Promise and Status of Myocardial Contrast-Enhanced Two-Dimensional Echocardiography: Delineation of Ischemic Risk Zone and Quantitation of Myocardial Perfusion Defects*

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The use of contrast agents during echocardiography is not new, and substantial qualitative evaluations with this approach have been reported (1–4). Recently, a JACC seminar (5) dealt with an extension of the contrast echo technique to the measurement of the size of underperfused myocardium and potentially to quantitation of myocardial blood flow. In the initial experimental studies (6,7), intracoronary or aortic root injection of a small amount of contrast agent, such as an agitated saline-Renografin mixture, enhanced two-dimensional echocardiographic images to a degree, allowing quantitative delineation of acute ischemic perfusion defects in short-axis left ventricular sections. Additional studies (8) demonstrated apparent safety and validated this technique in the dog. Refinements of the technique applied computer assist and digital subtraction methods (9,10), and problems in defining the myocardial contrast echoes have been examined (11).

Delineation and quantitation of myocardial ischemia or infarcted zone. The delineation of the ischemic risk zone in multiple cross sections has been logically applied by Kaul et al. (12) in this issue of the Journal. These authors satisfactorily correlated in dogs the echo contrast-derived ischemic risk region with various modes of regional dysfunction analysis, based on two-dimensional measurements obtained just before the administration of echo contrast agents. In vivo real time quantitation of the risk zone is of substantial interest, and can serve to normalize measurements of irreversible ischemic damage when coronary anatomy and collateral circulation vary substantially. Kaul et al. conclude that the myocardial contrast echo method will be a useful complement to current echocardiographic measurements of ischemic function. There is a need, however, to provide a perspective on the current state of the art and recognize problems that might be encountered in future applications.

Reviewing the data of Kaul et al. obtained during left anterior descending or left circumflex coronary artery occlusion in dogs (their Table 1), one becomes aware of discrepancies or difficulties in individually applying the general correlations. For example, in Dog 7, the preferred function analysis B yielded 73% extent of dysfunction in the papillary short-axis cross section of the left ventricle, which corresponded well with the 80% extent of the risk zone determined with contrast echo techniques. Yet, method B shows zero dysfunction for the high papillary section while contrast echocardiography yields a 33.6% perfusion defect. Thus, there is substantial variability, some of which may be attributed to the method of contrast delineation. More extensive comparisons should certainly be compiled in the closed chest model, rather than in open chest animals. There remain serious questions about the clinical application of myocardial contrast-echo delineation in the more common apical cross-sectional images of the left ventricle, and about the use of the technique in the presence of significant echo dropouts or poor quality of endocardial/epicardial interface definition. Finally, as has been pointed out by Kondo et al. (13) and Ten Cate et al. (14), it is necessary to bear in mind the effects of contrast agent administration on the heart. Since gaseous bubbles are needed in echo contrast methods, it is appropriate to require more information on the safety of intracoronary, aortic root or coronary venous injections. As revealed in a study by Ten Cate et al. (15), transpulmonary echo contrast studies of myocardium currently appear far from practicable.

Contrast echo computerization has been applied to analyze the dynamics of myocardial echo contrast appearance and disappearance (9,16) from which one can derive indexes such as "washout," which seem to correlate with coronary blood flow (14). If further developed and corroborated, a quantitative myocardial contrast echo methodology could be a useful tool in evaluating ischemic states and interventions affecting myocardial perfusion as well as cardiac function. Again, the clinical importance and potential of the technique are not yet clear.

Future improvements in contrast agents. Fundamental to all quantitative echocardiographic contrast methods is the use of quality-controlled microbubbles and well characterized contrast solutions. At this time, and in spite of several reports (17,18), no fully satisfactory echo contrast agent is available for myocardial perfusion studies. To assure safety, minimize measurement artifacts and approach characteristic
myocardial transit times, such an agent should have negligible myocardial effects and feature highly uniform and echogenic microbubbles that could readily pass through the microcirculation (18). In addition, there is as yet no satisfactory method of intravenous or right heart contrast administration for the quantitation of myocardial contrast echoes. The primary goal thus remains to develop echo contrast agents with sufficiently persistent highly uniform microbubbles of a diameter of 3 to 5 μ and capable of easy transit through the microcirculation. Among other complicating factors to be kept in mind is the major coronary hyperemia caused by certain agents (13), and a potentially unsatisfactory intensity of myocardial echo contrast enhancement when microbubbles are extremely small.

**Future clinical applications.** In spite of these words of caution and the evident challenges to be overcome, myocardial contrast two-dimensional echocardiography remains a highly desirable and apparently achievable technique. The relatively simple method reported in this issue of the Journal clearly indicates that a potential already exists for the useful application to study "risk areas." Aortic root and also coronary venous echo contrast injections (19) represent short-term solutions in anticipation of a more generally applicable right-sided or intravenous administration. Among new observations, a significant normal state phasic alteration in myocardial echo contrast intensity occurs during the cardiac cycle, and this effect might be applied to differentiate a state of ischemia during which this phasic intensity change is greatly reduced or eliminated.

We can expect selective application of myocardial contrast echocardiography in clinical studies, but clinical observations should be viewed with caution, particularly when the data involve insufficiently characterized agents or contrast agents with unspecified gas bubbles. Clinical reports should be examined in light of the potential problems I have indicated, particularly the limited or imperfect two-dimensional echocardiographic cross-sectional images and effects of contrast administration. A potential area of interest relates to myocardial echo contrast intensities after coronary occlusion and during the early reperfusion period. Contrast echocardiographic measurements of the ischemic zone as well as analysis of myocardial contrast washout might prove helpful in evaluating the effectiveness of the various acute reperfusion techniques that are receiving increasing attention.

**References**


