studies.” We believe that in abnormal studies, the proposed protocol may underestimate defect reversibility, particularly if there is inadequate delay between injections. Stress-induced hypoperfusion may not have fully resolved at the time of rest imaging. Additionally, absolute myocardial perfusion is higher with stress, so the proportion of Tc-99m taken up by the myocardium is higher following the smaller stress dose than the higher rest dose; this would tend to undermine the swamping effect.

Even with normal myocardial perfusion on stress images, it is important to evaluate all clinical data, planar images, gated images, and attenuation correction images, including computed tomography scans, to determine if the patient needs rest imaging. We agree that in addition to normal myocardial perfusion, patients must have normal cavity size to rule out reversible dilation, and an ejection fraction >50% with normal wall motion (1) to rule out post-ischemic stunning. We also propose that patients with normal stress images should also have rest images if the patient has angina during the stress test, hypotension with exercise, or ST-segment depressions meeting ischemic criteria during stress (4). Ischemic electrocardiograph changes, particularly during adenosine infusion, have been shown to be associated with an increased risk of future cardiac events (5), even with normal myocardial perfusion.

Still, there are other markers of significant coronary artery disease that, if noted, require rest images even with homogenous left ventricular perfusion on stress images. More specifically, patients with increased lung-to-heart uptake ratio (6) or increased right ventricular uptake (7) on stress images should have rest images before a study is considered nonischemic. Patients with calcification in the left main artery on computed tomography attenuation images should also have rest images even with normal stress images.

We believe that this protocol is suitable for patients with low-likelihood disease and no history of myocardial infarction. Rest images should be obtained if any of the aforementioned observations are made in the stress images. These precautionary measures may help avoid providing false reassurance to patients and providers when performing stress-only perfusion imaging.

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Normal Stress-Only Versus Standard Stress/Rest Myocardial Perfusion Imaging

Similar Patient Mortality With Reduced Radiation Exposure

We read the paper by Chang et al. (1) and accompanying editorial (2) with great interest. The insightful single-center study addresses safety of normal stress-only myocardial perfusion imaging (MPI). However, it raises some concerns.

Careful examination of the paper suggests a conundrum. Annualized crude death rate for the stress-only MPI group is significantly lower than stress and rest MPI. However, after adjustment for clinical factors associated with mortality (Table 3 of Chang et al. [1]) this difference in crude mortality, which is lower in the stress-only group, disappears. This, despite the fact that the stress-only group was significantly less likely to have these risk factors associated with higher mortality, both in aggregate (Table 1 of Chang et al. [1]) (mean number of risk factors: 1.33 ± 1.1 vs. 1.57 ± 1.1, p < 0.001) and for each individual risk factor. The fact that the stress-only group was older by 1.1 years cannot possibly, it seems, explain this effect of adjustment.

The study, although large, is retrospective and has all of the limitations of retrospective studies (3,4).

The stress-only study was performed in patients weighing <200 lbs. Hence, the study’s findings may be applicable to this subset of patients only, and furthermore, with the growing epidemic of obesity, its applicability will be further reduced. Chang et al. (1) did not indicate what percentage of these patients needed to undergo additional rest MPI. Additionally, height and/or body mass index were not considered in deciding stress-only protocol. With the same 200 lbs weight, a patient whose height is 60 inches would have a body mass index of 39.1 kg/m², whereas for a patient whose height is 72 inches, it would be 27.1 kg/m². The former patient (short and stubby) may present a significant challenge for the study’s findings may be applicable to this subset of patients only, and furthermore, with the growing epidemic of obesity, its applicability will be further reduced. Chang et al. (1) did not indicate what percentage of these patients needed to undergo additional rest MPI. Additionally, height and/or body mass index were not considered in deciding stress-only protocol. With the same 200 lbs weight, a patient whose height is 60 inches would have a body mass index of 39.1 kg/m², whereas for a patient whose height is 72 inches, it would be 27.1 kg/m². The former patient (short and stubby) may present a significant challenge for the stress-only MPI.

The end point was all-cause mortality derived from Social Security Death Index. Chang et al. (1) did not mention how many patients did not have a social security number and hence were lost to follow-up.

We do not have incidence of unstable angina pectoris, nonfatal myocardial infarctions, hospitalizations, revascularizations, and
information regarding quality of life, all of which add to morbidity and health care cost.

Chang et al. (1) also projected cardiac mortality on the assumption of data applicable to a general population, which may be inaccurate, as study patients have a higher cardiac risk profile than the population at large.

Among patients with a low (<5%) Bayesian likelihood of coronary artery disease and normal MPI transient ischemic dilation, incidence is reported to be 4.1%. Moreover, transient ischemic dilation may be the only scan abnormality in patients with severe multivessel disease producing balanced ischemia that can be missed on stress-only MPI. These patients will be clinically missed and not receive appropriate management.

The findings of this study (1) need to be validated in a large, randomized, prospective, multicenter study.

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Reply

We thank Drs. Bhalodkar and Blum for their interest in our report (1). They raise concerns regarding the adoption of a stress-only single-photon emission computed tomography (SPECT) imaging protocol based on our study results. Although ours was a single-center, retrospective trial, it represents data on almost 17,000 consecutive patients who had similar baseline characteristics and event rates as reported from other large centers that perform stress SPECT. In this regard, we feel our study results are applicable to most patients who are referred for SPECT imaging.

The perceived conundrum in event rates between the stress-only and stress/rest groups is probably explained by adjustment for baseline characteristics that included clinical variables, stress electrocardiogram results, and the type of stressor used (please see the Statistical Analysis section of Chang et al. [1]). The stress/rest group did have a significantly higher crude annual event rate than the stress-only group (2.92% vs. 2.57%), which was probably related to their significantly greater number of cardiac risk factors, higher incidence of coronary artery disease (CAD), and higher frequency of pharmacologic stress testing. Statistical significance was lost after adjustment for these variables.

We acknowledge the retrospective design of our study. However, the criteria used for defining a normal stress study and deciding who should undergo additional rest imaging were prospectively implemented in our laboratory before the start date of our study. In addition, only 2 cardiologists (J.J.M. and M.S.V.) interpreted all of the SPECT studies and only 1 (J.J.M.) from years 2001 through 2007. In this regard, our study had many features of a prospective trial with consistency in image interpretation.

Stress-only studies were not restricted to patients weighing <200 lbs. Rather, weight was used only to determine the initial isotope dose and not the imaging protocol. As shown in Table 2 of Chang et al. (1), 3,086 patients weighing >200 lbs underwent a stress-only procedure, which represented 38% of all stress-only patients and 53% of all patients weighing >200 lbs. Thus, our study results are applicable to patients of all body weights.

Only a small percentage of patients (1.7%) did not have assessment of all-cause mortality by the Social Security Death Index, and lack of follow-up was evenly distributed between stress-only (n = 137 or 1.7%) and stress/rest (n = 165 or 1.8%) groups. It is highly unlikely that the inclusion of these subjects would have altered our findings.

We agree that the incidence of nonfatal end points is important and can add to health care costs. Although we did not specifically address nonfatal events, our overall mortality results are strikingly similar to those reported by other investigators (2–6). Based on these similarities, there is no reason to assume that nonfatal end points would have differed between our stress-only and stress/rest cohorts.

Regarding the issue of transient ischemic left ventricular dilation, we recognize that this can, at times, be the only abnormality seen in patients with multivessel CAD. For this reason, all patients undergoing stress-only imaging had normal end-diastolic and -systolic volumes by gated SPECT and no evidence of post-stress left ventricular dilation on the initial perfusion images. We hope that all of these explanations have clarified our study results in a satisfactory manner.

We also thank Drs. Kim and Bokhari for their remarks regarding our paper (1). We agree that there are inherent benefits to a stress-only imaging protocol in view of growing shortages of technetium (Tc) 99m and concerns over radiation exposure. Stress-only imaging should also reduce imaging time in a large percentage of patients and decrease imaging costs.

We recognize that performing stress imaging as the first test could potentially underestimate detection of ischemia if the rest injection is not delayed for several hours. However, this is more of a theoretical concern than a practical one, because there has not been a study to convincingly demonstrate a reduction in ischemia detection based on a stress/rest imaging protocol. Conversely, a rest/stress protocol may potentially decrease the sensitivity of SPECT because of contamination by the rest dose. In this regard, there are inherent limitations to any same-day stress/rest or stress/stress protocol that uses separate injections of a Tc 99m radiopharmaceutical. Performing a 2-day protocol in patients with abnormal or equivocal studies is an optimal approach, although admittedly inconvenient to the patient.

We agree that it is important to evaluate all raw, perfusion, and gated SPECT image information before deciding whether a patient should have rest imaging. This is exactly what was done in our study.

We thank Drs. Bhalodkar and Blum for their interest in our report (1). They raise concerns regarding the adoption of a stress-only single-photon emission computed tomography (SPECT) imaging protocol based on our study results. Although ours was a single-center, retrospective trial, it represents data on almost 17,000 consecutive patients who had similar baseline characteristics and event rates as reported from other large centers that perform stress SPECT. In this regard, we feel our study results are applicable to most patients who are referred for SPECT imaging.

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