Stress-only imaging: We can rest assured

Brian G. Abbott, MD, FACC, FASNC^{a,b}

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From the early days of planar thallium, to more contemporary techniques using single photon emission computed tomography (SPECT) with technetium-based radiotracers, myocardial perfusion imaging (MPI) has been typically performed using two imaging sessions: immediately after stress, and at another time point after rest. Visual comparison of these two studies is then used to determine whether a perfusion abnormality is reversible and related to ischemia, fixed and secondary to myocardial infarction (MI), or potentially related to attenuation or artifact. From a diagnostic perspective, perfusion abnormalities have been demonstrated to have a very good positive predictive value for the presence of flow-limiting angiographic coronary artery disease (CAD). More importantly, from a prognostic standpoint, as the size and severity of the perfusion abnormalities increase, so does the short-term incidence of cardiac death and nonfatal myocardial infarction. Accordingly, when myocardial perfusion images are normal, the prognosis is excellent, with studies comprising tens of thousands of patients consistently demonstrating that the survival free from adverse cardiac events is <1% per annum.¹ The majority of these studies routinely employed rest-stress imaging protocols and visual interpretation with semiquantitative analysis.

Recent technical advances in SPECT-MPI including electrocardiographic gating, computer-aided quantification of defect size and severity with comparison to a normal database, and attenuation correction have been shown to provide added value to visual interpretation.

Employing one or more of these techniques can enhance diagnostic certainty, and increase reader confidence to consider perfusion images without significant abnormalities as unequivocally normal. In following, the next logical questions that would come to the mind of many physicians interpreting myocardial perfusion imaging studies are: If the stress images are completely normal, how will the acquisition and interpretation of rest images add to the stress study? Is a rest study still needed? The uncertainty about the answers to these questions is based on, up until recently, a lack of outcomes data examining an approach of performing stress-only imaging (i.e., not performing rest imaging in patients with initial normal stress images). Is the prognosis of patients with normal stress-only imaging as good as that demonstrated with conventional rest/stress protocols?

In this issue of the *Journal of Nuclear Cardiology*, Duvall and colleagues² provide us with additional data to allow us to the answer to these questions definitively. The authors report on a study comparing all-cause and cardiac mortality in a cohort of patients with a low pretest probability of CAD and normal results on a prospectively determined stress-only SPECT-MPI, to patients who underwent a standard rest-stress protocol with normal images. Overall mortality in the 1,673 with a normal stress-only study was no different than that in the 3,237 patients with normal results after conventional imaging with rest image acquisition. During 40 months for follow-up, total mortality and cardiac mortality were 2.7% vs 3.7%, and 0.4% vs 0.5%, in the stress-only cohort and rest-stress subjects, respectively. These findings demonstrate that the short-term prognosis in selected, low risk patients without known CAD and with a normal stress-only study is similar to those evaluated with a conventional rest-stress protocol.

This important study brings the cumulative reported experience of performing stress-only imaging to more than 10,000 patients. Recently, Chang and co-workers³ published their experience with stress-only imaging, noting similar total mortality in 8,034 patients with normal images using this approach, compared to 8,820 with a normal rest-stress study. The present study showed that total mortality with a normal stress study was similarly low, but notably, also demonstrated no differences in cardiac mortality. As such, it can now be definitively concluded that stress-only imaging protocols are safe and effective.

From the Warren Alpert School of Medicine of Brown University,^a Rhode Island Hospital, Providence, RI; Rhode Island Cardiology Center,^b East Greenwich, RI.

Reprint requests: Brian G. Abbott, MD, FACC, FASNC, Warren Alpert School of Medicine of Brown University, Rhode Island Hospital, Providence, RI; babbott@lifespan.org.

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OMITTING UNNECESSARY REST IMAGES

As the prognosis of patients with initial normal stress images is similar to those with normal results using a rest-stress protocol, rest imaging does not provide any important information in these patients, and is unnecessary. Conceivably, when stress images are normal, the only additional information that could be obtained from rest images would be a smaller left ventricular cavity size that would indicate the presence of stress-induced ventricular dilation or transient ischemic dilation (TID), which has been associated with an increased prevalence of multivessel CAD and worse outcome.⁴ The similar overall prognosis, and in particular no difference in *cardiac* mortality, suggests that TID does not have prognostic significance in patients with normal perfusion imaging. A recent study also reported no difference in outcome in patients with TID and normal perfusion compared to those without TID.⁵

PATIENT SELECTION

By design, Duvall and colleagues² prospectively determined the pre-test clinical risk for CAD and selectively employed a strategy of performing rest imaging first in those at low-to-intermediate risk, as these patients would also be expected to have a higher incidence of a normal stress study. Consequently, 86% of the stress only imaging studies were performed in outpatients or in the Emergency Department evaluation of acute chest pain, and >90% of the studies performed using initial stress imaging were normal. While an initial stress imaging protocol will likely have greater utility in low risk patients, prior studies have demonstrated its feasibility in patients with known CAD. The aforementioned recent study by Chang et al³ included 27% with known CAD, and 3% with prior MI.

PRACTICAL CONSIDERATIONS OF STRESS-ONLY IMAGING

Obviating the need to acquire and interpret rest images in the setting of normal stress-only perfusion images is clearly an attractive option from many perspectives. Laboratory throughput can be increased to permit more patients being imaged each day if patients with normal stress images are not brought back for rest images. However, this also requires that the stress study is reviewed and interpreted as normal. In our laboratory, an effort is made to review these “on-demand” when feasible, to make the decision as to whether rest images are needed. This protocol is also more convenient from a patient’s standpoint, as the shortened protocol reduces the time they must be present in the laboratory considerably.

For a study to be considered as normal, the stress images must show no significant perfusion abnormalities visually and with quantification demonstrating normal perfusion, normal left ventricular cavity size, and normal ejection fraction and wall motion by gated SPECT. If the stress study does not meet these criteria, rest imaging should be performed. It should be recognized that all studies to date evaluating a stress-only imaging protocol did employ some form of attenuation correction (AC). Is AC essential to be able to perform stress-only imaging? Not necessarily. AC can be helpful to discern mild abnormalities on visual inspection suspicious for diaphragmatic or breast attenuation, but if the perfusion images are normal both visually and quantitatively, AC does not add any meaningful information. Previous studies have shown that the addition of AC to gated SPECT imaging does increase reader confidence, and reduces the need for rest imaging while maintaining diagnostic accuracy.⁶ Availability of AC would likely increase the proportion of studies that can be performed as stress-only in a laboratory. However, added costs and lack of reimbursement have unfortunately limited the widespread proliferation of this technology. Prone imaging has also been shown to increase normalcy rates,⁷ and new camera designs may incorporate attenuation correction or make prone imaging more feasible, further reducing attenuation artifacts.

SUBSTANTIAL REDUCTION IN RADIATION EXPOSURE

Perhaps the greatest benefit of using a stress-only imaging protocol is the significant and important reduction in the dose of radiopharmaceutical administered. Duvall and colleagues² noted that the stress-only protocol avoided exposure to an additional 10 mCi of Tc-99m, with an overall 25% reduction in total radioisotope dose, using a weight-based protocol. Previous studies employing a low-dose protocol injecting 13.5 mCi of Tc-99m on average for the stress scan, have noted a >60% reduction in injected dose compared to conventional rest-stress imaging.³ Advances in hardware and software used in the acquisition and processing of SPECT studies now permit using even lower injected doses of radiopharmaceutical. Recent preliminary reports employing new solid state camera technology have noted diagnostic quality stress images with <12 mCi of Tc-99m,^{8,9} reducing radiation exposure to less than 5 mSv on average.⁹

SUMMARY

The findings of Duvall et al, put any concerns regarding the safety and efficacy of stress-only imaging to rest. Based on these findings, the stress study, with

low dose radiopharmaceutical if feasible, should be the initial scan in the majority, if not all, patients. Obese patients can also have a high dose stress first, with rest only if needed. As such, rest-stress protocols should be reserved for those with known CAD and prior infarction or left ventricular dysfunction. Incorporating quantification, and attenuation correction or prone imaging, will reduce the number of unnecessary rest images (and unnecessary radiation) when stress images are normal. Employing stress-only protocols in conjunction with emerging advances in camera and processing technology will lead to even greater reductions in radiation exposure. When the stress images are normal, we can now safely avoid rest imaging, and rest assured.

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