

Trials and Tribulations of Assessing New Imaging Protocols

Combining Vasodilator Stress With Exercise

Carlos D. Davila, MD, James E. Udelson, MD



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CME/MOC Objective for This Article: After reading this article the reader should be able to: 1) discuss the current available data on different configurations for exercise and vasodilator myocardial perfusion imaging (MPI); 2) compare the effectiveness and safety of studies adding vasodilator stress to submaximal exercise versus those studies adding exercise to pharmacologic stress; 3) express the potential limitations of current clinical practice for the design and implementation of large randomized clinical trials in cardiovascular imaging; and 4) summarize the background, design, results, and limitations from the "EXercise to Regadenoson in Recovery Trial" (EXERTT).

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From the Division of Cardiology and the CardioVascular Center, Tufts Medical Center, Boston, Massachusetts. Dr. Udelson is a consultant to Lantheus Medical Imaging, GE Healthcare, and Medtrace for imaging studies, but none of these is considered relevant to the topic at hand. Dr. Davila has reported that he has no relationships relevant to the contents of this paper to disclose.

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ABSTRACT

Among all patients referred for stress myocardial perfusion imaging (MPI), a substantial proportion in contemporary practice cannot exercise. Another group of patients are those who are thought to be able to achieve an adequate workload with treadmill (or bicycle) exercise but do not achieve at least 85% of maximum predicted heart rate without developing symptoms. There has been substantial interest and literature on the adjunctive use of vasodilator stress during the same visit to generate best-quality results for patients who do not exercise adequately. Current American Society of Nuclear Cardiology Guidelines recommend the possible use of vasodilator stress agents to supplement exercise in those patients who do not achieve target heart rate. However, optimal timing of administration is not clear. Herein, we summarize literature to date on the combination of vasodilator and exercise stress testing in light of the recently published Exercise to Regadenoson in Recovery Trial (EXERRT). (J Am Coll Cardiol Img 2018;11:494-504) © 2018 by the American College of Cardiology Foundation.

Among all patients referred for stress myocardial perfusion imaging (MPI), a substantial proportion in contemporary practice cannot exercise and routinely undergo pharmacologic stress testing, usually with vasodilator stress. Another group of patients are those who are thought to be able to achieve an adequate workload with treadmill (or bicycle) exercise but do not achieve at least 85% of maximum predicted heart rate without developing symptoms. In such patients, the exercise electrocardiogram (ECG) is nondiagnostic. MPI may retain overall sensitivity to detect presence of coronary artery disease (CAD) to a certain level of submaximal heart rate, but the important extent/severity variables may be compromised (1,2). Thus, there has been substantial interest and literature on the adjunctive use of vasodilator stress during the same visit for patients who do not exercise adequately to generate good-quality results for patients and referring physicians without the inconvenience of a second visit for pharmacologic stress (Central Illustration). Current American Society of Nuclear Cardiology Guidelines recommend the possibility of using a vasodilator stress agent to supplement exercise in those patients who do not achieve target heart rate (3), but Guidelines are silent on the exact timing of administration. Given that regadenoson can be given using bolus dosing at a fixed dose, it could be administered very quickly at the time that the submaximal nature of the stress test is apparent, in contrast to adenosine or dipyridamole. However, there is a report of greater

hemodynamic instability when regadenoson is given at peak exercise (4), and there have been reports of serious adverse events, including myocardial infarction, following administration of regadenoson, prompting warnings in the prescribing information by the Food and Drug Administration (FDA) (5).

Other studies have focused on the addition of exercise to pharmacologic stress during or immediately after infusion of vasodilator agents to capture some of the valuable functional information that is lost when performing pharmacologic stress alone (Central Illustration). The purpose of this article is to explore the currently available evidence on the combination of exercise and pharmacologic stress testing in light of the recently published EXERRT (Exercise to Regadenoson in Recovery Trial) (6). Here, we summarize all contemporary studies on vasodilator stress test and exercise in all configurations.

ADDING VASODILATOR STRESS TO SUBMAXIMAL EXERCISE

The recent report by Thomas et al. (6) on the design and results of the multicenter EXERRT critically evaluated the efficacy and safety of immediate administration of regadenoson early during the recovery period following a submaximal exercise stress. Previous reports on this topic of adding vasodilator stress to exercise have predominantly been

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