

## Consensus on the Interpretation of Exercise Echocardiography: Still Awaited

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Multiple studies published in the last 2 decades have demonstrated the usefulness of stress echocardiography in the diagnosis and prognosis of ischemic heart disease. In its pharmacological modalities, dobutamine stress echocardiography is used for the diagnosis of ischemic heart disease<sup>1</sup> to identify patients with a poor prognosis after acute myocardial infarction<sup>2</sup> and medically stabilized unstable angina.<sup>3</sup> It is also widely recognized in the detection of myocardial viability<sup>4</sup> due to its well-balanced sensitivity and specificity. The multicenter studies done by Picano's group popularized another pharmacological modality using dipyridamole.<sup>5</sup>

Although drugs are a priori easier and simpler to apply, they are not free from contraindications and risks, and these are more frequent in the case of dobutamine.<sup>6</sup> Furthermore, oxygen consumption induced by physical exercise and, thus, its ability to cause ischemia, is increased by the use of dobutamine. On the other hand, dipyridamole has shown low sensitivity (similar to the standard exercise stress test) in the detection of 1- or 2-vessel disease.<sup>7</sup> Thus, it seems natural that the indication for pharmacological stress echocardiography is increasingly restricted to those patients who cannot make physical efforts or to study myocardial viability.

Exercise echocardiography (EE) does not involve the shortcomings of using the electrocardiogram in the standard exercise stress test and is an effective alternative to radioisotopic techniques that use perfusion as a marker of ischemia. Not only are there technical advantages, such as its wide availability, but also clinical ones, since 2 investigations are done simultaneously: the baseline examination that identifies possible unknown diseases and assesses baseline ventricular function, and the analysis of

behavior under stress. Furthermore, it increases the prognostic value of clinical variables, the standard exercise stress test and resting echocardiography, as recently demonstrated.<sup>8</sup> It has the additional advantage of providing the results immediately, thus facilitating fast decision-making, which is also the case with pharmacological modalities. Treadmill stress echocardiography records the images immediately before and after exercise, with a narrow time-window for the acquisition of the postexercise examination, since the alterations in segment wall motion, induced by the ischemia, are resolved in 60-90 s. This specific issue can be resolved if stress is applied using bicycle ergometry, either in the standard or decubitus position, since segment wall motion can be then recorded over the time the test lasts and up to the maximal peak of the exercise.

In general, exercise echocardiography requires a high degree of specialization and is described as the most difficult technique out of all those carried out in echocardiography laboratories.<sup>9</sup> Thus, since its inception, there has been controversy regarding its degree of accuracy which has impeded its practical application. This is due to multiple factors, usually technical, such as image quality, the methodology used and, as in no other technique, the experience and skills of the operator.<sup>10</sup> In this case, the subjective, and thus qualitative, interpretation determines diagnostic accuracy which, in turn, is based on the observation of myocardial thickening before, during and after stress. Variability in interpretation, which is its main limitation, was analyzed in the now classic study by Hoffmann et al,<sup>11</sup> which identified subjective interpretation and the lack of uniform criteria in the acquisition and assessment of the images as causes of low inter-observer agreement. Subsequently, their second analysis, carried out 6 years later, demonstrated that intercenter agreement in the interpretation of dobutamine stress echocardiograms improved when using new techniques such as second harmonic imaging and digital imaging and by applying uniform reading criteria.<sup>12</sup>

A Spanish national multicenter study,<sup>13</sup> published in this issue of the REVISTA ESPAÑOLA DE CARDIOLOGÍA, analyzes intercenter agreement on the interpretation of EE which, surprisingly (as expressed by the authors),

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has not been studied until now. Using a very similar design to those studies which demonstrated improved intercenter variability with dobutamine stress echocardiography,<sup>14</sup> as well as the same criteria for interpretation, they also thoroughly analyze all the factors that affected sensitivity, specificity, and diagnostic accuracy regarding coronary artery disease in the 6 participating centers. The main conclusion of Peteiro et al<sup>13</sup> is that intercenter agreement on EE is moderate, with a Kappa coefficient of 0.48 (which is low rather than good). Here, experience and personal skills play a very important role in the interpretation of the studies from the different centers, such that this study and others report that the strictest centers, that is, those which assess the others as worse, achieve higher assessments regarding their images when evaluated by the other centers. However, it is also true, consistent, and clinically relevant, that the degree of agreement increases when the alterations that occur are not subtle or mild, but are more obvious. Thus, this is demonstrated in this study by the increase in the degree of agreement regarding 3-vessel disease, left anterior descending artery disease or baseline alterations in regional wall motion.

As was foreseeable, the blinded interpretation, i.e., without knowledge of patient data or their response to stress, has a lower probability of success and intercenter agreement. This fact is linked to the global accuracy of the technique which, in turn, has an inverse relationship to the degree of subjectivity in the interpretation, but not to the degree of image quality and, as seems to be demonstrated in this work, does not improve intercenter percentage agreement or the Kappa coefficient, regardless of the fact the studies were of optimal or suboptimal quality. This is a finding that contrasts with the reasons for the limited intercenter agreement on the interpretation of dobutamine stress echocardiograms carried out by Hoffmann, who demonstrated in a multivariate analysis that image quality, the severity of the alterations in induced wall motion abnormalities, and the obtained rate-pressure product were the factors that had a greater impact on the homogeneity of interpretation.<sup>14</sup> Perhaps it is because heart rates are higher when dobutamine is administered that the effect of image quality is a determining factor in the disparity of interpretations. However, it has been clearly demonstrated that the disparity of interpretations is related to including clinical data when interpreting a stress echocardiogram and that, without doubt, this has as much importance as the obtained images. The difference in sensitivity, specificity and diagnostic accuracy of the centers when analyzing their own cases and those of others is thus, not surprising.

Although including clinical data is important in any type of complementary test, it is the case that the interpretation of EE can be improved via one of the long-awaited major advances in this technique: the

possibility of objectively quantifying wall motion and its response to the various stress modalities. The use in clinical practice of some current techniques, such as tissue Doppler ultrasound or strain rate imaging, have clearly still not yielded everything expected from them regarding the need to reduce variability between observers and improve intercenter agreement. Other techniques, such as the application of transpulmonary contrast agents, have already demonstrated that the improvement in endocardial border resolution can improve the assessment of regional wall motion at rest and under stress,<sup>15</sup> and improve the capacity of stress echocardiography to detect coronary artery disease.<sup>16</sup>

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