Comparison Between Dobutamine Stress Echocardiography and Myocardial Perfusion Scan to Detect Viable Myocardium in Patients with Coronary Artery Disease and Low Ejection Fraction

HAKIMEH SADEGHIAN, JALIL MAJID-ARDAKAN, MASOUMEH LOTFI-TOKALDANY, CIROOS JAHANGIRI, MAHMOOD SHEIKH FATHOLLAHI

1Echocardiography Department, 2Nuclear Medicine Department, 3Research Department, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) are commonly used to detect viable myocardium. We designed this study to compare the results of these two methods in detecting myocardial viability.

Methods: We studied 736 segments from 46 patients (42 men, mean age 56 years), with coronary artery disease and impaired left ventricular systolic function (ejection fraction <40%), using low-dose DSE and 99mTc-sestamibi MPS. The two methods were compared in the detection of viability, primarily in dysfunctional and secondarily, in different anatomical segments.

Results: Of the 736 segments, 397 (53.9%) were normal or mildly hypokinetic and 339 (46.1%) dysfunctional. Of 49 severely hypokinetic segments, 33 (67.4%) were viable and 1 (2%) nonviable according to both methods, while discordant results were found in 15 (30.6%). Among 274 akinetic segments, both methods were concordant in 148 (54%) nonviable and 15 (5.5%) viable regions, while 111 (40.5%) segments showed discordance. Of 16 aneurysmal segments, 7 were viable according to MPS, but none showed contractile reserve on DSE. The two methods were concordant in 14.2% viable, 46.6% nonviable and discordant in 39.2% of all dysfunctional segments. Eighty-seven percent (98/113) of akinetic and 20% (8/41) of hypokinetic segments had 99mTc-sestamibi uptake, but did not show contractile reserve. There was more than 75% agreement in lateral basal, anterior apical and inferior apical segments.

Conclusion: The proportion of segments showing a positive response to dobutamine is significantly lower than those with technetium uptake. This suggests that the cellular mechanisms responsible for a positive inotropic response to adrenergic stimulation required a higher degree of myocyte functional integrity than those responsible for 99mTc-sestamibi uptake.

Low dose dobutamine stress echocardiography (DSE) and the myocardial perfusion scan (MPS) have been used to identify viable dysfunctional myocardium in patients with coronary artery disease and a low ejection fraction.1-5 Both techniques can detect coronary artery disease and provide prognostic information,1-5 thus guiding patient management decisions.6,7 Schinkel et al reviewed 17 direct comparative studies with different settings that used stress echocardiography and perfusion imaging in the same patients.8 The
study suggested that both techniques are useful in evaluating patients with chronic coronary artery disease, although small differences between their accuracy exist in different settings. To assess myocardial viability after acute infarction, the modalities seem to be equally sensitive, whereas stress echocardiography is the more specific test. In patients with chronic ischemic ventricular dysfunction, nuclear imaging has a high sensitivity for the detection of viable myocardium and a low specificity, whereas the converse is true for stress echocardiography.

The aim of this study was to assess the agreement and disagreement between the two methods in detecting viable myocardium, in either dysfunctional or different anatomical segments.

Methods

Forty-six consecutive patients (42 men, 4 women, mean age 56.39 ± 10.52 years) with chronic coronary artery disease (CAD) and impaired left ventricular systolic function (ejection fraction, EF <40% at rest) were evaluated by DSE and 99mTc-sestamibi tomography for the assessment of myocardial viability. All patients had CAD documented by angiography and the EF reported by angiography was used to select patients. The mean ejection fraction for the study group was 29 ± 9% (range 13-40%). The two studies were performed a maximum of 2 weeks apart.

Dobutamine stress echocardiography

Beta-blockers, calcium antagonists and nitrates were discontinued in patients at least 2 days before DSE. Echocardiography was performed with a 3.5 MHz transducer (VIVID 3 GE) under resting conditions and during each dobutamine infusion step. After baseline echocardiography, dobutamine infusion was administered using a mechanical pump. Dobutamine was delivered intravenously beginning at 5 µg/kg/min for three minutes, increasing by 5 µg/kg/min increments every three minutes until it reached 15 µg/kg/min for an additional three minutes. Blood pressure was measured periodically, and the 12-lead ECG was continuously monitored throughout the study and during the recovery phase. Grounds for termination of the infusion were a severe hypotensive or hypertensive response, significant arrhythmias, prolonged angina, significant electrocardiographic changes, appearance of new wall motion abnormalities in at least two segments, achievement of 85% of the maximum age-predicted heart rate, or completion of the protocol. Echocardiographic images were analyzed off-line and a 16-segment model was used, as suggested by the American Society of Echocardiography. The anatomical segments of the 16-segmental model are shown in Figure 1. Segmental wall motion at rest was scored on a four-point scale: 1. normal or mildly hypokinetic; 2. severely hypokinetic (decreased endocardial excursion and systolic wall thickening); 3. akinetic (absence of endocardial excursion and systolic wall thickening); and 4. dyskinetic or aneurysmal (paradoxical outward movement in systole).

Demonstration of wall thickening in a previously akinetic segment or normalization of thickening in a previously hypokinetic segment were considered as criteria of myocardial viability. A dysfunctional left ventricular segment was considered to have contractile reserve if infusion of dobutamine at 10 or 15 µg/kg/min resulted in an improvement in contractile function of at least one grade.

Myocardial perfusion scan

Myocardial single photon emission computed tomography (SPECT) was applied only at rest. After an overnight fast, patients underwent qualitative, semi-quantitative and quantitative SPECT, following intravenous administration of 20 mCi 99mTc-sestamibi under resting condition. Two tablets of sublingual nitroglycerin (TNG) equal to 0.8 mg of TNG were taken by patients 5 minutes prior to 99mTc-sestamibi injection. Computed tomography images were acquired one hour after infusion of the radiotracer.

Image acquisition was achieved with an Adoc dual head gamma camera without attenuation or scatter correction, using a low energy, all-purpose collimator and applying 180° SPECT. Transaxial tomograms were reconstructed: for each patient, six short-axis, three horizontal and three vertical long-axis slices were analyzed. A total of 16 myocardial segments per patient were studied. These segments were matched with the 16 segments evaluated by DSE. Tomographic views were analyzed by an experienced observer, who was unaware of the clinical data and echocardiograms. In each patient, two consecutive slices from the short axis series and two from the horizontal and vertical long axis series were selected from each set of images for visual analysis. Segments with a severe reduction of 99mTc-sestamibi activity (uptake below 50% of maximum uptake) were considered nonviable and all other segments...
were considered viable. Uptake was measured semi-quantitatively based on the visual interpretation of color scale.

**Statistical analysis**

Continuous variables are expressed as mean ± SD. The McNemar test was used in the analysis of discordant 99mTc-sestamibi tomography and DSE. The correlation between the two tests for the assessment of myocardial segment viability was expressed as percent agreement and value of Kappa (κ). We used the following grading system to evaluate agreement rate: poor agreement, a κ of 0.4 or less; moderate agreement, κ of 0.41 to 0.60; good agreement, κ of 0.61 to 0.80 and excellent agreement, κ greater than 0.80. If the value of κ was zero, we reported no agreement. A p-value <0.05 was considered statistically significant.

**Results**

A total of 736 myocardial segments from the 46 patients were evaluated. Regional contractile function, as assessed by resting two-dimensional echocardiography, demonstrated normal or mildly hypokinetic contraction in 397 (53.9%) segments and abnormal contraction in 339 (46.1%) segments. We excluded the 397 normal or mildly hypokinetic segments. The remaining 339 dysfunctional regions were included in further analysis. Of the 339 dysfunctional segments, 49 (6.7% of total) were severely hypokinetic at rest, 274 (37.2% of total) were akinetic, and 16 (2.2% of total) were aneurysmal.

**Stress echocardiography findings**

Of the 339 dysfunctional segments, 68 (20.1%) were viable and 271 (79.9%) nonviable by DSE. Viability was
found in 28/274 (10.2%) akinetic and 40/49 (81.6%) severely hypokinetic regions. All 16 aneurysmal segments were nonviable.

**Perfusion scan findings**

Of the 339 dysfunctional segments, 161 (47.5%) were viable and 178 (52.5%) nonviable. Results of resting two-dimensional echocardiography and MPS showed that 113/274 (41.2%) of akinetic, 41/49 (83.7%) of severely hypokinetic and 7/16 (43.8%) of aneurysmal regions were viable.

**Concordance and discordance between methods**

The two methods were concordant in 14.2% viable and 46.6% nonviable segments, and were discordant in detecting viability in 39.2% of segments. The Kappa value of 0.191 showed poor agreement between the two. Table 2 shows viability detected by DSE and MPS in hypokinetic, akinetic and aneurysmal segments. In the viability assessment of 49 severely hypokinetic segments, the two methods were concordant in 33 (67.4%) viable and 1 (2%) nonviable segments, whereas they were discordant in 15 (30.6%). Of 41 hypokinetic viable segments by MPS, 8 (20%) did not show contractile reserve by DSE. The agreement rate in these segments was 69.3%, $\kappa=0.060$. In the detection of viability of 274 akinetic segments, both methods were concordant in 15 (5.52%) viable and 148 (54%) nonviable segments, but discordant in 111 (40.5%) segments. The number of segments with resting wall motion abnormality that were considered viable by $^{99m}$Tc-sestamibi was significantly greater than the number of segments showing a contractile improvement in response to dobutamine (47.5% versus 20.1%, respectively; p<0.0001) (Table 1). Of 113 akinetic segments that were viable by MPS, 98 (87%) did not show contractile reserve by DSE. The agreement rate was also low among akinetic segments (59.3%, $\kappa=0.059$). The agreement rate in detecting viability in 16 aneurysmal segments was 56.3% (all nonviable by DSE and 9 nonviable by MPS). A comparison between DSE and MPS in the detection of viability of different functioning segments is shown in Table 3. Of 40 hypokinetic segments with a positive response to dobutamine 17.5% (7/40) did not show $^{99m}$Tc-sestamibi uptake, while of 28 akinetic segments with contractile reserve 46% (13/28) had no tracer uptake.

With respect to detecting viability in different anatomical segments, there was more than 75% agreement in lateral basal, anterior apical and inferior apical segments, but the value was lower in other anatomical segments.

**Discussion**

In patients with severe CAD and a low EF, the assessment of residual viability in regions with chronic contractile dysfunction is important for predicting improvement of function after revascularization. This study focused on a direct comparison between two widely used methods: dobutamine stress echocardiography and $^{99m}$Tc-sestamibi imaging for the assessment of viable myocardium.

In our study, a head-to-head comparison of the individual segments showed that the agreement rate between the two methods was 60.8%, with a disagreement rate of 39%.

**Table 1.** Viability detected by dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) in all dysfunctional segments.

<table>
<thead>
<tr>
<th></th>
<th>DSE</th>
<th>MPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viable</td>
<td>68/339</td>
<td>161/339</td>
</tr>
<tr>
<td>Non Viable</td>
<td>271/339</td>
<td>178/339</td>
</tr>
</tbody>
</table>

**Table 2.** Viability detected by dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) in hypokinetic, akinetic and aneurysmal segments.

<table>
<thead>
<tr>
<th></th>
<th>Viable ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSE akinetic</td>
<td>28/274 (10.2%)</td>
</tr>
<tr>
<td>DSE hypokinetic</td>
<td>40/49 (81.6%)</td>
</tr>
<tr>
<td>DSE aneurysmal</td>
<td>0/16 (0%)</td>
</tr>
<tr>
<td>MPS akinetic</td>
<td>113/274 (41.2%)</td>
</tr>
<tr>
<td>MPS hypokinetic</td>
<td>41/49 (83.7%)</td>
</tr>
<tr>
<td>MPS aneurysmal</td>
<td>7/16 (43.8%)</td>
</tr>
</tbody>
</table>

**Table 3.** Comparison between dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) in the detection of viability of different functioning segments.

<table>
<thead>
<tr>
<th></th>
<th>Agreement rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segments</td>
<td>Number</td>
</tr>
<tr>
<td>Severely hypokinetic</td>
<td>49</td>
</tr>
<tr>
<td>Akinetic</td>
<td>274</td>
</tr>
<tr>
<td>Aneurysmal</td>
<td>16</td>
</tr>
</tbody>
</table>

*Kappa was not calculated, because all aneurysmal segments were nonviable by DSE.*
rate of 39.2%. Similar results have been reported previ-
ounously. Panza et al reported 68% agreement between DSE and thallium scan and Bax et al found 72% agree-
ounment between DSE and technetium scan.

We observed discordance between the two meth-
ounods more frequently in akinetic segments that were vi-

able by 99mTc-sestamibi imaging, but did not show con-
tractile reserve by DSE (98/113 akinetic segments). Similar results were reported by Panza et al, who compared thallium imaging with dobutamine echo-

cardiography and showed that a large number of seg-

ments demonstrated thallium uptake but lacked contractile reserve. Of the 138 myocardial segments without contractile improvement shown by dobuta-

mine, 95 (69%) had normal, or mildly to moderately reduced thallium uptake and were therefore considered viable by thallium imaging. The authors suggested that these findings emphasized the difference in the mechanisms involved in the identification of myocardial viability by the two techniques; the cellular processes responsible for a positive inotropic response to adrenergic stimulation require a higher degree of myocyte functional integrity than those responsible for thallium uptake.

Studies comparing metabolic imaging with FDG (fluorin-18 fluorodeoxyglucose) by dobutamine echo-

cardiography to assess contractile reserve have also shown compatible results. Baer et al reported that dobutamine stimulation underestimates the number of segments with preserved FDG uptake. Sawada et al also reported a substantial percentage of the segments with FDG uptake (19%) that did not exhibit contractile reserve; thus, the amount of viable tissue required to determine the presence of metabolic activity is likely to be less than that required for detection of contractile reserve. Bax et al demonstrated that segments with both perfusion and contractile reserve have the least damage and fibrosis, while segments with perfusion but without contractile reserve have more damage/fibrosis, and segments lacking both perfusion and contractile reserve have the most severe damage/fibrosis. Our data confirm the fact that the number of akinetic segments considered viable by 99mTc-sestamibi under resting conditions is significantly greater than the number of those segments showing a contractile improvement in response to dobutamine.

We observed that 5.3% (20/374) of dysfunctional segments showed contractile reserve according to DSE, but did not show technetium uptake. Similarly, Panza et al reported 2% (6/311) of dysfunctional seg-

ments with similar presentation, but they explained this observation by the error inherent in the comparison of the two techniques, including poor anatomic correspondence of left ventricular segmentation in some patients. We think that this is more likely attributable to areas with non-transmural myocardial infarction, as explained by Armstrong. He argued that at a threshold of infarction of ~20% transmurality, rest function could be anticipated to be markedly abnormal. However, as 80% of the wall thickness is viable (due to the hibernating or normal myocardium), augmentation with low-dose dobutamine would result in improved function in that region. On the other hand, because the spatial resolution of radionuclide imaging techniques is not sufficient to determine myocardial thickness accurately, non-transmural myocardial infarction cannot be reliably detected on the basis of scintigraphic anatomy. On the basis of assumed kinetics of thallium activity, non-transmural infarction should be manifest as reduced overall wall activity. Discordance between the two methods in aneurysmal segments cannot be explained by this concept and could probably be attributed to the poor anatomic correspondence of left ventricular segmentation in some patients.

Although, at the moment, the most cost-effec-

tive imaging techniques to detect reversible contrac-
tile function are stress echocardiography and nu-
clear perfusion imaging, the use of newly developed echocardiography techniques such as tissue Doppler imaging during DSE has increased the sensitivity and specificity of echocardiography for detecting viability.

The most important limitation of this study was that we could not follow our patients after coronary artery bypass surgery. Echocardiographic findings after revascularization could help us to determine the specificity and sensitivity of each method. A second limitation arises from the concept that, although a similar 16-segment model was used for DSE and SPECT data, misalignment may have influenced the results.

**Conclusions**

There is a relation between 99mTc-sestamibi uptake and the presence of contractile reserve on DSE in patients with chronic coronary artery disease and left ventricular dysfunction. However, the proportion of segments with preserved technetium uptake is significantly greater than those showing a positive re-
responsive to dobutamine. This suggests that the cellular mechanisms responsible for a positive inotropic response to adrenergic stimulation require a higher degree of myocyte functional integrity than those responsible for $^{99m}$Tc-sestamibi uptake. The small number of segments with contractile reserve on DSE and without tracer uptake on perfusion scanning may be explained by the non-transmurality of myocardial infarction.

References

7. Brown KA. Do stress echocardiography and myocardial perfusion imaging have the same ability to identify the low-risk patient with known or suspected coronary artery disease? Am J Cardiol. 1998; 81: 1050-1053.

