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EDITORIAL COMMENT

Stress-Only Myocardial Perfusion Imaging

A New Paradigm*

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Although the acquisition protocols of myocardial perfusion imaging (MPI) have evolved over the past 4 decades, 2 sets of images (stress/rest) remain a standard practice (1). Even more sets are at times acquired for special indications (e.g., we described a protocol with 4 sets of images, rest/4-h delayed thallium-201 and high-dose/low-dose dobutamine gated technetium [Tc]-99m sestamibi to characterize dysfunctional myocardium as scar, hibernating or stunned) (2). The pros and cons of the 1-day stress/rest, 1-day rest/stress, and 2-day stress/rest have previously been discussed, and suffice it to say each has advantages and limitations (1).

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There are several potential reasons for acquiring 2 sets of images: differentiation of ischemia (reversible abnormality) from scar (fixed abnormality), increasing the confidence in recognition of artifacts, assessment of nonperfusion variables such as transient left ventricular dilation and post-stress stunning, and to have a more precise assessment of left ventricular ejection fraction (EF) when there is a gating problem with 1 of the 2 studies. Another reason, seldom acknowledged, is because of the tradition, and no wants to be accused of violating 4 decades of tradition! Finally, and in the spirit of the tradition, it is because the images are interpreted at the end of the day (because some readers might have several other concomitant commitments, such as clinic hours, hospital rounds, or cardiac catheterization), and it is more convenient for the reader (although not the patient) to have a standard policy of acquiring 2 sets of images on every patient. The laboratories using a rest/stress protocol or a dual isotope protocol (rest thallium-201/stress Tc-99m–labeled tracer) are by necessity committed to acquiring 2 sets of images, and those using a stress/rest protocol are committed to the same practice just because of the late reading time!

A more practical approach would be to use a stress/rest protocol, review the stress images as soon as they are completed, and if unequivocally normal (perfusion and function), omit the rest study (stress-only protocol). The advantages of this protocol are listed in Table 1. These advantages are very meaningful, considering the ever-increasing concerns about the health costs (especially imaging), the radiation exposure, and the oft-repeated criticism that MPI is a time-consuming procedure (unlike, say, stress echocardiography). The radiation exposure is reported to be in the range of 14 mSi for a typical stress/rest or rest/stress protocol and only 6 to 7 mCi for a high-dose stress-only study (and even lower if a smaller dose is used, 15 rather than 25 mCi) (3). The decrease in total dose of tracer needed is especially important currently, where there is a widespread shortage of Tc-99m supply. The stress-only protocol obviously requires a change in culture and is against the status quo of how we do imaging, but it is not difficult to implement, because we have been doing it in our own laboratory for more than 10 years, and it has enabled us to run a high-volume operation very efficiently. There is 1 senior reader who reads all images as soon as they are acquired and processed (all patients, 5 days/week) and communicates with the laboratory as to the need or lack of it for a rest study.

Alternative methods are on the horizon for decreasing imaging time by improvements in software and hardware, but these have not yet been widely used and await further validations (4).

A recent statement by the American Society of Nuclear Cardiology (5) concluded:

> The best use of a stress-only imaging strategy is likely to be in the selected low- or low-to-intermediate-risk population, in whom it is anticipated that the stress study will be normal. The limited data available seem to support the physician-guided highly selective use of this logical approach in this population. The American Society of Nuclear Cardiology believes that for the appropriate use of this strategy it is essential that the interpreting physicians be highly experienced and that the interpreting physicians make the decisions about who will benefit from resting images. Additional studies in this area are needed, particularly studies addressing clinical outcomes of patients who have decisions made on the basis of stress-only imaging. This strategy does not yet have sufficient data to support a widespread utilization.

In 2 prior reports, patients (116 patients in the first study, and 652 patients in the second study) with normal stress-only images had low event rates comparable to prior reports using 2 sets of images (6,7). Another preliminary report by Duvall et al. (8) in a much larger number of patients (1,673 patients with normal stress-only images, and 3,237 patients

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Table 1 Advantages of the Stress-Only Protocol

1. Saves time (it is the fastest protocol)
2. Increases laboratory efficiency (more patients could be studied/day/camera)
3. Decreases cost (billed as a single code rather than multiple codes [CPT code 78464 instead of 78465])
4. Improves patient convenience (less time in the laboratory and under the camera)
5. Decreases radiation exposure

with normal rest/stress images) also showed very low and comparable event rates in these patients regardless of whether 1 or 2 sets of images were obtained.

In this issue of the *Journal,* Chang et al. (9) provide convincing evidence that patients with normal stress-only images have the same low mortality as patients with normal images on the basis of evaluation of both the stress and rest images. These conclusions were derived from >16,000 patients, one-half of whom had stress-only images, and the median follow-up period was 4.5 years. All images were interpreted by experienced readers using visual analysis supplemented by quantitative analysis and attenuation correction (with external line sources), a method that has previously been shown to improve specificity by minimizing attenuation artifacts (6–10). These patients represented one-third of all patients imaged in their institution and one-half of all normal images. One would assume that these patients had a very low likelihood of coronary artery disease (CAD), but this was not the case, because 27% had known CAD and 58% of the remaining patients had intermediate probability of CAD. Furthermore, most patients had pharmacological stress testing, and many were inpatients, groups that are known to be at higher risk.

The salient features for performing stress-only images are listed in Table 2. This study examined the all-cause mortality and did not provide information on cardiac mortality or nonfatal myocardial infarction, but on the basis of their estimates of the relation between cardiac and all cause mortality, the cardiac mortality is estimated to be low and in accordance with prior reports (11–15). Also in accordance with prior studies, patients with known CAD or diabetes or

Table 2 Requirements for Stress-Only Images

1. Good quality images
2. Experienced reader
3. The stress study is done as the initial study
4. The tracer dose is selected per accepted guidelines, and a large dose is used only if the patient would otherwise have qualified for a 2-day study.
5. Interpretation soon after acquisition and processing
6. Unequivocally normal perfusion and function, by visual and quantitative analysis. The interpretation should equally be unequivocal.
7. Attenuation correction increases reader's confidence but is not a necessity for stress-only imaging paradigm
8. This paradigm of stress-only imaging could be applicable to exercise and pharmacological stress testing and to patients with known or unknown coronary artery disease

Table 3 Personal Recommendations in Special Circumstances

Issue	Recommendation
Positive ST segment response but normal stress images	Do not recommend rest imaging
Over-correction with attenuation correction methods (e.g., improvement of inferior defect but a new anterior defect)	Recommend rest imaging
Suboptimal quality images due to hot spots, motion, or low counts	Recommend repeating the stress images
Depressed ejection fraction, large left ventricular cavity, or poor gating	Recommend rest imaging

those who underwent pharmacological stress testing had higher mortality than their counterparts, but this was true in patients with stress-only and in those with 2 sets of images. Unlike other studies that used hazard ratios or odds ratios, this study used the time ratio (TR) from the accelerated failure time models. The odds ratio is generated from the logistic model to assess the risk of death when the time of death is not known. The hazard ratio from the Cox proportional hazards model is used to assess the risk of death when the time to death is known. The Cox model assumes that the hazards over time are consistent. When this assumption is violated, the TR is used; a TR of 2 means doubling survival, whereas a TR of 0.5 means reduction in survival by 50% in those with versus those without a given predictor.

The attenuation correction used in this study was also used in the study by Gibson et al. (7) and Duvall et al. (8) discussed earlier, but in this study, attenuation correction was used to confirm that a study is normal but was otherwise not used in the decision-making process. This is an important attribute of this study, because it makes the results applicable to other sites that do not use attenuation correction.

It is important not to confuse the issue of when to use stress-only imaging; patients with abnormal or equivocal stress images require rest imaging to resolve the problem and characterize the abnormality as to whether fixed or reversible. Our general rule is "when in doubt, obtain a rest image."

There are special issues that need further studies, and these are listed in Table 3. One might argue that stress-only images deprive the reader of other imaging variables such as transient ischemic dilation and post-stress stunning. The latter should not be an issue as per selection criteria; the patients with stress-only images have normal wall motion/EF. This reviewer is not convinced that transient ischemic dilation is a risk factor in the absence of perfusion defects or depressed EF.

The health costs, radiation dose, and patient comfort demand that we become flexible in our selection of imaging protocols; the status quo is no longer tenable. This change in imaging protocol combined with recent and future developments should radically change the perception that

MPI is an all-day procedure. The current article reinforces this concept and provides assurance that omitting the rest study does not compromise patient safety. The nonperfusion data seldom change the outcome of the patients in the presence of normal perfusion and function (1,14,15). The American College of Cardiology, the American Society of Nuclear Cardiology, the Centers for Medicare and Medicaid services, and the third-party payers should make note of this new paradigm in imaging, because it is applicable to a sizable proportion of patients, and its impact on cost and safety is substantial.

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REFERENCES

1. Iskandrian AE, Garcia EV, editors. Nuclear Cardiac Imaging: Principles and Applications. 4th edition. New York, NY: Oxford University Press, 2008:703–18.
2. Narula J, Dawson MS, Singh BK, et al. Noninvasive characterization of stunned, hibernating, remodeled and nonviable myocardium in ischemic cardiomyopathy. J Am Coll Cardiol 2000;36:1913–9.
3. Einstein AJ, Moser KW, Thompson RC, Cerqueira MD, Henzlova MJ. Radiation dose to patients from cardiac diagnostic imaging. Circulation 2007;116:1290–305.
4. Slomka PJ, Patton JA, Berman DS. Advances in technical aspects of myocardial perfusion SPECT. J Nucl Cardiol 2009;16:255–76.
5. Des Prez RD, Dahlberg ST, Einstein AJ, et al. Stress-only myocardial perfusion imaging. ASNC Announcement. J Nucl Cardiol 2009;16:329.
6. Gal R, Ahmad M. Cost-saving approach to normal technetium-99m sestamibi myocardial perfusion scan. Am J Cardiol 1996;78:1047–9.
7. Gibson PB, Demus D, Noto R, Hudson W, Johnson LL. Low event rate for stress-only perfusion imaging in patients evaluated for chest pain. J Am Coll Cardiol 2002;39:999–1004.
8. Duvall W, Wijetunga M, Klein T, Hingorani R, Henzlova M. The prognosis of normal stress-only SPECT myocardial perfusion imaging (abstr). J Am Coll Cardiol 2009;53 Suppl A:287A.
9. Chang SM, Nabi F, Xu J, Raza U, Mahmarian JJ. Normal stress-only versus standard stress/rest myocardial perfusion imaging: similar patient mortality with reduced radiation exposure. J Am Coll Cardiol 2009;55:221–30.
10. Heller GV, Bateman TM, Johnson LL, et al. Clinical value of attenuation correction in stress-only Tc-99m sestamibi SPECT imaging. J Nucl Cardiol 2004;11:273–81.
11. Berman DS, Hachamovitch R. Risk assessment in patients with stable coronary artery disease: incremental value of nuclear imaging. J Nucl Cardiol 1996;3:S41–9.
12. Shaw LJ, Iskandrian AE. Prognostic value of gated myocardial perfusion SPECT. J Nucl Cardiol 2004;11:171–85.
13. Iskandrian AE, Garcia EV, Faber T, Mahmarian JJ. Automated assessment of SPECT myocardial perfusion imaging. J Nucl Cardiol 2009;16:6–9.
14. Berman DS, Kang X, Slomka PJ, et al. Underestimation of extent of ischemia by gated SPECT myocardial perfusion imaging in patients with left main coronary artery disease. J Nucl Cardiol 2007;14:521–8.
15. Lima RS, Watson DD, Goode AR, et al. Incremental value of combined perfusion and function over perfusion alone by gated SPECT myocardial perfusion imaging for detection of severe three-vessel coronary artery disease. J Am Coll Cardiol 2003;42:64–70.

Key Words: myocardial perfusion imaging ■ radiation exposure ■ risk stratification ■ single-photon emission computed tomography ■ stress testing.