

## Editorial Comment

# Gated Myocardial Perfusion Imaging for Measuring Left Ventricular Function\*

ROBERT O. BONOW, MD, FACC

Chicago, Illinois

Myocardial perfusion imaging has undergone major advances in recent years. Contributing to this progress has been the development of new technetium-99m (Tc-99m)-based perfusion tracers, pharmacologic stress agents and single-photon emission computed tomographic (SPECT) techniques, along with concomitant advances in quantitative and semiquantitative methods to assess myocardial perfusion, function and viability.

Gated SPECT imaging represents the most recent important advance in the evolution of this field. By applying electrocardiographic gating during acquisition of the tomographic perfusion images, gated SPECT takes full advantage of the properties of Tc-99m perfusion agents, namely, high count rates and stable myocardial distribution with time. Because the tracer distribution in the myocardium is stable, spatial and temporal changes in myocardial tracer activity during the cardiac cycle reflect regional myocardial wall motion and wall thickening. Because the diagnostic and prognostic power derived from knowledge of left ventricular function can be added to that provided by assessing myocardial perfusion, gated SPECT has rapidly gained widespread acceptance and is now used on a routine clinical basis in a growing number of laboratories.

The accuracy of gated myocardial perfusion SPECT for evaluating left ventricular function has been well established. Assessment of regional wall motion and regional systolic wall thickening, at least by experienced observers, correlates well with regional wall motion and wall thickening data obtained by two-dimensional echocardiography (1). As in any other method requiring visual interpretation of regional left ventricular function, there is an obligate learning curve in the qualitative assessment of regional function and the potential for considerable interobserver variability. A major step forward in gated SPECT technology has been the development of objective, automatic and reproducible techniques to calculate left ventricular ejection fraction (2,3) that have been well

validated with radionuclide ventriculography and which eliminate the interobserver issues. The study by Johnson et al. (4) in this issue of the Journal confirms the excellent reproducibility of ejection fraction measurements by gated myocardial perfusion SPECT, which is equivalent to that established over a decade ago by radionuclide ventriculography (5).

In laboratories using a 2-day protocol for stress–rest myocardial perfusion imaging with Tc-99m compounds, electrocardiographic (ECG) gated acquisitions work well during acquisition of the rest images. However, for a variety of logistic, clinical and patient satisfaction issues, many laboratories have adopted single-day stress–rest protocols, using either a low dose–high dose imaging protocol with a Tc-99m agent or a dual-isotope protocol using thallium-201 for the rest study, followed by a Tc-99m agent for the stress study (6). In these situations, ECG gating is usually performed during acquisition of the stress images. Although the tracer is administered during stress and the perfusion images represent relative myocardial blood flow during stress, the measurement of left ventricular function represents function at the time of image acquisition itself, which may take place 30 to 60 min after stress. Thus, this approach is assumed to provide a combined assessment of stress myocardial perfusion and rest left ventricular function. Under most circumstances, this assumption is valid, and the measurement of resting left ventricular ejection fraction is accurate. However, Johnson et al. (4) identify an important limitation of this approach, a limitation that heretofore has not been fully appreciated.

Johnson et al. (4) point out that the post-stress ejection fraction measured by this technique does not necessarily represent the rest left ventricular function. Among 61 patients with reversible ischemia studied with a 2-day stress-rest Tc-99m protocol, 22 patients (36%) manifested a significantly lower ejection fraction measured on the post-stress gated images than that measured on the true rest study on a separate day. Although the difference between the rest and post-stress ejection fractions was only slightly greater than the reproducibility limit of 5% in several of these patients, this difference was more substantial in the majority, measuring  $\geq 8\%$  in 13 patients and  $\geq 10\%$  in 8. This effect was observed in none of the 20 patients in a separate group without reversible perfusion defects, in whom there was excellent agreement between ejection fractions measured after stress and at rest.

Johnson et al. (4) interpret the reduced post-stress ejection fraction in over one-third of patients with inducible ischemia as a manifestation of prolonged stress-induced myocardial stunning, persisting during the 30- to 60-min period before imaging began (and during the subsequent imaging period itself of roughly 16 min). Exercise-induced myocardial stunning is a well recognized phenomenon that has been described by many investigators (7–9), and this may indeed account for the observations in the current study by Johnson et al. This interpretation is supported by two of the authors' observations: 1) The reduced post-stress ejection fraction was caused by reduced chordal shortening of the ischemic segments and; 2)

\*Editorials published in *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

From the Division of Cardiology, Northwestern University Medical School, Chicago, Illinois.

Address for correspondence: Dr. Robert O. Bonow, Division of Cardiology, Northwestern University Medical School, 250 East Superior Street, Suite 524, Chicago, Illinois 60611. E-mail: r-bonow@nwu.edu.

**Abbreviations and Acronyms**

ECG	= electrocardiographic
Tc-99m	= technetium-99m
SPECT	= single-photon emission tomography (tomographic)

the magnitude of the depression of post-stress ejection fraction relative to the rest ejection fraction correlated with the severity of reversible ischemia, as estimated by the summed defect reversibility score.

There is another possible mechanism for the observation of reduced ejection fraction on post-stress images versus rest gated images that would appear plausible, in at least some patients. Unlike standard planar gated blood pool imaging or gated blood pool SPECT imaging, in which the calculation of ejection fraction is not dependent on ventricular geometry, the calculation of ejection fraction by gated myocardial perfusion SPECT requires identification of the endocardial border. In patients with ischemic myocardium, with reduced endocardial tracer uptake, the automatic edge detection algorithm (which is based on myocardial tracer activity) may fail to identify the endocardial border accurately in regions with the greatest ischemia. This would result in an overestimation of the severity of the wall motion abnormality and an underestimation of chordal shortening and ejection fraction. This possible effect is illustrated in Figure 1 in the report by Johnson et al. (4), in which reduced counts in the ischemic anterior wall in the post-stress long-axis images gives the impression of a dramatic and acute thinning of the anterior wall compared to the rest anterior wall thickness. It is thus uncertain whether the resulting increase in chordal length from the center of the ventricle to the anterior endocardial edge along chord 3 in the post-stress images of Figure 1 is more apparent than real.

It is noteworthy that the two observations that support the possibility of stunning as the mechanism for ejection fraction underestimation also support the possibility of endocardial border misregistration: Reduced ejection fraction is related to reduced chordal shortening in ischemic zones, and the magnitude of ejection fraction underestimation is related to the magnitude of reversible ischemia. In addition, there are two other findings that give credence to the possibility of misidentification of the endocardial border rather than stunning in some patients: 1) The underestimation of ejection fraction was observed not only in a high percentage of patients who underwent exercise stress but also in an equal percentage of patients who underwent pharmacologic stress with dipyridamole. Myocardial ischemia would most likely not be as severe with dipyridamole as to induce stunning to the same frequency and extent as exercise-induced ischemia. 2) The underestimation of ejection fraction on post-stress images was unrelated to the time delay between termination of stress and imaging. One would anticipate a greater likelihood of stunning in patients imaged shortly after exercise than in those imaged 1 h later.

Thus, either physiologic or methodologic factors (or both) may contribute to the observation of reduction in ejection fraction by gated myocardial perfusion SPECT when derived from post-stress images compared with true rest images in many patients with inducible ischemia. The extent to which myocardial stunning contributes to this effect requires further study and could be addressed in future investigations in a series of patients with reversible ischemia in whom sequential gated acquisitions are obtained over the course of several hours after administration of a single dose of a Tc-99m tracer at peak stress. If stunning is operative, early impairment in left ventricular function on gated imaging should resolve over several hours despite persistence of the perfusion defect. If the reduction in ejection fraction is related to endocardial border misregistration, the persistent perfusion defect would be associated with persistent reduction in the calculated ejection fraction.

Regardless of the mechanism or mechanisms involved, Johnson et al. (4) have identified an important limitation of post-stress gated myocardial perfusion SPECT for measuring left ventricular function, and their conclusions are compelling. Gated measurements of ventricular function made on post-stress images appear to accurately reflect rest left ventricular function in patients with normal myocardial perfusion or those with only irreversible perfusion defects, but these measurements must be interpreted very cautiously in patients with reversible myocardial ischemia.

## References

1. Chua T, Kiat H, Germano G, et al. Gated technetium-99m sestamibi for simultaneous assessment of stress myocardial perfusion, postexercise regional ventricular function and myocardial viability: correlations with echocardiography and rest thallium-201 scintigraphy. *J Am Coll Cardiol* 1994;23:1107-14.
2. Germano G, Kiat H, Kavanagh P, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med* 1995;36:2138-48.
3. Nichols K, DePuey EG, Rozanski A. Automation of gated tomographic left ventricular ejection fraction. *J Nucl Cardiol* 1996;3:475-82.
4. Johnson LL, Verdesca SA, Aude WY, et al. Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi tomograms. *J Am Coll Cardiol* 1997;30:1641-8.
5. Bonow RO, Kent KM, Rosing DR, et al. Improved left ventricular diastolic filling in patients with coronary artery disease after percutaneous transluminal coronary angioplasty. *Circulation* 1982;66:1159-67.
6. Berman DS, Kiat HS, Van Train KF, Germano G, Maddahi J, Friedman JD. Myocardial perfusion imaging with technetium-99m sestamibi: comparative analysis of available imaging protocols. *J Nucl Med* 1994;35:681-8.
7. Homans DC, Sublett E, Dai XZ, Bache RJ. Persistence of regional left ventricular dysfunction after exercise-induced myocardial ischemia. *J Clin Invest* 1986;77:66-73.
8. Kloner RA, Allen J, Cox TA, Zheng Y, Ruiz CE. Stunned left ventricular myocardium after exercise treadmill testing in coronary artery disease. *Am J Cardiol* 1991;68:329-34.
9. Ambrosio G, Betocchi S, Pace L, et al. Prolonged impairment of regional contractile function after resolution of exercise-induced angina: evidence of myocardial stunning in patients with coronary artery disease. *Circulation* 1996;94:2455-63.