Myocardial Contrast Echocardiography: An Innovative Technique to Assess Myocardial Perfusion in Hypertensive Patients

Roxy Senior

Myocardial contrast echocardiography (MCE) is an ideal imaging tool for the assessment of the myocardial microcirculation. At baseline, approximately 8% of left ventricular mass is constituted by blood present in the microcirculation termed myocardial blood volume (MBV), 90% of which is comprised of blood in the capillaries. The MCE measures microcirculatory flow because it uses gas-filled microbubbles that are inert, remain entirely within the vascular space, and possess an intravascular rheology similar to that of red blood cells (RBC). Furthermore, MCE has good spatial and temporal resolution. When microbubbles are administered as a constant infusion and once a steady state is achieved (approximately 1 to 2 min), the acoustic intensity measured from the myocardium after background subtraction (to eliminate native backscatter from myocardial tissue) provides a measure of MBV fraction. An excellent correlation was observed between signal intensity obtained from a region of interest in the myocardium of patients with capillary density obtained from the biopsied myocardium of the same region.1 At steady state, when microbubbles within the myocardium are destroyed with high-energy ultrasound pulses, the rate of microbubble reappearance reflects RBC velocity or blood velocity. Because myocardial blood flow (MBF) constitutes a volume of blood moving at a certain mean velocity, the product of MBV fraction and myocardial microvascular flow reflects myocardial microvascular flow.2 Therefore, unlike other clinical methods that measure MBF, this approach provides an assessment of two components of capillary (tissue) perfusion (ie, MBV and myocardial blood velocity).

How does MCE detect flow-limiting coronary artery disease (CAD)? During hyperemia, in the absence of significant tachycardia, myocardium subtended by normal coronary artery shows no change in microbubble signal intensity, because microvascular volume remains constant. However, in the presence of coronary stenosis hyperemia results in a decrease in MBV proportional to the severity of stenosis. This occurs because capillary volume decreases (MBV fraction is predominantly capillary) to maintain a constant capillary hydrostatic pressure in the presence of a decrease in precapillary pressure. Because capillaries do not have smooth muscles, they cannot constrict. The only way capillary volume can decrease is if capillary units functionally shut off, resulting in a lower number of microbubbles in the myocardium and a resultant perfusion defect on MCE. This mechanism is also responsible for the occurrence of perfusion defect with radionuclide imaging. Capillary derecruitment, combined with a lesser increase in RBC velocity, forms the basis for stenosis detection in CAD. At rest, normally, because the RBC velocity in capillaries is 1 mm/sec, after destruction of microbubbles in the myocardium it takes approximately 5 sec to fill the ultrasound beam, as the elevation of the ultrasound beam is 5 mm. During hyperemia the normal myocardium fills in 1 sec because hyperemic flow increases five times, whereas in regions subtended by coronary stenosis, the rate of filling is slower depending on the severity of stenosis. In case of milder stenosis, the filling abnormality may be only confined to the subendocardium, which may be seen on MCE but not radionuclide imaging because of the higher spatial and temporal resolution of MCE. Thus, MCE is more sensitive than radionuclide perfusion imaging in detecting reversible perfusion defects in intermediate flow-limiting stenosis.3 MCE by virtue of its ability to measure both resting and hyperemic myocardial blood flow can also measure MBF reserve.

The study by Aggeli et al4 demonstrated the value of MCE for the detection of CAD in hypertensive patients. Systemic hypertension is a strong risk factor for CAD, but the prevalence of CAD in such patients is moderate. An
exercise electrocardiogram (ECG) is the most widely used technique for the assessment of CAD, but it has a relatively low sensitivity and specificity compared with imaging techniques such as stress echocardiography and single-photon emission computed tomography (SPECT) imaging. Stress echocardiography is excellent for the assessment of CAD, but its sensitivity tends to be compromised in patients with significant left ventricular hypertrophy (LVH). Perfusion techniques like SPECT may suffer from low specificity, because hypertensive patients may have microvascular disease in the absence of large vessel CAD and often asymmetrical LVH, which result in a relative difference in tracer uptake leading to apparent perfusion abnormalities even in the absence of microvascular disease and CAD. The MCE in this scenario is an ideal technique. Perfusion defect in the presence of vaso-dilator stress almost always occurs when there is significant epicardial coronary stenosis. Microvascular disease is manifested as delayed microbubble filling of the myocardium after a destructive phase. These differential effects on the kinetics of MCE and differential manifestation as a result may allow MCE to accurately classify patients with and without CAD as opposed to microvascular disease. In the study by Aggeli et al MCE was equivalent to SPECT for the detection of CAD with a tendency toward higher sensitivity of MCE compared with SPECT. The latter is likely because MCE, by virtue of its superior spatial resolution compared with SPECT, is likely to identify mild subendocardial ischemia due to CAD more effectively. The high specificity of both techniques is unexpected. However, it is likely because the number of patients with significant LVH may be low (the mean LV mass index was only 118 gm/m² in this study), or because of hypertensive patients may have microvascular disease in the absence of large vessel CAD and often asymmetrical LVH, which result in a relative difference in tracer uptake leading to apparent perfusion abnormalities even in the absence of microvascular disease and CAD. The MCE in this scenario is an ideal technique. Perfusion defect in the presence of vaso-dilator stress almost always occurs when there is significant epicardial coronary stenosis. Microvascular disease is manifested as delayed microbubble filling of the myocardium after a destructive phase. These differential effects on the kinetics of MCE and differential manifestation as a result may allow MCE to accurately classify patients with and without CAD as opposed to microvascular disease. In the study by Aggeli et al MCE was equivalent to SPECT for the detection of CAD with a tendency toward higher sensitivity of MCE compared with SPECT. The latter is likely because MCE, by virtue of its superior spatial resolution compared with SPECT, is likely to identify mild subendocardial ischemia due to CAD more effectively. The high specificity of both techniques is unexpected. However, it is likely because the number of patients with significant LVH may be low (the mean LV mass index was only 118 gm/m² in this study), or because of hypertensive patients may have microvascular disease in the absence of CAD.

However, the investigators should be congratulated for performing this study, as this is the first comparative study in hypertensive patients. This study clearly underscores the value of MCE, which is a bedside technique without exposure to radiation.

References