iVIEW

EDITOR'S PAGE

Stress-Only CMR

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"Black swan" events are by definition unexpected (even if the "black swan" has been visible before) and come with catastrophic consequences. One such occurrence is the current coronavirus pandemic, which is likely to have a considerable impact on the practice of medicine in as yet unknown ways. A likely consequence will be a significant economic downturn and constrained budgets, resulting in even higher pressure to optimize our diagnostic and therapeutic pathways. To survive the cost pressure, diagnostic studies will have to evolve significantly: they must be fast, use the most cost effective approach, and result in a therapeutic consequences or management guidance. Shorter examinations require focus on the core question, standardized image acquisition and procedures, and rapid, increasingly automized data analysis and reporting. Cost-effectiveness requires more research, but also using the knowledge we have to reduce unnecessary diagnostic and therapeutic procedures.

In this issue of *iJACC*, Rijlaarsdam-Hermsen et al. (1) provide information on one strategy that seems promising and yet opens up new questions. The investigators used stress-only perfusion cardiovascular magnetic resonance (CMR) in patients with stable chest pain and coronary artery calcium (CAC) scores >0 to guide patients to invasive angiography. They found obstructive coronary artery disease (CAD) in only 3% of patients in the group without typical angina and CAC scores <100 and 16% among patients with nonanginal chest pain and CAC scores ≥400. This is the first study showing the advantage of using CAC as a gatekeeper for CMR stress testing, and it adds to the evidence that rest perfusion can be safely skipped in most perfusion CMR studies, a strategy

also supported by the latest Society for Cardiovascular Magnetic Resonance standardized acquisition consensus (2). D'Angelo et al. (3) previously demonstrated that scar imaging (late gadolinium enhancement) can be done with a 0.1-mmol dose of a gadolinium-based contrast agent without loss of image quality or diagnostic information and a shorter wait time between contrast injection and scar imaging. Cine imaging can be performed after perfusion and before late gadolinium enhancement, reducing total scan time for a fully standardized CMR examination to approximately 15 to 20 min. Such comprehensive examinations must become the standard for CMR to increase patient throughput and reduce costs. However, the core question remains: how can we maximize the clinical effectiveness of diagnostic procedures in patients with chest pain? Several strategies are currently advocated: the use of better pretest probability assessments (4), incorporating gatekeeping methods (1), sequential imaging (5), value-added testing such as computed tomographic (CT) fractional flow reserve and CT perfusion (6), and finally hybrid imaging (7) of various forms. However, all of these must now pass once again through the critical filter of economics and newer evidence such as that from the ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial (8).

One possible change that could find new proponents might be avoiding most diagnostic imaging for CAD. However, no imaging would make sense only if we would stop revascularizing patients with stable angina and would accept giving up on risk assessment (both excluding high-risk anatomy such as left main coronary artery and detecting high event

risk), as well as making a correct diagnosis. Such consequences are neither perceivable without some imaging, nor would they contribute to the best possible patient management. Coronary calcium, ischemia, and vulnerable plaques are all important predictors of future events, and knowledge about them can guide the type and extent of risk-modifying therapy and lifestyle changes.

The proponents of a "one-stop shop" approach could argue for cardiac computed tomography in all patients with chest pain independent of pre-test likelihood, supported by CT fractional flow reserve in those with potentially hemodynamically significant coronary stenoses. This approach is advocated by the United Kingdom's National Institute for Health and Care Excellence guidelines (9) and is based mainly on the notion that exclusion of CAD can be done with limited effort and costs using CT angiography. Advances in CT perfusion (10) could substantially buttress this argument. This approach is also supported by the high negative predictive value of CT angiography and data from the SCOT-HEART (Scottish Computed Tomography of the HEART Trial) trial (11), demonstrating that knowledge of coronary anatomy and plaques improves outcomes. In contrast, this approach has the disadvantage that the majority of patients will have negative results on computed tomography, which requires nephrotoxic contrast agents, a rare, but not negligible prevalence of allergic reactions and some ionizing radiation, thus also adding significantly to the overall cost. CMR imaging allows a combination of function, scar imaging, mapping, and perfusion and can serve as an attractive "go to" test; it is well validated, allows precise quantitation and a high degree of automation (12), and is one of the few tests that shows noninferiority compared with an invasive fractional flow reserve-based strategy for the management of stable CAD (13). However, it will have to overcome limited availability and the need for a high degree of expertise.

A Bayesian approach might continue to find favor despite evidence against it (9). Performing computed tomography in the lower range of pre-test likelihoods and stress imaging in patients with intermediate to high pre-test probability is advocated the European Society of Cardiology guidelines on chronic coronary syndromes (14). This approach is highly evidence based for the diagnosis of CAD, as it allows a reliable rule-out in the lower pre-test probability group and a rule-in with testing for significant CAD and significant ischemia in the intermediate to high pre-test likelihood group. According to these guidelines, patients with very high pre-test likelihood should proceed directly to invasive angiography. Two recent studies challenge these guidelines. First, MR-INFORM (MR Perfusion Imaging to Guide Management of Patients With Stable Coronary Artery Disease) (13) has demonstrated that patients with high pre-test likelihood can also be safely guided by noninvasive perfusion CMR, thus reducing unnecessary invasive angiography in this specific patient group. Second, the ISCHEMIA trial (8) challenges the need to assess patients invasively for prognostic reasons but reveals utility for relief on symptoms. Symptomatic relief, however, requires a correct diagnosis of the underlying problem, which can frequently be determined using CMR imaging with a combination of function, scar imaging, mapping, and perfusion.

Sequential imaging, where one proceeds to the next test only if a low-cost efficient test produces abnormal results, has found some favor and is supported by at least 1 small randomized controlled trial (15). A combination of CAC scoring and perfusion CMR is a variation that strategy and now has evidentiary support (1). This approach reduces the need for invasive angiography, while minimizing the need for perfusion scanning in those with low calcium burden, further shortening the CMR study and eliminating the need to apply vasodilator stress in a considerable group of patients. Using biomarkers alone for predicting CAD has been less than conclusive so far (16), and a combination of imaging and biomarkers might improve performance. Hybrid imaging—using multiple modalities around the same time (either individually or on the same machine, as with positron emission tomography/computed tomography or positron emission tomography/magnetic resonance)—is attractive but may not adequately fulfill its promise at this time (17).

Value-added testing, using CMR or CT angiography, might become one of the more attractive avenues for cost-effective imaging. Some strategies might provide important insights regarding anatomy, physiology (18), blood flow quantitation, microvascular health (19), and information about the vessel wall (20) and prognosis in the same test environment. Both computed tomography and CMR allow this, and rapid advances, including automation (12,21) and machine learning (22), may allow novel paradigms. For example, it would be interesting to investigate whether a CAC scan (without CT coronary angiography) and a noncontrast CMR study could be combined in a specific group of patients, obviating the need for contrast injection or even vascular access for a stressor administration (23), which could

considerably increase patient throughput and offer testing at a much lower cost than currently possible. Whether such multimodality approaches can save costs needs to be determined.

We need to start focusing less on the diagnosis of CAD and guidance toward revascularization and concentrate more on strategies and their effectiveness to establish a final diagnosis and optimally and individually guide patient management in a cost-effective way.

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