Table 1. Coefficient Estimates of Our Statistical Model Adjusted for Baseline Values and Confounding Factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Delta</th>
<th>Intercept</th>
<th>Baseline</th>
<th>Mild Hypertension</th>
<th>Duration of Symptoms</th>
<th>Amiodarone Treatment</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(yes vs. no)</td>
<td>(months)</td>
<td>(yes vs. no)</td>
<td>(metoprolol vs. carvedilol)</td>
</tr>
<tr>
<td>VEB/h 6 mo</td>
<td>38.93</td>
<td>−0.33*</td>
<td>−37.93</td>
<td>−0.27</td>
<td>−25.89</td>
<td>28.67</td>
<td></td>
</tr>
<tr>
<td>VEB/h 12 mo</td>
<td>53.03</td>
<td>−0.32</td>
<td>−119.38*</td>
<td>−0.39</td>
<td>−39.10</td>
<td>101.26*</td>
<td></td>
</tr>
<tr>
<td>Couplets/h</td>
<td>6 mo</td>
<td>−0.52</td>
<td>0.046</td>
<td>0.23</td>
<td>0.03</td>
<td>0.21</td>
<td>0.83</td>
</tr>
<tr>
<td>Couplets/h</td>
<td>12 mo</td>
<td>−0.337</td>
<td>−0.118</td>
<td>−0.887</td>
<td>0.004</td>
<td>−1.121</td>
<td>1.818*</td>
</tr>
<tr>
<td>NSVT/h 6 mo</td>
<td>−0.02</td>
<td>−0.33*</td>
<td>−0.005</td>
<td>0.0004*</td>
<td>−0.02</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>NSVT/h 12 mo</td>
<td>−0.03</td>
<td>−0.10</td>
<td>−0.03</td>
<td>0.0005*</td>
<td>−0.01</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05.

NSVT = nonsustained ventricular tachycardia; VEB = ventricular ectopic beats.


Pharmacologic Stress Echocardiography: Can We Forget “State-of-the-Art” Protocols?

In a recent issue of the Journal, Fragasso et al. (1) reported on the comparison of different stress imaging modalities for the detection of coronary artery disease in hypertensive patients. Their final conclusion was that stress echocardiography appears to be the most valuable tool for predicting significant coronary artery disease, and that among pharmacologic stressors, dobutamine stress echocardiography should be the first choice. In my opinion, this statement should be read with caution. First of all, the authors applied protocols of stress testing that do not represent the accepted "state-of-the-art" modalities of pharmacologic echocardiography. In case of a negative stress test response, atropine was not used either during dobutamine or dipyridamole echocardiography. Although they mentioned that atropine coadministration improves the diagnostic power of both tests, they explicitly stated that the accuracy of dobutamine stress remains higher. I must disagree with this statement. It is well known from a large-scale, multicenter study, that in a group of patients taken off beta-blockers (such as those studied by Fragasso et al.), atropine coadministration dramatically increases the sensitivity of dipyridamole testing, whereas it only mildly affects the sensitivity of dobutamine echocardiography (2). Atropine coadministration with dobutamine markedly increases the test sensitivity in a group taking beta-blockers (3). Moreover, in a meta-analysis of 12 reports comparing head-to-head dipyridamole and dobutamine echocardiography, there was no significant difference in the diagnostic accuracy of both tests. Dobutamine was more sensitive in patients with one-vessel disease, but this advantage disappeared in patients with multivessel disease. The specificity of dipyridamole was consistently higher, and the accuracy of the two tests was similar (4). The result of the meta-analysis is perfectly in agreement with the data of Fragasso et al., showing that the accuracy of the two tests is similar, with a higher sensitivity of dobutamine in single-vessel disease and a higher specificity of dipyridamole in patients with normal coronary arteries. Interestingly, Astarita et al. (5) have recently studied dipyridamole/atropine echocardiography and perfusion scintigraphy in hypertensive patients with a positive exercise electrocardiography test. Using the same selection criteria of Fragasso et al., they also showed a similar sensitivity and higher specificity of...
dipyridamole stress echocardiography versus perfusion scintigraphy. In contrast to Fragasso et al., Astarita et al. used a “state-of-the-art” atropine protocol, and they in fact observed that dipyridamole sensitivity was raised to 88%. Stress echocardiography protocols have evolved rapidly in recent years. When the diagnosis is the target, atropine coadministration should be used. When prognostic stratification is the reason for testing, a high dose without atropine, even in hypertensive patients (6), provides excellent stratification (7).

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REFERENCES


REPLY

We are grateful to Dr. Varga for his comments on our report (1), because his letter gives us the opportunity to further clarify our opinion. Like others (2), in the past, we have used dipyridamole for the diagnosis of coronary artery disease, but we (3) have been unable to reproduce the diagnostic accuracy reported by some groups. Interestingly enough, the near totality of these data comes from a single institution. In our study, we decided not to use atropine to assess the intrinsic strength of the individual stressors. The sensitivities and specificities for perfusion scintigraphy, dipyridamole and dobutamine echocardiography were 98% and 36%, 61% and 91%, 88% and 80% respectively. As a consequence, accuracy, which takes in account both sensitivity and specificity, was not significantly different between the three tests, although dobutamine appeared to perform better (84%) than dipyridamole (74%) and scintigraphy (71%). Furthermore, in patients with one-vessel disease, the performance of dipyridamole was very poor, with a sensitivity of 31%. We do not think that the addition of atropine could have increased this figure to an acceptable level, especially if we take into account that, in this subgroup, the sensitivities of dobutamine and scintigraphy were 85% and 95%, respectively. Indeed, we believe that such differences are enough to justify our statement that dobutamine echocardiography (as well as rest/stress myocardial perfusion scintigraphy) are better than dipyridamole echocardiography in these patients. We cannot afford the risk of missing so many patients with coronary artery disease in such a high-risk group. In addition, this statement is also justified by pathophysiologic considerations. Dobutamine increases oxygen demand by increasing contractility, heart rate and systolic blood pressure. These features make dobutamine an ideal stressor in hypertension. In contrast, dipyridamole produces coronary vasodilation, with little “myocardial stress,” as defined by changes in the rate–pressure product and a lesser likelihood of causing myocardial ischemia. This is why dipyridamole yields high sensitivities when used with scintigraphy, where perfusion abnormalities are thought to represent areas of altered blood flow rather than areas of ischemia; however, this is also why its sensitivity is low when used with echocardiography.

Surely, the addition of atropine improves sensitivity, but it also leaves misdiagnosed a large proportion of patients with single-vessel disease. Furthermore, although dipyridamole is considered a safe test, most patients experience considerable side effects. Aminophylline is administered at the end of the test, and, when atropine has also been given, sustained sinus tachycardia usually ensues, causing discomfort and making the duration of the test as long as dobutamine testing. On the basis of these considerations, we think that dobutamine provides the best performance for the diagnosis of coronary artery disease in hypertensive patients (and beyond). Our feeling (allowed in a letter!) is that most cardiologists around the world share the same opinion.

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REFERENCES


Overdosing With Prostacyclin in Primary Pulmonary Hypertension

Rich and McLaughlin (1) reported excessively high rest cardiac outputs in 12 of 55 patients with primary pulmonary hypertension (PPH) treated with intravenous prostacyclin, all of whom had...