Bolus injection or continuous infusion for the assessment of myocardial blood flow during perfusion stress echocardiography?

We read the recent article by Wejner-Mik et al. in the Journal with great interest and we congratulate them on their study which re-emphasizes both the clinical value of myocardial contrast echocardiography (MCE) and specifically the prognostic value of dipyridamole MCE. Both real-time and triggered imaging techniques were used, highlighting the robust nature of each method. We wish to highlight certain methodological aspects which may be of use in planning future studies.

First, the contrast agent (Optison) was administered by repeated bolus injections rather than a continuous intravenous infusion. The pioneering scientific experiments that established the ability of MCE to assess myocardial blood flow (MBF) used a continuous infusion. The myocardial signal assessed visually as contrast intensity reflects the concentration of microbubbles within the myocardium. When the entire myocardium is fully saturated with microbubbles, the signal intensity denotes the capillary blood volume. Any alteration of signal must, therefore, occur predominantly from a change in capillary blood volume. Consequently, one of the basic physiological principles of MCE is that the myocardium should be fully saturated with microbubbles prior to destruction-replenishment imaging. This steady-state can be achieved with a bolus injection if the microbubbles persist for long-time periods (e.g. as with the contrast agent LightLab, used in the recent multicentre RAMP trials).

Continuous infusion of contrast has several other advantages. First, titrating the rate of infusion allows one to individualize the dose needed for each patient, secondly, there is more time to acquire images with an infusion, whereas with a bolus injection the degree of opacification deteriorates rapidly with time. Thirdly there are reduced contrast artefacts with infusion use (e.g. shadowing, blooming, or swirling) and, fourthly, use of an infusion allows quantification of MBF. Additionally, calculation of MBF at rest and stress yields the coronary flow reserve, which has both diagnostic and prognostic benefit in a variety of conditions. The EAE guidelines on contrast echocardiography recommend continuous infusion for the assessment of myocardial perfusion.

Secondly, as the authors themselves acknowledge, the population studied were a high-risk cohort—all had been referred on clinical grounds for cardiac catheterization and, indeed, 75% were found to have significant coronary artery disease. We therefore propose that further studies in a low-intermediate risk cohort will also be of clinical value, as it is frequently such patients in whom functional imaging tests are requested.

In conclusion, we again commend the authors on their work and for achieving lengthy follow-up in a large cohort to inform us of the prognostic significance of dipyridamole MCE in a high-risk patient population. However, we have certain methodological suggestions as described above and, in particular, propose that the optimal method for assessing myocardial perfusion during MCE is with a continuous intravenous infusion of contrast.

References


LETTERS TO THE EDITOR