Contrast Echocardiography. Does it Have a Future?

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In the past thirty years echocardiography has revolutionized cardiologic investigation. The non-invasive access to anatomy, physiology, and heart diseases has become increasingly broader. Since the introduction of the M-mode technique and, progressively, of two-dimensional echocardiography, Doppler, color flow mapping, transesophageal echocardiogram, and use of physical or pharmacologic stress, different methodologies have been added in pursuit of the optimization of cardiac assessment using ultrasound, and all of them have become consolidated in the clinical practice. Among the most recent techniques, real-time 3D echocardiography, assessment of ventricular function with tissue Doppler and strain-strain rate, and the use of contrast can be pointed out.

Actually, the pursuit of contrast echocardiograms is not novel and has progressed slowly. In 1968, at the beginning of the history of echocardiography, in tests performed during cardiac catheterization, the injection of liquids in the cardiovascular system was observed to allow the formation of small bubbles that produced a cloud of echoes[1]. These bubbles, however, had large diameters in relation to the microcirculation, and could not pass through pulmonary capillaries, a fact that limited their use to a few clinical applications. In 1984, with the use of microbubbles with diameter lower than 10μ, the pulmonary capillary barrier was crossed and the left cavities could be opacified with sonicated albumin[2]. In the 1990's, countless studies on the development of contrast agents and technological advances in equipment were conducted, which made detailed assessments of the left cavities possible, and the expected investigation of the coronary artery circulation became closer to fullfilment[3-7].

Research on contrast agents have aimed at obtaining an agent with microbubbles able to pass through capillaries with the least diameter possible, with a long-lasting stability, acoustic impedance different from that of tissues, higher concentration, low toxicity, and rapid metabolism and excretion[8]. With these purposes, we can interfere with: (1) the size of the microbubbles, (2) the gas that fills them, and (3) the substance that forms their outer layer. As regards the size, microbubbles should be smaller than 10μ; however, within this range the largest bubbles are more stable. Gases are preferably heavy, inert and not very soluble, whereas albumin, phospholipid, carbohydrate, or biopolymer capsules enable a higher stabilization[6,9]. First-generation contrast agents are represented by Albunex™ (air filled microbubbles and sonicated albumin in the outer layer), and by Levovist™ (air filled and galactose with traces of palmitic acid in the outer layer).

In the second generation, the gas medium was replaced by fluorcarbon gases, providing the compounds with more stability. Its main representative is PESDA (Perfluorocarbon-Exposed Sonicated Dextrose Albumin)[4], a non-processed product prepared in a hospital environment, to be used within 24 hours. It is injected in bolus or continuous infusion, has a low cost in comparison with other agents, and is the most widely used contrast agent in Brazil.

Other contrast agents of this generation are Optison™[10] and Definity™, the latter being recently marketed in Brazil[11]. SonoVue™, an agent containing phospholipid and sulphur hexafluoride – the first to be authorized in Europe for the assessment of myocardial perfusion, should also be pointed out. Several other products are being studied at the clinical development phase, and some are considered third-generation contrast agents[12].

In relation to technological advances of equipment mainly aimed at the optimization of contrast examinations, we should point out the types of imaging provided by ultrasound and the mechanical index applied to the responses from microbubbles. As regards some types of imaging, second harmonic, Doppler harmonic, ultra-harmonic or third harmonic, Power Doppler harmonic, and pulse inversion imaging (real-time imaging) have been developed. All these techniques aim at improving the imaging obtained both from tissues, by means of two-dimensional echocardiogram, and from microbubbles reflecting the contrasted area. The mechanical index regulates the amount of ultrasonic energy transmitted, determining the degree of microbubble destruction. It may range from 0.1 to 1.0; lower indexes (0.1-0.3) with little bubble destruction are preferable for perfusion studies, and indexes between 0.4-0.8 for a better definition of

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endocardial borders.

With such advances, how does the clinical application of contrast echocardiography stand? Its use in the improvement of definition of endocardial borders is well-established and has been applied in studies at rest and stress with a significant contribution to the optimization of imaging. The major challenge, however, is related to the use of contrast echocardiography in coronary artery disease, with myocardial perfusion studies that focus on aspects of the anatomical and functional diagnosis in the chronic disease, contribution in acute coronary syndromes, assessment of myocardial viability and prognostic factors. In the United States, the Food and Drug Administration (FDA) has authorized microbubbles only to improve the definition of the borders, but not for the assessment of myocardial perfusion up to the moment. This restriction certainly discourages the practical development of the methodology. In Europe, in turn, the use of SonoVue™ is also allowed for myocardial perfusion studies, which brings forward a broader dissemination of this technology in that continent.

In Brazil we face the difficulties of high costs of commercially available contrast agents and payment restrictions on the part of health management organizations, since the procedure is not included in the old price tables, and the new Brazilian Hierarchical Classification of Medical Procedures has been slowly adopted by HMOs. As regards scientific research, technology has been widely applied in different approaches on coronary artery disease[15-18] with fully satisfactory results.

Wei et al[19] study compared the usefulness of dipyridamole stress PB 127 myocardial contrast echocardiography with SPECT under similar conditions, and verified that the consonance for classification of patients as normal versus abnormal was 84%.

After exclusion of false-negative SPECT scans consonance increased to 93%, leading to the conclusion that myocardial perfusion study using contrast echocardiography was very satisfactory for the detection of coronary artery disease. Additionally, the utilization of new computer software has allowed the quantification of contrast flow in the myocardium, which increases the diagnostic accuracy of the method and reduces the variability between observers[20].

In conclusion, contrast echocardiography is perceived as a non-invasive method with no ionizing radiation that provides information on anatomy and microcirculation and is readily available at bedside. It allows quick results, with a good cost-benefit ratio, so its use in the clinical practice both to enhance definition of cavity borders and to study myocardial perfusion is supported by repeated scientific investigations. For all these reasons, we believe that the method undoubtedly has a future.

Potencial Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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