques for studying both anatomy and pathophysiology.

References