A helping hand for regadenoson tests

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Noninvasive stress testing is ideally performed by allowing patients to exercise to maximal capacity. However, not all patients are able to perform sufficient exercise or are on medications that blunt the necessary heart rate increase. For these individuals, pharmacologic stress testing is performed, often with adjunctive treadmill exercise. Low-level exercise has been combined with pharmacologic stress for years, and has been shown to reduce side effects and improve image quality.[1-6] Pharmacologic stress has also been combined with symptom-limited exercise in suitable patients as a means to obtain valuable functional data while ensuring adequate stress.[7-12]

Since its approval in 2008, regadenoson has become the most commonly used vasodilator used in pharmacologic perfusion imaging surpassing adenosine and dipyridamole.[13] Although it involves an off-label use of the agent, interest and experience in protocols combining symptom-limited exercise and pharmacologic stress is increasing.[14] That regadenoson can be administered as a bolus injection has invited the study of such protocols with this agent. Studies to date have shown that combining regadenoson with some form of exercise is feasible and safe.[5,6,9-12] However, some patients we intend to stress with regadenoson cannot walk on a treadmill. What can we do for these patients to enhance their experience and improve image quality?

In this issue of the journal, Janvier et al prospectively evaluate the safety, feasibility, and hemodynamic and imaging impact of a less commonly utilized exercise modality—handgrip—in combination with regadenoson administration.[15] In this study, patients being evaluated for stable coronary artery disease were prospectively assigned to either a standard regadenoson (Reg) protocol or to a combined handgrip-regadenoson (HG-Reg) protocol. For the HG-Reg group, isometric handgrip exercise was started 2 minutes prior to regadenoson administration and continued for 5-7 minutes after the infusion.

Feasibility of this protocol was measured by certain hemodynamic measurements such as heart rate and blood pressures variability between the study groups. Maximum heart rates were greater in the exercise group (HG-reg), but mean systolic blood pressures were similar between the two groups. Blood pressure fluctuations, particularly significant decreases in systolic blood pressure, were less likely in the HG-Reg group. Fewer patients in the HG-Reg group had any side effects of the test; however, typical vasodilator side effects such as chest discomfort were similar in both groups. Consistent with previous studies of utilizing exercise with pharmacologic stress protocols, myocardial image quality was at least comparable, if not better, in the HG-Reg group. Another benefit touted by the authors is that, because handgrip exercise resulted in a limited heart rate response, the potential risk of the ''double stress'' is significantly reduced, adding to the safety of this protocol.

Issues to keep in mind regarding this study include the small cohort sizes and the lack of comparison of ischemia detection. Then again, this was just a preliminary study primarily focusing on safety and feasibility. A nice next step from this group would be the determination of the diagnostic ability of this protocol using a comparison of ischemic burden based on imaging results. In addition, a specific device was utilized for the handgrip exercise (CanDo® Digi-Flex® Hand Exerciser, not mentioned in the paper). It is not clear to us how this was used. Was the handgrip continuous or repeated? Was one hand used or two? Another question, but one this study was not designed to answer, is if the device is

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needed at all. Many nuclear laboratories have had patients unable to walk do handgrip exercise—opening and closing their hands repeatedly—in an attempt to reduce side effects. While our experience would tell us that handgrip without a device may be useful for this purpose, that has not been proven yet.

Nonetheless, the authors should be commended for systematically studying the addition of a simple exercise to regadenoson stress, showing the benefits that they did. We disagree, however, with a statement in their conclusion that this protocol has advantages to adding symptom-limited exercise to regadenoson. These are really two different groups of patients. The protocol of Janvier et al is appropriate for patients who cannot safely walk on a treadmill. For patients who appear to be able to perform a reasonable amount of exercise we would advocate performing symptom-limited exercise with regadenoson administered if target heart rate is not achieved. We will leave the specifics of how that is done to the individual laboratories, but administration soon after peak exercise seems to be the safest method while still allowing the assessment of functional capacity and exercise-induced symptoms, and without unduly prolonging the stress test.[12]

The greatest opportunity of the protocol presented by Janvier et al is to significantly improve the tolerability of regadenoson while maintaining image quality and lab efficiency in a growing population of patients who are unable to exercise significantly. For these patients, this protocol is attractive. It is simple, adds no significant risk to the patient, and presents nuclear cardiology laboratories with another alternative method to perform adequate stress while maximizing patient comfort.

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