

Can Be Useful to Assess Whether Dobutamine Echocardiography Can Induce Myocardial Damage for Diagnostic and Prognostic Purposes in Coronary Artery Disease?

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The value of pharmacological stress echocardiography using dobutamine (EDOB) in the diagnosis and prognosis of ischemic heart disease in its diverse forms of presentation has been extensively demonstrated in the medical literature.

Effort or pharmacological stress techniques combined with effort or resting cardiac radionuclide perfusion scans are the traditional imaging techniques used for the detection of residual ischemia in the risk stratification of the coronary syndrome. In patients with unstable angina, the high prognostic value of the exercise stress test with thallium-201 and technetium-99m-sestamibi radionuclide perfusion scanning has been demonstrated.¹ Likewise, radionuclide scanning with thallium-201 combined with dipyridamole has been shown to be safe when performed soon after myocardial infarction, and useful for predicting cardiac events during follow-up.² The exercise stress test combined with the radionuclide perfusion scan using technetium-99m-sestamibi or the pharmacological test with dipyridamole and the same radionuclide marker can detect residual ischemia when performed soon after myocardial infarction, as well as predict cardiac events during follow-up in the first year.³ The prognostic value of the pharmacological stress test with dobutamine in combination with Tc-sestamibi radionuclide scans has also been evaluated in large groups of patients with chest pain.

EDOB is a technique that has been much used in echocardiography laboratories and its usefulness has been evaluated extensively in populations with a suspected or known diagnosis of coronary artery

disease. In the last decade, the routine use of stress echocardiography has led to the application of this technique in the risk stratification of patients with acute coronary syndromes. Preliminary studies have already demonstrated the usefulness of bidimensional echocardiography in evaluating the prognosis of patients with unstable angina, disclosing that the presence or exacerbation of segmental motility anomalies is associated with a greater incidence of cardiac events.⁴ Nevertheless, its use in patients with unstable angina has not been studied much. In our center we performed EDOB on 122 patients with unstable angina and low-to-intermediate risk who had been stabilized with medical treatment 48 h after hospital admission.⁵ The one-year survival rate without cardiac events (unstable angina, infarction, or cardiac death) was significantly better in patients who had a negative test result for ischemia, even after considering that 78% of the patients were taking beta-blockers and only 25% of the patients reached submaximum heart rate. The divergence between the two groups was already apparent in the first months after hospital discharge and persisted throughout the 2-year follow-up period. The positive result of EDOB was an independent prognostic factor for events during follow-up and, along with left ventricular function, the most powerful prognostic factor.

As is well-known, EDOB also has been shown to be very useful in the study of myocardial viability, with a good sensitivity and greater specificity than other imaging techniques.⁶ For that reason, it is often used in conjunction with radionuclide techniques to obtain maximum sensitivity and specificity from the combined techniques. Likewise, it is used to stratify risk in patients who will undergo non-coronary surgery.

Nevertheless, in routine practice, the maximum exercise test limited by symptoms, with electrocardiographic control of ischemia, continues to be the preferred complementary test for the diagnosis of ischemic heart disease because it is easily performed and provides additional information about the patient's

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functional capacity.

The limitations that restrict its universal application derive, on the one hand, from the impediments to physical exercise that a large proportion of patients with ischemic heart disease have and, on the other hand, the presence of baseline ECG anomalies like bundle-branch block, left ventricular hypertrophy, pre-excitation, or digitalis treatment. These anomalies interfere with the evaluation of ST-segment changes during exercise. In these cases the strategy of using imaging techniques to detect myocardial ischemia has been a routine practice for the last two decades. Comparative studies have established that stress echocardiography and radionuclide perfusion studies offer a similar level of accuracy in the diagnosis of ischemic heart disease and have a similar capacity for detecting the location and, to a lesser degree, extension of coronary artery disease.⁷ Both techniques have strong and weak points; for instance, echocardiography requires less equipment and is less expensive than radionuclide perfusion techniques. In addition, at the current stage of technological development, in which second-harmonics imaging and transpulmonary contrast materials have been incorporated, the quality of the studies has improved. In spite of such advances, the technique continues to be operator-dependent, which is a drawback in the case of less experienced operators. For this reason, the use of the cardiac radionuclide perfusion scans has been recommended in cases of deficient acoustic window and in patients who, in addition to impediments to physical exercise, have a contraindication for dobutamine. However, the recommendation for stress echocardiography stands fast for patients with physical limitations and a contraindication for vasodilator drugs like dipyridamole. The use of stress echocardiography has also been recommended in patients with hypertrophy or left bundle-branch block because it seems to be more specific, and the patient can be monitored to take immediate action in situations that might be less evident or in doubt, such as possible destabilization or severe ischemia.⁷

The main limitation of EDOB and, by extension, any type of stress echocardiography, is interobserver variability. This variability is intimately linked to the quality of the studies as well as the severity of the motility disturbances originated, as indicated by Hoffmann in an analysis of the causes of this variability. As demonstrated in the study by this author, this variability could be reduced by standardizing studies with respect to the onscreen image, which should be in digital loop format, and interpretation criteria.⁸

It is also clear that stress echocardiography protocols to facilitate the execution of these studies and improve results have evolved in recent years.

Consequently, if dipyridamole is used instead of dobutamine for the diagnosis of ischemic heart disease, atropine must be administered to improve sensitivity. However, if the reason for performing stress echocardiography is prognostic stratification, high doses of dipyridamole should be used without atropine, even in hypertensive patients, to obtain an excellent stratification.⁹ Similarly, modifications have been made in the drug doses given, whether dipyridamole¹⁰ or dobutamine is used, in order to shorten the study time.

In a new attempt to improve the capacity and diagnostic accuracy of EDOB in the diagnosis of coronary artery disease, Pastor et al propose, in a provocative article published in this issue of the journal, a new method based on the determination of the troponin T (TnT) curve before and after EDOB in a group of patients distributed equally between patients with suspected and known ischemic heart disease.¹¹ In fact, if only because patients are separated by the presence or absence of elevation of markers of myocardial damage, their proposal results in a stratification of patients into high risk and low risk groups, and not just the detection of coronary artery disease in a given patient. Thus patients are defined not only by this new definition of myocardial infarction, but also by the criteria used in clinical trials to classify patients with acute coronary syndrome.

Until now, the experience reported with this subject has been scarce and the findings have been somewhat contradictory. In two studies that used TnT or TnI, respectively, to determine if dobutamine infusions cause myocardial lesions in two study groups of 20 and 27 patients with serious coronary artery lesions who underwent assessment of cardiac viability, no elevation of troponins was found.^{12,13} In another recent study, Wang et al¹⁴ analyzed TnI values immediately before performing EDOB in 117 patients with stabilized acute coronary syndrome. In multivariate analysis, the variables associated with TnI elevation are the time when EDOB became positive and the presence of motility anomalies in baseline circumstances, which indicates the presence of more residual ischemia and a history of infarction. From this it can be deduced that EDOB has the same clinical value as the finding of troponin elevation 70±2 h after hospitalization for an acute coronary syndrome.

If the results of the study of Pastor et al¹¹ are confirmed in other studies with a larger number of patients, we may have to reconsider the protocols used in EDOB and any other ischemia provocation method employing detection techniques that induce troponin elevation. However, with the exception of this and other methodological questions, such as the value of serial extractions, the addition of trustworthy prognostic information obtained by the determination of the myocardial damage markers would be an important

qualitative jump for stress echocardiography techniques, particularly since we know from evidence obtained in experimental studies that troponin T also rises in the absence of necrosis, although in such cases the elevation is small.¹⁵

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