Contrast Stress Echocardiography
Completing the Picture From Image Enhancement to Improved Accuracy and Prognostic Insight

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The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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Echocontrast contrast agents have great value in combination with stress echocardiography. Their conventional role is to enhance left ventricular borders during suboptimal imaging, and the test is widely, if not universally, applied for this purpose.1 The use of echocardiographic contrast agents unequivocally improves endocardial resolution,2,3 facilitating concordant test interpretation,4 and there are probable diagnostic benefits,5 especially for less-expert readers. The evaluation of myocardial perfusion with echocardiographic contrast agents, long considered a holy grail of echocardiography, has become feasible as a result of improved understanding of microbubble–ultrasound interaction, equipment development, and significant efforts from a relatively small number of clinical investigators. The development of a feasible approach for myocardial contrast echocardiography has led to a number of recent reports that demonstrate improvement in the accuracy of stress echocardiography,6,7 particularly for the identification of single-vessel disease, and the recognition of the true extent of coronary disease, a facet that is commonly underestimated with stress echocardiography.

The article by Tsutsui et al8 in this issue of Circulation represents another landmark in the clinical evaluation of myocardial contrast echocardiography. These investigators evaluated the prognostic value of myocardial perfusion imaging in 788 patients undergoing myocardial contrast echocardiography. The use of myocardial perfusion imaging significantly increased the proportion of studies recognized as abnormal, from 26% to 41%, with not only an increased recognition of ischemia but also a recognition of ischemia within areas thought to have infarction. As in previous literature, the extent of multivessel disease was better appreciated with contrast echocardiography. During a median follow-up period of nearly 20 months, 58 patients died and 17 suffered a nonfatal myocardial infarction, giving an overall event rate of 9.6%. The 3-year event-free survival rates in patients with ischemia and fixed perfusion defects were 84% and 86%, respectively, compared with 95% in patients with normal perfusion and normal wall motion, 82% in patients with abnormal perfusion but normal wall motion, and 95% in patients with normal perfusion and normal wall motion. Multivariate analysis showed that abnormal perfusion was an independent predictor of adverse outcome, with wall motion excluded from the model. Moreover, abnormal perfusion added significant incremental value to clinical analysis, resting, and stress wall motion assessment.

These results are important on two levels. On clinical grounds, they document the incremental value obtained from adding myocardial contrast to stress echocardiography, defining not only a diagnostic but also a prognostic benefit. The combination of both this and the previous diagnostic work suggests that rather than contrast only being applied to selected stress echocardiograms, in which image quality is imperfect, it may add significantly to the diagnostic and prognostic content of all stress echocardiograms. On a pathophysiological level, the results of the study provide some provocative information about the relative prognostic impact of myocardial perfusion and function. Previous studies with stress echocardiography have suggested that left ventricular function responses to stress are prognostically powerful, and in comparisons with myocardial perfusion assessment using SPECT both in head-to-head trials6,10 and meta-analyses,11 the prognostic significance of abnormal wall motion responses to stress and abnormal perfusion have been considered analogous. In contrast, the results of the study of Tsutsui et al8 suggest that the perfusion data are prognostically more meaningful and indeed appear to outweigh the wall motion data.

This discrepancy with the previous literature with regard to the prognostic implications of abnormal flow and function may reflect the superiority of myocardial contrast over SPECT or the inferiority of wall motion analysis in this trial as compared with the previous literature. From a prognostic standpoint, there is little evidence to suggest the superiority of echo assessment of perfusion compared with SPECT assessment, with a negative SPECT scan conferring a <1% annualized risk,11 less than that reported in this study. The wall motion analysis in this study, which gave a 2.4% annualized event rate in patients with normal wall motion, does exceed that in recent reports (Table).7,8,12-17 There may be two important explanations for this. First, low mechanical index imaging was used for both interpretation of wall motion and perfusion. Despite the authors’ recent report that high and low mechanical index imaging have similar sensitivity,18 this modality has potentially poorer endocardial resolution and frame rate as compared with standard imaging. Second, the criteria for positivity with wall motion were
Results of Recent Studies of Stress Echocardiography to Predict Events in Groups of >1000 Patients With Chronic Stable Coronary Disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Stress</th>
<th>No. Patients</th>
<th>Mean F/U, mo</th>
<th>Annualized Event Rate, %</th>
<th>Positive Test</th>
<th>Negative Test</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsutsui et al6</td>
<td>Dob</td>
<td>788</td>
<td>20</td>
<td>10.6</td>
<td>2.4</td>
<td></td>
<td>All-cause mortality+MI</td>
</tr>
<tr>
<td>Sicari et al12</td>
<td>Dpy or Dob</td>
<td>7333</td>
<td>31</td>
<td>3.0</td>
<td>1.2</td>
<td></td>
<td>Total mortality</td>
</tr>
<tr>
<td>Marwick et al13</td>
<td>Dob</td>
<td>3156</td>
<td>46</td>
<td>9.5</td>
<td>1.1</td>
<td></td>
<td>Cardiac mortality</td>
</tr>
<tr>
<td>Poldermans et al14</td>
<td>Dob</td>
<td>1659</td>
<td>36</td>
<td>2.7–6.7</td>
<td>1.3</td>
<td>Hard events</td>
<td></td>
</tr>
<tr>
<td>Yao et al17</td>
<td>Tml or Dob</td>
<td>1500</td>
<td>32</td>
<td>3.1–5.2</td>
<td>0.9</td>
<td></td>
<td>Cardiac death+MI</td>
</tr>
<tr>
<td>McCully et al12</td>
<td>Tml</td>
<td>1325</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td>...</td>
</tr>
<tr>
<td>Elhendy et al7</td>
<td>Tml, men</td>
<td>3322</td>
<td>38</td>
<td>3.6</td>
<td>1.0*</td>
<td></td>
<td>Cardiac death and MI</td>
</tr>
<tr>
<td>Tml, women</td>
<td>2476</td>
<td>38</td>
<td></td>
<td>2.6*</td>
<td>0.6*</td>
<td></td>
<td>PV—relates to exWMSI &lt;1.25*</td>
</tr>
<tr>
<td>Marwick et al16</td>
<td>Tml</td>
<td>5375</td>
<td>66</td>
<td>2.7</td>
<td>1.1</td>
<td></td>
<td>Total mortality</td>
</tr>
</tbody>
</table>

F/U indicates follow-up; Dob, dobutamine; Dpy, dipyridamole; Tml, treadmill; PV, predictive value; and exWMSI, exercise wall motion score index.

Conservative (wall motion abnormalities were only identified if they were present in ≥2 segments), which would have reduced the number of positive scans by wall motion and led to patients with 1 abnormal segment being included in the group with normal wall motion.

The perfusion data gathered from myocardial contrast echocardiography vary from the data reported from SPECT imaging. It is possible that information gathered about the microvasculature using myocardial contrast echocardiography is incremental to wall motion in a way that SPECT perfusion data are not. Such a finding is at odds with our present understanding of the relative contributions of stress-induced wall motion and perfusion abnormalities and needs to be evaluated further in subsequent studies. In the meantime, however, the study of Tsutsui et al6 defines for the first time that myocardial contrast echocardiography is predictive of outcome in patients with known or suspected coronary artery disease.

Disclosure

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References


Key Words: Editorials ■ contrast media ■ coronary disease ■ echocardiography
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