LETTERS TO THE EDITOR

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

We read the recent article by Wejner-Mlik et al.1 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.2 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.3 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 Imagify4, used in the recent multicentre RAMP trials).5

Continuous infusion of contrast has several other advantages.5 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 echocardiography5 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

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Bolus injection for the assessment of perfusion during stress echocardiography has several limitations, but also certain advantages

We would like to thank Dr Shah and Professor Senior for their interest in our recent article regarding the prognostic value of stress myocardial contrast echocardiography (MCE)7 and for their insightful comments concerning methodology of our study.

Indeed, contrast administration by bolus injections has several limitations, such as unsuitability for advanced quantitative analysis, decreased diagnostic time window and more risk of acoustic shadowing affecting the far field image quality.7–9 It is true that the calculation of myocardial blood flow and replenishment curve-derived quantitative indices requires a stable microbubbles concentration. All the benefits from infusion notwithstanding, we believe that slow manual administration of individually adjusted boluses of contrast can provide satisfactory images for qualitative analysis. In our previous study based on bolus injections of contrast, perfusion assessment by real-time MCE was precluded by suboptimal image quality only in 5% of segments at rest and in 5.2% during stress.6 According to our experience, this is partly due to the immediate visual feedback between myocardial signal intensity and the rate of injection. Thus, we hypothesized in our study that visually assessed differences in myocardial contrast intensity may provide valuable prognostic

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