JACC: CARDIOVASCULAR IMAGING VOL. 3, NO. 2, 2010

ISSN 1936-878X/10/$36.00
PUBLISHED BY ELSEVIER INC. DOI:10.1016/j.jcmg.2009.12.006

iVIEW

EDITOR'S PAGE

Contrast Echocardiography: Over-Achievement in Research, Under-Achievement in Practice?

Thomas H. Marwick, MD, PhD,* Jagat Narula, MD, PhD†

This issue of *iJACC* focuses on the topic of contrast echocardiography. Starting more than 25 years ago, work with intracoronary injections demonstrated collateral flow, no-reflow, and the importance of the pre-capillary arterioles to coronary physiology (1). The development of transpulmonary agents allowed contrast echocardiography to be used for the noninvasive assessment of myocardial perfusion initially using high- and subsequently low-mechanical index using destruction/replacement imaging. The quantitation of ultrasound microbubbles, which are intravascular tracers, has taught us lessons regarding myocardial blood flow velocity and myocardial blood volume.

Left ventricular (LV) opacification (2) is the main approved indication for transpulmonary contrast agents. The use of these agents has expanded the reach of echocardiography into situations where it was previously compromised by image quality, including severe obesity, pulmonary disease, ventilated patients, and chest wall problems. Even in patients where noncontrast imaging is less challenging, apical pathology such as thrombi, apical hypertrophic cardiomyopathy, and noncompaction are more readily identified with contrast agents. Noncontrast echocardiography underestimates LV volumes by 30% to 40% and ejection fraction by 3% to 6%, both of which may have material impact on decisions in patients with valvular disease or heart failure under evaluation for device therapy. These findings have an important clinical impact in decision making, and even in medically managed patients, the accurate assessment of LV remodeling has been shown to be linked to outcome (3). In a randomized controlled trial, the use of contrast during stress echocardiography improved the sensitivity and specificity of the technique (4). These findings add to an existing literature regarding improvements in the feasibility and reliability of wall motion scoring. The cost-effectiveness of this technique has been identified in studies demonstrating a reduction of downstream use of other imaging modalities, as well as studies documenting the benefits of improved accuracy of stress echocardiography (5,6). In the context of this evidence base, the ongoing lack of clinical uptake of contrast echocardiography is truly striking. Despite the fact that approximately 10% of echocardiograms are to some extent uninterpretable, the use of LV opacification remains <1%. A number of challenges are still posed for the echocardiographic community regarding the use of contrast, including needs for training, regulatory issues allowing sonographers to inject agents, and appropriate benchmarking of contrast use.

The use of myocardial contrast for the assessment of perfusion remains one of the holy grails of echocardiography (7). Currently, no contrast agent is approved for this indication. The potential applications of an echocardiographic tool for the assessment of myocardial perfusion are extensive, including during stress echocardiography for ischemia, assessment of viability, and the evaluation of myocardial perfusion in patients in the emergency department. Nonetheless, there is good evidence that the combination of contrast perfusion during stress echocardiography improves accuracy and the evaluation of prognosis (8). In the assessment of viable myocardium, the extent of contrast defects is proportionate to outcome in acute myocardial infarction, and in patients with

From the *Cleveland Clinic, Cleveland, Ohio; and the †University of California-Irvine, Irvine, California. Dr. Marwick has received grant support from GE Medical Systems, Siemens, Philips, and Lantheus Medical Imaging.

chronic LV dysfunction, the use of contrast perfusion may identify flow in segments lacking contractile reserve. Nonetheless, quantitation remains difficult with this modality. Barriers include attenuation, signal from tissue, and incomplete bubble destruction. Some investigators have used the intracavitary signal to minimize the plateau intensity for absolute estimation of myocardial blood flow, but this has not reached general use. Even the subjective evaluation of myocardial perfusion using contrast echocardiography is difficult, with problems related to attenuation, lung and rib shadowing, apical bubble distraction, and the lack of an approved indication.

A specific indication of contrast echocardiography is its place in the emergency department (9). The current clinical tools for the assessment of patients presenting with chest pain, including the historical evaluation of pain and electrocardiography, are limited, and particularly so in the context of 70% to 90% of patients presenting with chest pain symptoms eventually lacking a cardiac diagnosis. This field is a source of inappropriate expenditure in patients being unnecessarily admitted to hospitals, as well as medicolegal liability when the diagnosis of coronary disease is missed. Possibly as a consequence, there are now multiple competing modalities for this indication, including single-photon emission computed tomography, computed tomography, magnetic resonance imaging, and various types of stress testing. In this setting, the role of contrast echocardiography is unclear, given the technical challenges of acquisition. However, when these logistic issues can be addressed, the evidence indicates that the outcomes with using contrast echocardiography for evaluation of these patients is similar to that obtainable with single-photon emission computed tomography.

Despite all of this work, the future of contrast echocardiography is unclear. Although the indications for LV opacification should clearly grow, driven by the combination of contrast with 3-dimensional echocardiography (10), the reality is that contrast has been difficult to incorporate into the workflow of many echocardiography laboratories. Likewise, the combination of bioengineering of molecular probes with myocardial contrast delivery would enable targeted therapies to be directed towards ischemia and transplant rejection (11). However, the difficulties experienced with obtaining a U.S. Food and Drug Administration approved indication for perfusion, now unsuccessful after a number of attempts, are an ongoing source of concern regarding the long-term viability of this modality.

Address for correspondence:
Jagat Narula, MD, PhD
Editor-in-Chief, *JACC: Cardiovascular Imaging*
3655 Nobel Drive, Suite 630
San Diego, California 92112
E-mail: narula@uci.edu

REFERENCES

1. Kaul S. Myocardial contrast echocardiography: a wondrous journey! J Am Coll Cardiol Img 2010;3:212–8.
2. Chahal NS, Senior R. Clinical applications of left ventricular opacification. J Am Coll Cardiol Img 2010;3:188–96.
3. Dwivedi G, Janardhanan R, Hayat SA, Lim TK, Senior R. Improved prediction of outcome by contrast echocardiography determined left ventricular remodelling parameters compared to unenhanced echocardiography in patients following acute myocardial infarction. Eur J Echocardiogr 2009;10:933–40.
4. Plana JC, Mikati IA, Dokainish H, et al. A randomized cross-over study for evaluation of the effect of image optimization with contrast on the diagnostic accuracy of dobutamine echocardiography in coronary artery disease: the OPTIMIZE trial. J Am Coll Cardiol Img 2008;1:145–52.
5. Kurt M, Shaikh KA, Peterson L, et al. Impact of contrast echocardiography on evaluation of ventricular function and clinical management in a large prospective cohort. J Am Coll Cardiol 2009;53:802–10.
6. Moir S, Shaw L, Haluska B, Jenkins C, Marwick TH. Left ventricular opacification for the diagnosis of coronary artery disease with stress echocardiography: an angiographic study of incremental benefit and cost-effectiveness. Am Heart J 2007;154:510–8.
7. Porter TR, Xie F. Myocardial perfusion imaging with contrast ultrasound. J Am Coll Cardiol Img 2010;3:176–87.
8. Dolan MS, Gala SS, Dodla S, et al. Safety and efficacy of commercially available ultrasound contrast agents for rest and stress echocardiography: a multicenter experience. J Am Coll Cardiol 2009;53:32–8.
9. Wei K. Utility contrast echocardiography in the emergency department. J Am Coll Cardiol Img 2010;3:197–203.
10. Jenkins C, Moir S, Chan J, Rakhit D, Haluska B, Marwick TH. Left ventricular volume measurement with echocardiography: a comparison of left ventricular opacification, three-dimensional echocardiography, or both with magnetic resonance imaging. Eur Heart J 2009;30:98–106.
11. Lindner JR. Molecular imaging of myocardial and vascular disorders with ultrasound. J Am Coll Cardiol Img 2010;3:204–11.