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EDITORIAL COMMENT

Pharmacological stress: a useful exercise?

E. E. van der Wall

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Over the past years cardiovascular magnetic resonance (CMR) imaging has been increasingly used to detect the presence of coronary artery disease and to assess its functional consequences to the myocardium [1]. Several approaches have been applied to detect coronary artery disease with CMR including direct visualization of coronary arteries and bypass grafts [2–4] (magnetic resonance coronary angiography), the characterization of myocardial tissue [5–8] (delayed contrast enhancement) or the visualization of the effects of induced ischemia [9–17] (wall motion analysis or perfusion measurements). The latter is particularly valuable in clinical decision making since the detection of epicardial coronary luminal narrowing alone does not necessarily predict its hemodynamic consequences to the underlying myocardium.

In the last decades, pharmacological stress has been extensively evaluated as an alternative stress method and is particularly advised to those patients who are not able to perform adequately either due to limited exercise capability or a disabling disease. With the development of rapid gradient systems and the routine application of advanced CMR scanner systems, it has become possible to perform cine imaging of the heart at rest and under stress conditions with CMR. Since space is limited within the MR scanner bore and patient movement impairs image quality, pharmacological stress is preferred for CMR imaging. Research efforts have been focused on the definition of the clinical role of magnetic resonance pharmacological stress for the detection of inducible wall motion abnormalities, preferably using dobutamine stress magnetic resonance (DSMR) [18–30]. High-dose DSMR proved to be highly accurate for the detection of inducible wall motion abnormalities and its usefulness for determination of patient prognosis has been shown [18–24]. DSMR at low-dose dobutamine levels was found to be highly predictive of functional improvement of resting wall motion abnormalities after coronary revascularization procedures (detection of viable myocardium) [25–27].

For induction of ischemic wall motion abnormalities, adenosine/dipyridamole or dobutamine are routinely used and the outcome is often considered alike and interchangeable. In a landmark study by Paetsch et al. [31], the results of a direct comparison of dobutamine stress CMR, adenosine stress CMR and adenosine stress CMR perfusion as assessed during a single, combined examination with all stress tests were evaluated against coronary angiography as the standard of reference. This study proved that dobutamine was superior to adenosine stress for the detection of inducible wall motion abnormalities related to the presence of epicardial coronary

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E. E. van der Wall (✉)
Department of Cardiology, Leiden University Medical Center, P.O. Box 9600, Leiden, The Netherlands
e-mail: e.e.van_der_wall@lumc.nl

stenoses > 50%, with DSMR and adenosine stress CMR, yielding an overall diagnostic accuracy of 86 and 58%, respectively. Only for the detection of coronary artery stenosis > 75%, a reasonably good diagnostic accuracy of adenosine stress CMR was found. Based on this study, adenosine was not considered suitable the detection of inducible wall motion abnormalities resulting from epicardial coronary stenoses. This finding is physiologically quite understandable as adenosine is a vasodilatory agent not necessarily inducing an ischemic response but rather a maldistribution of flow [32, 33]. This phenomenon explains the absence of wall motion abnormalities in the absence of true myocardial ischemia. As a result, adenosine in conjunction with advanced CMR imaging might be better suited for direct assessment of perfusion abnormalities rather than detection of wall motion abnormalities.

Several studies have addressed the value of adenosine in conjunction with CMR imaging in terms of safety, diagnostic accuracy and prognosis [34–39]. Recently, Greenwood et al. [40] determined the safety and diagnostic accuracy of adenosine-stress CMR perfusion imaging early after acute ST elevation myocardial infarction (STEMI) compared with standard exercise tolerance testing in 35 patients admitted with first acute STEMI. All patients underwent a CMR imaging protocol which included rest and adenosine-stress perfusion, viability, and cardiac functional assessment. Adenosine stress CMR imaging was well tolerated in all patients and no complications occurred. CMR was more sensitive and more accurate than exercise testing for detecting significant coronary artery stenosis, and more sensitive for predicting revascularization. It was concluded that adenosine-stress CMR imaging is a safe procedure early after acute STEMI and identifies patients with significant coronary stenosis more accurately than conventional exercise tolerance testing. Pilz et al. [41] recently showed that a normal adenosine stress CMR predicted a very low cardiac event rate and an excellent 1-year prognosis in 128 patients with suspected coronary artery disease. Adenosine-stress CMR imaging may therefore serve as a reliable non-invasive gatekeeper in reducing the number of redundant coronary angiographies.

In the present issue of the *International Journal of Cardiovascular Imaging*, Karamitsos et al. [42] determined the safety and tolerance of adenosine stress CMR first-pass perfusion imaging in 351 patients with suspected or known coronary artery disease. In total, 233 patients (76%) were found to have significant coronary artery disease of whom 128 patients (36%) had multi-vessel disease. There were no deaths, myocardial infarctions, or episodes of bronchospasm during the CMR study. Transient second (Mobitz II) or third-degree atrioventricular block occurred in 27 patients (8%). There were no sustained episodes of advanced atrioventricular block. Patients on beta-blocking agents or calcium-channel antagonists were not at increased risk for atrioventricular block. Transient chest pain was the most common side effect in 199 subjects (57%). The present study differs from previous studies by (1) including a large percentage (86%) of patients with angiographic data, (2) a prolonged infusion time (4 min instead of 3 min routinely), and (3) more importantly, the procedure was safe in patients with multi-vessel disease. A limitation of the study was the rather short follow-up time of 1 h after administration of adenosine. However, given the very short half-time (<10 s) of adenosine, major side effects beyond one hour of administration are not to be expected. Besides, aminophylline is a very useful and efficient antidote to adenosine.

To summarize, it can be concluded that adenosine is a very suitable agent for stress CMR perfusion imaging, as it is well-tolerated and safe even in patients with severe coronary artery disease. Consequently, adenosine stress CMR imaging is a valuable adjunctive modality in assessing myocardial perfusion abnormalities with prognostic implications in patients with suspected and known coronary artery disease.

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