Evaluation of Myocardial Perfusion by Means of Contrast Echocardiography

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Introduction

In 1980 DeMaria [4] reported that injection of an ultrasonic contrast medium in the left ventricle or the aorta causes an increase in echo intensity in the myocardium. He speculated that this observation might suggest a possibility of evaluating myocardial perfusion. Since this first report a number of experiments in laboratory animals have been performed with a variety of different ultrasonic contrast media. These studies have shown that reproducible demonstration of a myocardial perfusion defect is possible after total occlusion of a coronary vessel [2, 9–12, 22, 24, 27]. Attempts have been made to correlate the kinetics of the myocardial contrast effect with actual myocardial blood flow [13, 17, 25, 28, 29]. Myocardial contrast echocardiography is currently an interesting experimental method for evaluation of myocardial ischemia. Initial clinical studies have proven that the technique is well tolerated, and it is to be expected that myocardial contrast echocardiography will be performed in humans in the future [16, 20, 23].

Principles of Myocardial Contrast Echocardiography

The increase in myocardial echo intensity found after intracoronary or aortic injection of an ultrasonic contrast medium is caused by small air bubbles contained in the contrast medium [18]. Since the air bubbles measure 5–50 μm and are much smaller than the wavelength of the ultrasound beam, it is scattering rather than reflection of the ultrasound beam at the surface of the air bubbles which causes the contrast effect. Since the resolution of most conventional ultrasound systems ranges from 1 to 4 mm, one may assume that increased intensity of the contrast effect at a given location is not due to scattering from a single air bubble, but results from total scattering at this location. Increased echo intensity is found in the myocardium as long as the air bubbles remain stable, are not absorbed, or do not traverse the myocardial capillary bed.

A number of different ultrasonic contrast agents have been used for myocardial contrast studies. These include saline solution containing CO₂ [4], gelatin microspheres [1], a mixture of H₂O₂ and blood [12], hand-agitated glucose solutions [15], and a hand-agitated mixture of renographin and saline [27]. The ultrasonic contrast agents were successful in demonstrating myocardial perfusion defects, but proved unsuitable for evaluation of myocardial blood flow, since the
air bubbles in the solutions are too large to pass through the myocardial capillary bed [5]. In vivo studies using an optical microscope defined the average bubble diameter of gelatin microspheres at 76 μm, a mixture of H₂O₂ and blood at 50 μm, and a hand-agitated mixture of renographin and saline at 16 μm [1, 12, 28]. It should be noted that air bubbles may coalesce in vitro, resulting in larger bubble size. In one case air bubbles measuring 85 μm were found with H₂O₂. Studies in the capillary bed of the cat show that bubbles larger than 10 μm cause temporary obstruction of the microcirculation lasting a few seconds to several minutes, when the bubbles either shrink or collapse [5].

In our series a new ultrasonic contrast agent SHU 454 was used, since this agent is superior to other ultrasonic contrast media in reproducibility of the contrast effect [26]. Mean bubble size is 3.0 μm, and 95% are smaller than 7 μm. One may assume that the air bubbles pass unimpeded through the capillary bed. Sonication – preparation of a 70% sorbitol solution with ultrasonic energy – produces small air bubbles averaging 6 ± 2 μm diameter [26, 29].

**Side Effects of Ultrasonic Contrast Agents**

Studies of the hemodynamic and morphological effects of ultrasonic contrast agents have varied widely. It has been shown that injection into the coronary arteries or the aortic root results in slight hemodynamic changes of short duration. Gelatin microspheres, a mixture of H₂O₂ and blood, and the mixture of renographin and saline cause a slight decrease in aortic pressure [1, 12, 13, 27]. Highly concentrated glucose solutions and SHU 454 result in increased myocardial blood flow [15, 25], which was attributed to the high osmolality of the solutions rather than to the air bubbles themselves. It is conceivable that the air bubbles might cause ischemia, which is followed by an increase in blood flow. However, there were no characteristic changes in hemodynamic variables such as left ventricular diastolic pressure as possible signs of ischemia after injection of ultrasonic contrast agents. Temporary T-wave flattening or ST-segment depression was observed in the electrocardiogram with almost all ultrasonic contrast agents. An increase in ventricular premature beats was reported after administration of high concentrations of H₂O₂ [12]. Gilliam et al. [8] observed temporary disorders of regional wall motion after intracoronary injection of a solution containing renographin and saline. We recorded no changes in regional wall motion after injection of SHU 454 into the coronary artery. Kondo et al. [15] did not observe disorders of regional wall motion after injection of 50% glucose and 30% renographin solutions.

Histologic studies with the optical microscope failed to demonstrate morphological changes in the heart after arterial administration of SHU 454 and a mixture of renographin and saline [8, 25]. Santoso et al. [23] injected hand-agitated Haemaccel with average bubble size of 12 μm and found no increase in cardiac enzymes in 16 patients.