Myocardial Contrast Echocardiography

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Myocardial contrast echocardiography (MCE) is an imaging tool for the assessment of the myocardial microcirculation. It utilizes gas-filled microbubbles that are inert, remain entirely within the vascular space, and possess an intravascular rheology similar to that of red blood cells.\(^1,2\)

During an intravenous infusion of these microbubbles and attainment of a steady state, the microbubbles are destroyed with high energy ultrasound and the rate of microbubble replenishment within the ultrasound beam is measured (Figure 1), which represents mean red blood cell velocity.\(^3\)

Normally, the beam fills within 5 seconds when resting flow is normal. It takes longer to fill when flow is reduced and fills faster at hyperemic flows. When the beam is fully replenished, the ultrasound signal represents relative blood volume within the beam, which translates to the volume of blood within the myocardium itself. Normalizing this value to the signal from the left ventricular cavity provides a measure of blood volume fraction.\(^3\)

Therefore, unlike other experimental and clinical methods that measure myocardial blood flow (MBF), this approach provides an assessment of the 2 individual components of nutrient tissue (capillary) perfusion: Blood volume fraction and flow velocity. The product of the two is proportional to MBF. Other than the heart,\(^3,4\) this method has been used successfully and accurately for the measurement of tissue perfusion in the skeletal muscle,\(^5\) skin,\(^6\) brain,\(^7\) and kidney.\(^8\) In this update, we shall review the clinical use of this technique in 2 clinical settings: Acute myocardial infarction (AMI) and detection of coronary artery disease (CAD).

**Acute Myocardial Infarction**

In AMI, MCE can define the area at risk and confirm the success of reperfusion.\(^9\) MCE has been clinically shown to be superior for the detection of acute coronary syndromes in the emergency department compared with routine evaluation.\(^10\) A day or two after reperfusion (when hyperemia has abated), it can define the region with no-reflow, which approximates infarct size.\(^11\) Consequently, MCE can be used to determine the spatial extent of viable tissue post-infarction.\(^12,13\)

MCE can also be used to define the extent of collateral perfusion during coronary occlusion and hence to predict the ultimate infarct size (provided mechanical intervention does not increase the infarct size from microembolism of atherosclerotic debris or from reperfusion injury).\(^14\) The extent of collateral perfusion during coronary occlusion has been shown to correlate with the extent of viable myocardium.\(^15\) The case discussed below illustrates an example of a patient with AMI who had extensive collateral flow.

A 67-year-old man presented to the emergency department with recurrent chest discomfort lasting for several months and culminating in sustained pain over the past 2 weeks. The ECG showed diffuse, non-specific ST-T wave changes. An echocardiogram revealed regional dysfunction in the left ventricular apex and the adjacent interventricular septum. MCE (Figure 2A and Movie I) depicted lack of filling of the apex at shorter pulsing intervals when the rest of the myocardium had already opacified. At longer pulsing intervals, most of the apex also opacified except for a small subendocardial region. Coronary angiography revealed an occluded left anterior descending artery (Figure 2B and Movie II). Therefore, despite an occluded infarct-related artery, adequate perfusion was seen in the apex,

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The Movies are available in an online-only Data Supplement at http://www.circulationaha.org.

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albeit at a slower rate. The subendocardial region of the myocardium that did not opacify even at long pulsing intervals was bereft of collateral flow and was therefore likely to undergo necrosis unless the infarct-related artery was immediately opened. Nevertheless, the worse-case scenario AMI was likely to be small and limited to the endocardium, even if the infarct-related artery was not opened.

Detection of Coronary Artery Disease

If there is no prior AMI, detection of CAD requires some form of stress testing. For MCE, we prefer a coronary vasodilator, although dobutamine is also sometimes used. The advantage of a vasodilator is shorter examination time, fewer side effects, and easier image interpretation because of absence of tachycardia and tachypnea-induced cardiac motion. It is currently not possible to perform MCE in patients exercising on the treadmill. For interpretation, end-systolic images acquired at rest and stress are placed side-by-side. In this manner, we can compare the same region within the stress and rest images at the same pulsing interval. Unlike nuclear cardiology, we do not compare different regions within the same image.

As stated earlier, the ultrasound beam should replenish in 5 seconds at rest if the resting flow is normal. If maximal hyperemia (5 times normal flow) is achieved with a vasodilator, then the stress image should fill in 1 second. Thus, the 5-second rest image should look exactly like the 1-second stress image. A lack of this finding suggests reduced coronary blood flow reserve. If this finding is regional, it indicates the presence of CAD. When this finding is global, it usually indicates reduced flow reserve due to other systemic conditions, such as hypertension, diabetes, or hyperlipidemia.

When we perform vasodilator stress, we prefer intermittent high mechanical index imaging as shown in Figure 2. During dobutamine stress, however, we prefer low mechanical index imaging in order to simultaneously examine regional function, shown in the case discussed below. In addition to the rapid filling seen with dobutamine, we also see an appreciable increase in myocardial opacification because dobutamine increases myocardial blood volume. At low doses, dobutamine is a vasodilator, and at higher doses it recruits more capillaries to meet the increased myocardial oxygen needs. Lack of increase in myocardial opacification also indicates the presence of CAD. Similar to vasodilators, dobutamine can cause a decrease in myocardial blood volume distal to a stenosis, resulting in a perfusion defect. The decrease of blood volume occurs from capillary de-recruitment in an attempt to maintain a constant capillary hydrostatic pressure in the face of a decrease in perfusion pressure caused by hyperemia.

An 80-year-old woman was referred for dobutamine stress echocardiography because of atypical chest pain. She had left ventricular hypertrophy with generalized repolarization changes on the ECG. She under-
went both regional perfusion and regional function assessment using a constant infusion of Definity during low mechanical index, real-time MCE that allows simultaneous assessment of regional perfusion and function (at 20 Hz instead of the usual 30 Hz). The patient demonstrated no perfusion defect at rest (Figure 3A and Movie III), but developed a defect at a dose of 20 μg · kg⁻¹ · min⁻¹ at a time when wall motion was still normal (Figure 3B and Movie IV). At a dobutamine dose of 40 μg · kg⁻¹ · min⁻¹, both perfusion and function became abnormal (Figure 3C and Movie V). Note that the normal region shows increased myocardial opacification compared with baseline and lower dobutamine dose. Coronary angiography revealed a proximal left circumflex artery stenosis and a dominant left coronary system.

Because of the ischemic cascade, perfusion abnormalities precede wall motion abnormalities as shown above and therefore have a higher sensitivity both for the detection of CAD, as well as for identification of multivessel disease.

Conclusions
MCE is a rapid bedside method for assessing myocardial perfusion both at rest and stress. It has been performed safely in several thousand patients. As of yet there is no ultrasound contrast agent that has been approved for MCE by the US Food and Drug Administration. Most of the clinical experience gained has been in the research setting. Once ultrasound contrast agents are approved for MCE and reimbursement is determined, this modality should experience increased use in clinical cardiology.

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References

