Clinical Applications of Ultrasonic Enhancing Agents in Echocardiography: 2018 American Society of Echocardiography Guidelines Update

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This document is endorsed by the following American Society of Echocardiography International Alliance Partners: the Argentinian Federation of Cardiology, the British Society of Echocardiography, the Canadian Society of Echocardiography, the Chinese Society of Echocardiography, the Echocardiography Section of the Cuban Society of Cardiology, the Indian Academy of Echocardiography, the Indian Association of Cardiovascular Thoracic Anaesthesiologists, the Iranian Society of Echocardiography, the Japanese Society of Echocardiography, the Korean Society of Echocardiography, the Saudi Arabian Society of Echocardiography, and the Vietnamese Society of Echocardiography.

Keywords: Echocardiography, Contrast, Guidelines, Imaging

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The following authors reported no actual or potential conflicts of interest in relation to this document: Sahar S. Abdelmoneim, MBBCH, MSc, MS, FASE, Michelle Bierig, MPH, ACS, RDCS, FASE, Linda D. Gillam, MD, FASE, Shelby Kutty, MD, PhD, MHCM, FASE, Wilson Mathias, Jr., MD, and Flordeliza Villanueva, MD. The following authors reported relationships with one or more commercial interests: Thomas R. Porter, MD, FASE, has received educational support from Bracco Imaging and is a speaker at Bracco Imaging educational programs. He has received prior grant support from Lantheus Medical and GE Healthcare. He has received equipment support from Philips Healthcare. Sharon L. Mulvagh, MD, FASE, has served as a consultant for Bracco Diagnostics and has received investigator-initiated research grants from GE Healthcare, Lantheus Medical Imaging, and Bracco Diagnostics. Harald Becher, MD, PhD, has received research support (software), a research grant, and an honorarium for satellite symposia and courses from Bracco and research support (software) from Siemens and Philips. J. Todd Belcik, BS, ACS, RDCS, FASE, has presented talks on behalf of Bracco. Jonathan Choy, MD, MBA, FASE, has served as a course director and speaker and has received an unrestricted educational grant from Philips Healthcare, has served as a consultant for Bracco Imaging, and was on the advisory board for Aspen Canada. Nicola Gaibazzi, MD, PhD, has served as a lecturer and consultant and has participated in sponsored studies for Bracco Imaging. Rajesh Janardhanan MD, MRCP, FASE, has served on the speakers bureau for Lantheus. Howard Leong-Poi, MD, FASE, has served on the speakers bureau for Lantheus and as a site investigator for a clinical trial run for Bracco Imaging. Jonathan R. Lindner, MD, FASE, has received an investigator-initiated grant from GE Healthcare. Michael L. Main, MD, FASE, has received research grants from Bracco Imaging and Boston Scientific and has served as a consultant for Boston Scientific. Margaret M. Park, BS, ACS, RDCS, RVT, FASE, has served on the speakers bureau for Lantheus Medical and was a Sonographer Contrast Task Force member for Bracco Imaging. Roxy Senior, MD, DM, has received speaking fees from Philips Healthcare, Bracco Imaging, and Lantheus Medical Imaging.

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0894-7317/$36.00

https://doi.org/10.1016/j.echo.2017.11.013

Abbreviations

2D = Two-dimensional
3D = Three-dimensional
ASE = American Society of Echocardiography
CAD = Coronary artery disease
CHD = Congenital heart disease
CMRI = Cardiac magnetic resonance imaging
COR = Class of recommendation
CPT = Current Procedural Terminology
CT = Computed tomography
DSE = Dobutamine stress echocardiography
DUS = Diagnostic ultrasound
ECG = Electrocardiography
ED = Emergency department
FDA = US Food and Drug Administration
ICU = Intensive care unit
IV = Intravenous
LOE = Level of evidence
LV = Left ventricular
LVEF = Left ventricular ejection fraction
LVO = Left ventricular opacification
MBV = Microvascular blood volume
MCE = Myocardial contrast echocardiography
MI = Mechanical index
MP = Myocardial perfusion
OR = Odds ratio
PAD = Peripheral arterial disease
RCT = Randomized controlled trial
RTMCE = Real-time myocardial contrast echocardiography
RWM = Regional wall motion
SPECT = Single-photon emission computed tomography
STEMI = ST-segment elevation myocardial infarction
TEE = Transesophageal echocardiography
TTE = Transthoracic echocardiography
UEA = Ultrasound enhancing agent
UTMD = Ultrasound-targeted microbubble destruction
VLMI = Very low mechanical index

I. INTRODUCTION

The use of ultrasound enhancing agents (UEAs) has become an integral component of echocardiography practice. Since the 2008 American Society of Echocardiography (ASE) consensus statement on clinical applications of ultrasound contrast agents,[1] there have been several important developments that require the document be revised into a guidelines paper.

1. The term *ultrasound contrast agents*, describing a class of products comprising microbubbles to enhance ultrasound signals,[2-5] was replaced with the less conflicting term *ultrasound enhancing agent*. Although the Writing Group understands the need for this terminology in helping patients and referring physicians distinguish these substances from iodinated contrast agents or gadolinium chelates, it was considered equally acceptable to refer to these agents as contrast agents and the imaging techniques as contrast echocardiography or myocardial contrast echocardiography (MCE).
2. The Intersocietal Accreditation Commission has required that policies be in place for UEA use (section 1.6.2.4B, updated June 1, 2017) in specific clinical settings in which UEAs are required.[6]
3. The safety of UEAs has been documented in several different clinical scenarios (stress echocardiography, pulmonary hypertension, intracardiac shunting) as well as in emergency department (ED), critical care, and pediatric settings.[5] Propensity-matched studies have not only documented safety but also demonstrated the potential value and importance of early UEA use in improving patient outcomes (Table 1). These large single- and multicenter studies have led to changes in the US Food and Drug Administration (FDA) boxed warnings regarding UEA use in pulmonary hypertension, critical care settings, and more recently, known or suspected right-to-left shunts.
4. Numerous clinical trials have demonstrated the safety and efficacy of UEAs in new stress echocardiography settings (dipyridamole, adenosine, regadenoson, bicycle, and treadmill), as well as in different resting conditions in which regional wall motion (RWM) and perfusion information provide significant incremental value in predicting patient outcomes (Table 2).
5. The use of myocardial perfusion (MP) imaging with UEAs has increased, specifically in the setting of stress echocardiography, chest pain evaluation in the ED, and in the evaluation of intracardiac masses.[25,34,35] The American Medical Association Current Procedural Terminology (CPT) Panel approved a category III ("emerging technology") CPT code (+0439T) for "myocardial contrast perfusion echocardiography; at rest or with stress, for assessment of myocardial ischemia or viability" (effective July 1, 2016) for the use of perfusion imaging as an add-on to the following base CPT codes: 93306, 93307, 93308, 93350, and 93351. Although this category III code is not reimbursed by the Centers for Medicare and Medicaid Services in the United States, approval of this code acknowledges the significant incremental value of MP with UEAs in several clinical settings.