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EDITORIAL COMMENT

Stress Testing in the Obese

Are We Finally Getting the Bigger Picture?*

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Obesity has reached epidemic proportions at a global level with multiple adverse medical and societal implications (1). It is a major determinant for the development of cardiovascular risk factors such as diabetes and hypertension, and independently predisposes to cardiac conditions such as coronary artery disease, heart failure, and sudden cardiac death (2). Therefore, identification of an accurate method for cardiac risk stratification in obese patients is of ultimate importance. In addition to being a high-risk group, obese patients, however, often present diagnostic challenges when we need to evaluate them for the presence of myocardial ischemia. Basic tests such as exercise electrocardiography are partially hampered by artifacts as a result of adipose tissue.

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Moreover, overweight patients are often not able to reach the minimal heart rate threshold for an adequate test result because of general deconditioning. Thus, pharmacological stress testing in conjunction with an imaging technique is the preferred approach. Although numerous diagnostic approaches are available, there is an apparent discrepancy between the extent of the clinical problem associated with obesity and the amount of published data on using imaging-based cardiac stress testing.

Because stress echocardiography in obese subjects is often limited by a low acoustic window, there has been some uncertainty about the accuracy of the test. The diagnostic accuracy can be improved by the use of contrast agents, but the prognostic value of stress echocardiography in this patient population remains vague (3). Single-photon emission tomography (SPECT) with stress perfusion analysis may be an overall more commonly applied test in obese patients, but it is also handicapped by suboptimal image quality resulting from relevant photon attenuation and a decreased signal-to-noise ratio. Currently, there are conflicting data regarding the prognostic value of a negative SPECT examination in obese patients (4,5).

More recently, coronary computed tomography angiography (CTA) has been established for the assessment of CAD and is particularly regarded for its high negative predictive value (6,7). However, the image quality of coronary CTA is also compromised in obese patients (8). Although newer protocols may improve image quality and the visualization of distal coronary vessels, the fundamental question regarding the clinical relevance of intermediate stenoses will continue to be unanswered, thus supporting the imperative for functional testing (9).

Despite the abundance of data on obesity as a cardiovascular risk factor, very little data have been published on the characteristics, accuracy, or prognostic value of stress cardiac magnetic resonance (CMR) in this population. In this issue of *iJACC*, Shah et al. (10) are the first to report their findings on the feasibility and usefulness of vasodilator stress CMR perfusion imaging for the assessment of cardiac prognosis in 285 patients with a body mass index $\geq$30 kg/m^2. The investigators should be commended for their effort in conducting this study, with over 89% of patients achieving diagnostic-quality studies. CMR image quality is probably least affected by obesity compared with the alternative techniques although increased body habitus introduces noise and the larger field of view decreases the in-plane resolution of the images. The

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main limitations of CMR have been the size of the bore and the table weight limits. This has been mostly overcome by the recent development of large-bore systems. Analyzing their data on a mid-term follow-up basis, Shah et al. (10) identified a strong association of inducible ischemia with major adverse cardiac events (MACE), whereas patients with neither ischemia nor late gadolinium enhancement had a very low annual rate of 0.6 % for MACE, which is in accordance with previous data in nonobese patients (11).

Generally, stress testing with CMR has become an important diagnostic and prognostic tool in the evaluation and management of patients with known or suspected coronary artery disease (11,12). Given the unique advantages of CMR in providing detailed information on function, perfusion, and scar tissue, the results of this study do not come as a surprise. The authors address an important topic, and their data contribute to the definition of the clinical usefulness of vasodilator stress CMR for accurate risk stratification in this difficult population.

A number of issues need to be considered before the results of Shah et al. (10) can truly represent the prognostic utility of stress CMR in this population. The study was performed retrospectively over a period of almost 10 years, including 3 different scanners using 1.5- and 3.0-T. During recent years, CMR myocardial perfusion techniques have achieved very high image quality with the advancement of hardware and software settings. With the increasing adaptation of wide-bore 3.0-T systems for CMR, it is likely that the diagnostic quality of stress CMR on obese patients will continue to improve. The investigators do not provide more specific information on diagnostic image quality, and a nonobese control group was not included in this study. Prospective inclusion of patients and a more rigorous trial design may lead to different results. However, the high number of diagnostic cases and the excellent outcome data of this study suggest a high diagnostic and prognostic value of CMR in this study group. It is noteworthy that the prognostic association between inducible ischemia and MACE remained robust when patients undergoing early revascularization were censored. However, because of the limited number of hard events, the current study does not have adequate statistical power to define a threshold extent of inducible ischemia in obese patients. Experience from larger CMR trials suggests that ischemia >10% of left ventricular myocardium defines high risk, which is similar to prior stress nuclear imaging data (13,14).

There are several areas for future work. Can the results of the current study be translated to other CMR stress protocols, for example, dobutamine–atropine stress CMR? Wallace et al. (15) have already demonstrated that dobutamine–atropine stress CMR is a suitable testing modality for accurately providing prognostic information in obese women. Ischemia in the form of stress-inducible wall motion abnormalities was identified as a predictor of survival. Recently, the CE-MARC (Clinical Evaluation of MAgnetic Resonance imaging in Coronary heart disease) study demonstrated that adenosine stress CMR is more sensitive and has a higher negative predictive value than SPECT in a nonobese group (12). Whether these results can be transferred to obese patients will have to be addressed.

The question of which method may offer the optimal approach in obese patients remains currently unanswered and will need to be addressed by future prospective studies. Nonetheless, the results from Shah et al. (10) reflect an important experience in which valuable lessons have been learned and provide encouraging evidence in the clinical role of stress CMR in the obese patient.

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