American Society of Echocardiography Guidelines and Recommendations for Contrast Echocardiography: A Summary for Applications Approved by the U.S. Food and Drug Administration

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The American Society of Echocardiography published a Guideline document on the clinical applications of contrast agents (also termed "ultrasound enhancing agents [UEAs]) in echocardiography in 2018.[1] This document represented a comprehensive update of the original Consensus Statement on the use of ultrasound contrast agents published in 2008,[2] and of the Guidelines for use of contrast echocardiography for cardiac sonographers published in 2014. These guidelines provide information on the entire scope of use of UEAs in cardiovascular ultrasound, with the intent to be inclusive of all applications where contrast has been shown to improve diagnostic accuracy, patient care, or cost-effectiveness. The current document provides a summary of recommendations for use and best practices extracted from these documents for left-ventricular cavity opacification (LVO) which is the primary on-label cardiovascular application for ultrasound contrast. All recommendations in this document satisfy the following criteria: (i) they conform to the indications and dosing approved by the United States Food and Drug Administration (FDA); (ii) have been judged by expert consensus to have a recommendation grade of Class I (strong) or Class II (moderate); and (iii) have a level of evidence grade that is based on moderate to high-quality evidence from well-designed randomized or non-randomized trials.

Contrast Agents

Commercially-available UEAs that are approved for use by the United States FDA are composed of encapsulated microbubbles.[4-6] The use of microbubbles as UEAs is based on their ability to undergo volumetric oscillation (compression and expansion) in the pressure fluctuations of the ultrasound field.[7,8] Microbubble vibration can occur without compromise of its integrity (stable cavitation), or can be accompanied by either sudden or gradual destruction from exaggerated non-linear oscillation (inertial cavitation) which occurs when ultrasound is delivered at high ultrasound pressure amplitude and close to the ideal resonant frequency for microbubbles. Inertial cavitation or non-linear stable cavitation produce a strong acoustic signature that can be separated from tissue with specially-designed and commercially available imaging protocols.[3,7]

There are currently three UEAs (**Table 1**) approved by the United States FDA for LVO during echocardiography in order to better define the blood pool and the endocardial borders. These microbubbles share some common properties. They all contain an inert bio-compatible high-molecular weight gas, and are encapsulated with a lipid or protein shell. Optison (perflutren protein-type A microspheres, GE Healthcare, Marlborough, MA) is composed of octafluoropropane contained within a shell of denatured human serum albumin.[4] Definity (perflutren lipid microspheres, Lantheus Medical Imaging, North Billerica, MA) is composed of octafluoropropane contained within a lipid monolayer, the primary component of which is a phospholipid with a hydrocarbon tail oriented inward and a polar group oriented outward. Lumason (sulfur hexafluoride lipid-type A microspheres, Bracco Diagnostics, Princeton, NJ) also is contained within lipid monolayer but contains a sulfur

TABLE 1 – COMMERCIALLY AVAILABLE UEAS APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION

Name	Manufacturer/vial contents	Mean diameter	Shell	Gas	Contraindications
Lumason (sulfur hexafluoride lipid-type A microspheres)	Bracco Diagnostics, 5 mL	1.5–2.5 μm (maximum 20 μm, 99% ≤10 μm)	Phospholipid	Sulfur Hexafluoride	Allergy to sulfur hexafluoride
Definity (perflutren lipid microsphere)	Lantheus Medical Imaging, 1.5 mL	1.1–3.3 μm (maximum 20 μm, 98% ≤10 μm)	Phospholipid	Perflutren	Allergy to perflutren
Optison (perflutren protein type-A microspheres)	GE Healthcare, 3.0 mL	3.0–4.5 μm (maximum 32 μm, 95% ≤10 μm	Human albumin	Perflutren	Allergy to perflutren/ blood products

hexafluoride gas. The use of high molecular weight gases with relatively low solubility and diffusivity limits the outward diffusion of gas from its core, thereby improving stability after intravenous injection.[9] Encapsulation not only reduces outward gas diffusion, but also serves in many cases to reduce surface tension. This latter feature enhances the production and stability of microbubbles that are relatively uniform in size and sufficiently small (<6 μm) to pass unimpeded through the pulmonary and systemic capillary beds.[2,10]

All of the commercially-available UEAs are approved for use only with intravenous injection. There are differences between agents in terms of storage conditions, shelf life, and methods for pre-injection preparation which include hand agitation (Optison), addition of saline and hand agitation (Lumason), and mechanical agitation (Definity).

Key Points:

1. The only FDA-approved use in cardiovascular disease is for LVO using IV injections.
2. All commercially-produced UEAs (Optison, Definity, Lumason) are encapsulated with albumin or lipid, and contain safe high-molecular weight gas.
3. UEAs have a range of average size between 1.1 and 4.5 μm, thereby allowing them to pass unimpeded through the pulmonary and systemic microcirculation.
4. There are agent-related differences in storage and pre-administration preparation protocols.

Recommendations for Imaging of UEAs

The signals generated by UEAs are dependent on the acoustic pressure and the frequency of the transmitted ultrasound, which commonly is reflected by the mechanic index (MI) displayed on imaging systems and calculated by dividing the peak negative acoustic pressure amplitude by the square root of the centerline transmission frequency.[7,8] At conventional frequencies used during echocardiography, low MI (0.05-0.2) imaging can produce stable cavitation with oscillations that are asymmetric and non-linear in terms of their relationship with pressure.[11] At higher MIs, microbubble shell integrity is compromised from exaggerated oscillation and gas loss. This response results in reproducible and rapid destruction of microbubbles at MI>0.5. Contrast-specific imaging methods have been developed for both high-MI and low-MI imaging that rely on detecting non-linear microbubble signals, and have been extensively reviewed elsewhere.[3,7]

The use of UEAs for LVO ordinarily involves the continuous observation of contrast enhancement throughout the cardiac cycle, which requires imaging at MIs that do not rapidly compromise microbubble integrity. Accordingly, low-MI contrast-specific imaging algorithms are now routinely used when performing contrast echocardiography. In general, imaging at MI 0.2-0.5 will produce non-linear acoustic signals that are strong enough to allow simple contrast-specific imaging algorithms that rely on filtering to detect harmonic frequencies (multiples of the transmit frequency).[1,11] However, continuous high-frame rate imaging at these MIs can sometimes produce microbubble destruction, which often results in swirling artifacts especially in the near-field. Imaging at MI ≤0.2 largely avoids microbubble destruction, but the non-linear signals received are not strong. Therefore, multi-pulse algorithms including power-modulation, pulse-inversion, or combinations thereof are used to increase signal-to-noise by efficiently eliminating almost all background tissue signal.[2,7,12]

The dosing parameters for UEAs vary according to agent. Bolus injections by hand of UEAs followed by a saline flush are approved for all agents. Bolus injections are the most simple in terms of pre-injection preparation. Disadvantages of bolus injections are that microbubble concentration is not constant over time and there can be severe attenuation or shadowing of far-field structures caused by high instantaneous contrast agent density. Continuous infusions of UEAs are also approved for use with Definity. This approach has the disadvantage of requiring infusion pumps, extension tubing, and more preparation time. However, this approach provides the benefit of stable and consistent UEA concentrations, and avoids the need to interrupt scanning for repetitive bolus administration.

There are practical approaches for optimizing contrast-enhanced images for LVO beyond the use of contrast-specific presets that increase signal-to-noise ratio. While the MI reflects the transducer output, the actual acoustic pressures within the body will vary according to anatomic considerations. For example, the MI may need to be increased for patients who are large or have significant lung attenuation. With regards to artifacts encountered during LVO, swirling or lack of contrast particularly at the left ventricular (LV) apex when imaging from apical views can occur from near-field destruction of UEAs. This artifact can be addressed by lowering the MI, switching to multi-pulse algorithms that are more effective at low MI, and adjusting the acoustic focus to the near-field. Attenuation caused by high concentrations of microbubbles can be addressed not only by reducing contrast dose, but also by several seconds of high MI (0.8-1.2) imaging to “clear” contrast through inertial cavitation. For multi-pulse techniques used with low MI imaging, far-field attenuation tends to be least with modalities that use power—or amplitude—modulation since they rely on imaging at the fundamental rather than higher harmonic frequencies and, therefore, are less susceptible to attenuation. Inability to view segments due to rib attenuation can be addressed by adjusting the imaging plane to focus on a single wall or segment. With high blood pool concentration of contrast or with techniques with high signal-to-noise ratio, opacification of the myocardium itself can occur from contrast residing within the myocardial microcirculation, thereby impairing the discrimination between endocardium and LV cavity. This problem can be addressed by a brief (5 to 15 frames) application of high-MI imaging, sometimes called flash impulses, which reduces tissue signal relative to cavity.[1]

Key Points:

1. Manufacturers should provide users with information on the contrast-specific algorithms employed on their systems and how to readily access them.
2. Imaging system presets for UEAs should be considered a "starting point;" users should be familiar with changes in system settings that are likely to improve image quality and reduce artifacts for individual patients.

Recommendations for Imaging:

1. Low-MI imaging, including the use of non-linear and multi-pulse detection methods with or without brief high-MI flash impulses, should be used to image UEAs during assessment of regional and global LV function.
2. Contrast agents can be given by bolus injection; certain agents can be administered by continuous infusion.
3. Imagers should become familiar with common artifacts when imaging UEAs and approaches used to minimize their impact on image quality.

Clinical Applications for LV Volumes, LVEF, and Regional Wall Motion

All three UEAs commercially available for LVO have been evaluated in multicenter trials with regards to their ability to improve the identification of the left ventricular borders for assessment of LV systolic function and regional wall motion. The sections below represent a summary of recommendations from the 2018 update of guidelines for the clinical application of UEAs in resting echocardiography.

LV Volumes. According to the American Society of Echocardiography and European Association of Cardiovascular Imaging guidelines for LV chamber quantification, volumetric measurements should be based on tracing the interface of the compacted myocardium and the LV cavity, excluding the LV trabeculae.[13] The use of UEAs is recommended when accurate dimensions and volumes cannot be readily obtained because of the poor quality of endocardial visualization. Unenhanced two dimensional (2D) echocardiography may underestimate LV volumes not only because of inadequate visualization, but also because of foreshortening and exclusion of the portion of the LV within non-compacted trabecular surfaces. Use of UEAs may overcome these technical errors by allowing the true longitudinal axis of the left ventricle to be measured, as well as enabling accurate tracing of endocardial borders by detection of intra-trabecular blood volume, and clear delineation of the endocardial border. End-diastolic volume measurements determined by enhanced echocardiography have been shown to be significantly larger than those without UEAs, irrespective of 2D or 3D echocardiographic techniques.[14-17] The use of UEAs has been shown to provide greater accuracy and closer correlation with cardiac magnetic resonance imaging (CMR), and to avoid systematic underestimation of LV volumes measured with unenhanced echocardiography compared to CMR.[14,18] It should be mentioned that differences in the normal range of LV volumes for contrast versus unenhanced echocardiography have not been established.

LV Ejection Fraction. The quantitative assessment of LVEF becomes particularly important when patients are considered for a defibrillator or cardiac resynchronization therapy, when patients are monitored for the effects of potentially cardiotoxic medications (i.e. chemotherapeutic agents), or in patients with valve disease who are being evaluated for intervention (e.g., aortic and mitral regurgitation). In these circumstances, accuracy and reproducibility are of critical importance. Many studies have demonstrated that the use of UEAs can increase the accuracy of LVEF measurements, including when compared with CMR.[14,15,17,18] Multicenter studies have confirmed that inter-observer variability is significantly reduced with UEAs, resulting in similar intraclass correlation coefficients when compared with CMR.[14,15] Although unenhanced three dimensional (3D) echocardiography has improved the reproducibility and reliability of serial measurement of LVEF, the use of UEAs has not yet been shown to further improve 3D echocardiography test-retest variability,[19] although this may be related to the fact that optimization of 3D contrast imaging and integration with volumetric analysis software is at an early stage.

Regional Wall Motion. Analysis of regional wall motion at rest is subject to significant inter-observer variability. Inherently, wall motion is a subjective assessment without a gold standard, and is in part dependent on image quality, highlighting the importance of being able to accurately detect the endocardium throughout ventricular systole. It is also important to note that visual wall motion assessment relies on evaluation of wall thickening, and thus both the endocardium and epicardium must be identified. A multicenter study has demonstrated that inter-observer agreement for regional wall motion was highest in patients who underwent enhanced echocardiography compared to both unenhanced echocardiography and CMR.[20] UEAs also significantly improve the agreement for regional wall motion when compared to CMR.[14] While UEAs are not recommended when the heart cannot be imaged because of chest deformity or lung hyper-expansion, they should be utilized for regional wall motion analysis whenever views can be obtained but endocardial border delineation is inadequate for interpretation based on their ability to increase diagnostic yield.[21]

Critical Care and Emergency Department Settings. Echocardiography is frequently technically difficult in intensive care unit (ICU) patients based on patient-related factors including mechanical ventilation, wound dressings,

and difficulty in patient positioning; underscoring the particular need for UEAs in this patient population. Because of the need to establish safety of UEAs in critically-ill patients in the ICU, propensity-matched studies in critically-ill patients who underwent TTE have shown either no difference in short-term mortality between patients undergoing echocardiography with versus without UEA, or a significantly lower mortality in those receiving UEAs.[22,23] While there is no direct evidence that UEAs played a causative role in the mortality difference in one of the trials, it is possible that earlier and more accurate diagnostic testing in these critically ill patients resulted in earlier provision of life-saving medical therapy. With regards to clinical impact, the use of UEAs in a select group of ICU patients with poor acoustic windows has been shown to reduce the likelihood for echocardiography to be judged as technically difficult by almost 90%, and converts non-diagnostic studies to diagnostic in virtually all of the studied patients.[24] Accordingly, there was a significant management change (avoidance of downstream diagnostic testing, an important medication change, or both) in over 1/3 of patients. Although there were many benefits of using UEAs in these critical care studies, the primary benefit was improving regional and global LV systolic function analysis.

UEAs have also been used to improve care in patients presenting to the emergency department (ED) with chest pain. Most of these patients do not manifest electrocardiographic ST-segment elevation, and many patients with acute myocardial infarction do not describe typical angina-quality chest discomfort.[25] Additionally, conventional cardiac biomarker assessment has low sensitivity for detection of myocardial necrosis in the early hours of acute myocardial infarction. Given these limitations, echocardiographic assessment of global and regional wall motion has been suggested as an adjunct to the traditional evaluation of patients presenting to the ED with suspected myocardial ischemia.[26] The use of UEAs for assessing regional function has been shown to enhance the diagnosis of ischemic heart disease in patients presenting to the ED with chest pain, and to provide important prognostic information.[27] There is also evidence that the use of echocardiography with UEAs is cost-effective in patients presenting to the ED based on the low event rate in patients with normal studies who can be safely dismissed directly from the ED.[28]

Recommendations for Imaging:

1. For routine resting echocardiographic studies, UEAs should be used when two or more LV segments cannot be visualized adequately for the assessment of LV function (LVEF or regional assessment), and/or in settings in which the study indication requires accurate analysis of regional wall motion.
2. Contrast echocardiography should be used in all patients in whom quantitative assessment of LVEF is important to prognosis or management of the clinical condition.
3. LV volumes obtained during contrast echocardiography are typically larger than those measured without UEAs, and therefore chamber quantification guidelines should be applied with caution when applying normal ranges. The normal range for LVEF does not appear to be different.
4. UEAs are recommended in all technically difficult ICU and ED patients to more quickly and accurately diagnose potentially life-threatening conditions and to reduce the need for downstream diagnostic testing. Contrast echocardiography should not be withheld on the basis of any particular diagnosis or co-morbidity.
5. In patients presenting to the ED with suspected myocardial ischemia and non-diagnostic ECG, regional function assessment with UEAs adds incremental diagnostic and prognostic value over traditional clinical and ECG evaluation.

Detection of Intracardiac Abnormalities

The clinical utility of UEAs for LVO extends beyond the visualization of endocardial borders and the assessment of LV volumes and LV systolic function. The opacification of the LV cavity also allows the detection, characterization, and diagnosis of intracardiac abnormalities such as masses (**Figure 1**) and conditions that influence the shape and contour of the LV. It is worth noting that many of these applications are designed to overcome limitations imaging the apex that arise from near-field clutter artifacts.

Intracardiac Thrombi. Intracardiac thrombi pose serious clinical risks with regards to systemic embolization. Likewise, treatment with antithrombotic agents can also impose significant risk, and their use must be appropriately justified. Therefore, accurate detection and diagnostic management of cardiac thrombi is essential. Despite advances in other imaging modalities, echocardiography remains the initial tool for diagnosis and risk stratification in patients predisposed to developing cardiac thrombi. The use of UEAs facilitates LV thrombus detection by providing opacification within the cardiac chambers to demonstrate the 'filling defect' appearance of an intracardiac thrombus. UEAs can increase sensitivity for detecting LV thrombus, and also improve the negative predictive value, or likelihood that a thrombus is truly absent when not visualized on echocardiography.[29-31] It is recommended that non-traditional "off-axis" views be obtained in order to visualize the entire apex while imaging with UEAs. While delayed enhancement CMR has the highest sensitivity and specificity for detection of LV thrombi,[29] performance of echocardiography with a UEA is a more clinically feasible initial test. However, CMR should be considered when echocardiography with UEAs fails to detect an intracardiac thrombus but clinical suspicion persists.

Intracardiac Masses. 2D echocardiography is usually the primary initial diagnostic imaging modality offering real-time, high spatial and temporal resolution for evaluation of cardiac masses. Although numerous echocardiographic criteria have been developed to define cardiac masses, diagnostic errors and misclassifications can lead to unnecessary surgery or inappropriate anticoagulation. The use of UEAs may potentially avoid these diagnostic errors.[32] Intracardiac masses can be a normal variant of cardiac structure such as a false chord, accessory papillary muscle, or prominent trabeculation, or can be pathologic such as thrombus, vegetation, or tumor. Any suspicious cardiac mass, when not clearly evident on baseline images, can be confirmed or refuted after injection of intravenous UEAs for better delineation of structures. Just as with unenhanced echocardiography, off-axis images and longer loop acquisitions may be required to identify and characterize intracardiac thrombi or masses.

Apical Abnormalities in Patients with Hypertrophic Cardiomyopathy. The apical variant is present in about 7% of hypertrophic cardiomyopathy patients but may not be detected by routine unenhanced echocardiography because of incomplete visualization of the apex. When apical hypertrophic cardiomyopathy is suspected but not clearly documented or excluded, UEAs should be applied to evaluate for the characteristic spade-like appearance of the LV cavity in diastole and vigorous apical myocardial wall thickening.[2] Complications associated with apical hypertrophy can also be readily visualized, such as apical aneurysm formation and thrombi (**Figure 2**). The presence of an apical aneurysm has been associated with adverse outcomes, including arrhythmic events and thromboembolism.[33] However, echocardiography even with UEAs can result in false negative results in the case of very small apical aneurysms, or if contrast-specific

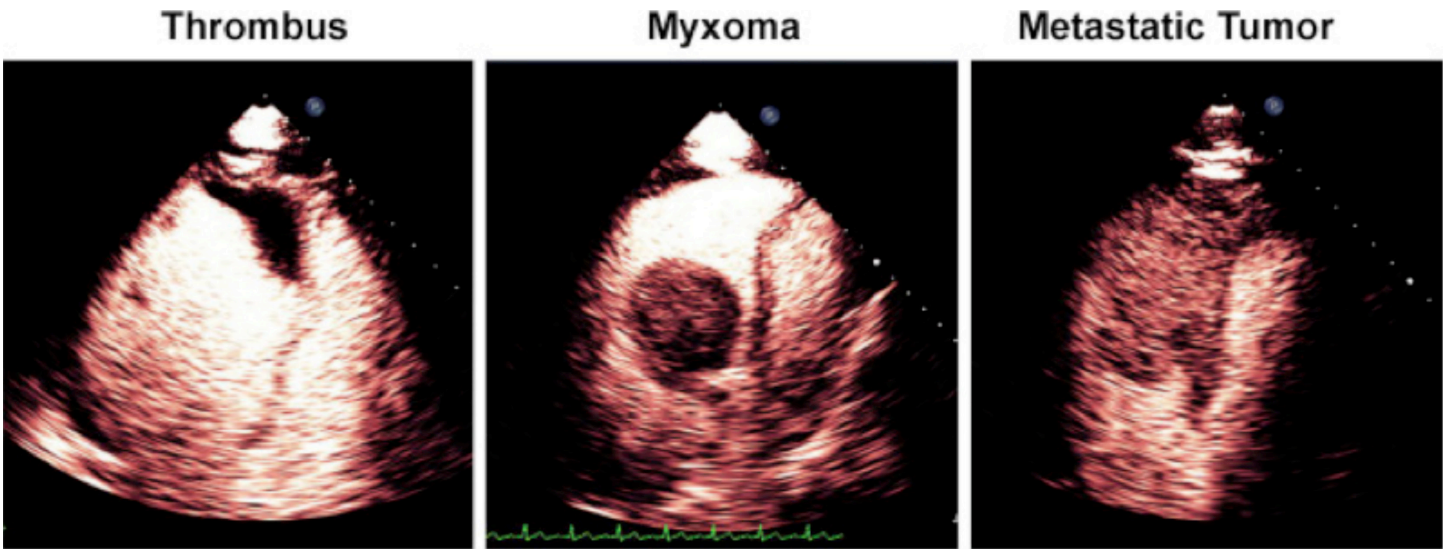

Figure 1 – Modified apical four-chamber images of intra-cardiac masses in three separate patients receiving UEAs during transthoracic echocardiography. Reproduced with permission.[1]

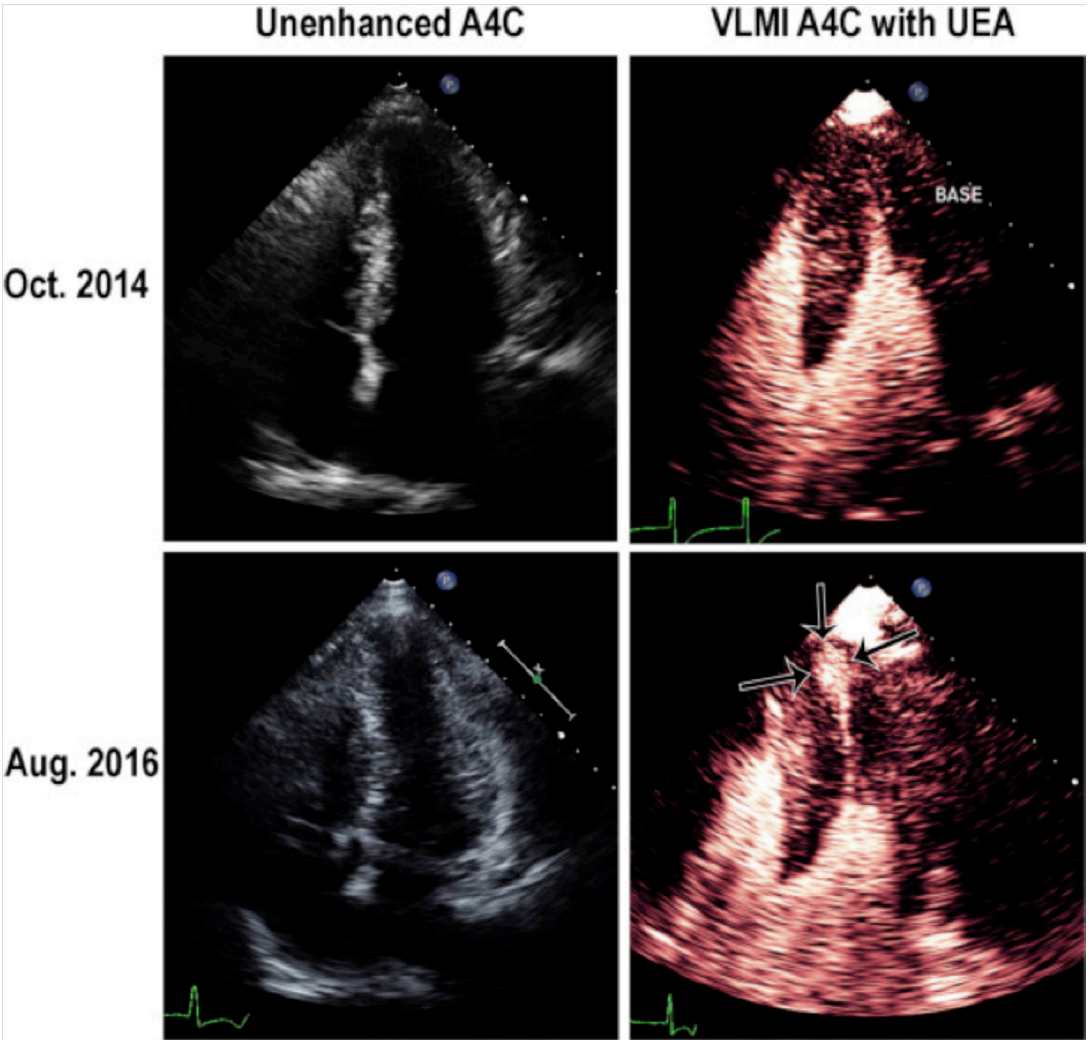

Figure 2 – Apical four-chamber end-systolic images of a patient with apical hypertrophic cardiomyopathy at two separate dates illustrating the development of an apical aneurysm which is better appreciated on the study with UEA. Reproduced with permission.[1]

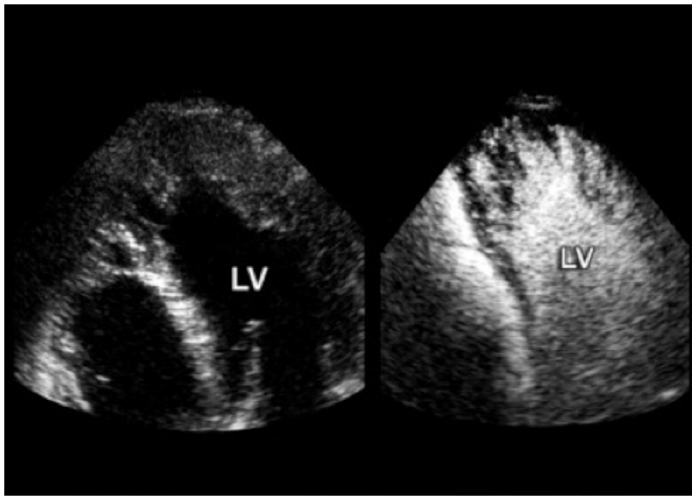

Figure 3 – Apical four-chamber view of a non-contrast and a contrast-enhanced transthoracic echocardiogram illustrating the presence of non-compaction cardiomyopathy. The true extent of the compacted and non-compacted myocardium can be better appreciated on the study using UEAs. Reproduced with permission.[2]

imaging machine settings are not optimized.[34] Accordingly, adjustment of settings mentioned previously for optimal evaluation of the LV apex is recommended.

Noncompaction Cardiomyopathy. Noncompaction of the myocardium is an uncommon but increasingly recognized abnormality that can lead to heart failure, arrhythmias, cardio-embolic events, and death.[35] It is due to alterations of myocardial structure with thickened, hypokinetic segments that consist of two layers: a thin, compacted subepicardial myocardium and a thicker, noncompacted subendocardial myocardium. Echocardiography with UEAs may be helpful in identifying the characteristic deep inter-trabecular recesses by showing microbubble-filled intracavitary blood between prominent LV trabeculations when LV noncompaction is suspected but inadequately seen by conventional 2D imaging (**Figure 3**).[3] It may be useful to use an MI setting that is somewhat higher than usual (MI 0.3-0.4) to better distinguish the myocardial trabeculations in the noncompacted myocardium from UEA presence within the deep recesses.[3] The use of higher MI at real-time frame rates destroys the low-velocity microbubbles within the trabecular myocardium before they can replenish, while the higher-velocity inter-trabecular microbubbles in the LV cavity can replenish, permitting better delineation of the noncompacted layer.

Complications of Myocardial Infarction. LV aneurysm, an often asymptomatic complication of a prior myocardial infarction, is a common apical LV abnormality. True aneurysms are characterized by thin walls and a dilated apex, which may be akinetic or dyskinetic and involve the full thickness of the ventricular wall. These findings are usually readily detected on unenhanced echocardiographic imaging. However, if the apex is not completely visualized, an apical aneurysm may go undetected until a UEA is used. Other complications that can be better detected using UEAs in selected patients with suboptimal views include LV pseudoaneurysm, free wall rupture, and ischemic ventricular septal defects.[36] As previously mentioned, UEAs may also be helpful in detecting LV thrombus and the threshold for using them should be low in those at high risk for thrombus based on the presence of an aneurysm or extensive area of akinesis. The use of UEAs can also help detect the presence of non-ischemic ventricular diverticulum, although the clinical implications of this are not well established.

Recommendations for Imaging

1. UEAs should be used in patients in whom LV thrombus cannot be ruled in or out with non-contrast echocardiography.
2. UEAs should be considered in patients in whom structural abnormalities of the LV, such as noncompaction cardiomyopathy, apical hypertrophy, and aneurysms, cannot be adequately assessed on non-enhanced echocardiography.
3. UEAs should be used for the diagnosis or exclusion of pseudoaneurysms.

Safety and Lab Policy

Studies examining the safety of commercially-produced UEAs have been performed in a variety of patient populations including inpatients, outpatients, critically ill patients, patients with pulmonary hypertension, and those on mechanical circulatory support.[23,37-41] In all of these studies, there have been no reported deaths, and no increases in myocardial infarction rate or mortality in comparison to the control population. There are no safety data published in pregnant patients or children under age 5. There are no agents that are approved by the U.S. FDA for use in the pediatric population for the cardiovascular on-label use of UEAs for LVO in echocardiography. Studies have demonstrated that life-threatening reactions with UEAs are extremely rare, occurring in approximately one in 10,000 doses.[37] The most serious events include hypersensitivity reactions that are thought to be not immunoglobulin-E-mediated, but rather pseudoanaphylactic reactions from complement activation.[42,43] These rare reactions can include shock, bronchospasm, throat swelling, flushing, skin changes, and hypoxemia. Other adverse events that have been reported with UEAs are infrequent and mild, and include headache, weakness, fatigue, palpitations, nausea, dizziness, dry mouth, altered sense of smell or taste, dyspnea, urticaria, and back pain. Administration should be halted for any symptoms potentially related to UEAs.

In 2016, the FDA removed the contraindication for UEA use in patients with known or suspected right-to-left, bi-directional, or transient right-to-left cardiac shunts for all three commercially-produced UEAs. With regards to other contraindications, Optison should not be used in patients with known or suspected hypersensitivity to perflutren (the generic name for the UEA), blood, blood products, or albumin. Definity is contraindicated in patients with known or suspected hypersensitivity to perflutren. Lumason is contraindicated in patients with a history of hypersensitivity reactions to sulfur hexafluoride lipid microsphere components or to any of the inactive ingredients in Lumason.

Because of the rare reactions to UEAs (1 in 10,000), it is advised by the ASE, and mandated by the Intersocietal Accreditation Commission (IAC), that a policy be in place for early identification and rapid response to these acute and severe reactions. All personnel, including sonographers, registered nurses, exercise physiologists, and physicians, should be familiar with the early identification of an allergic reaction and the appropriate treatment. Allergy kits which include auto-injectable epinephrine should be available and easily accessible in all areas where UEAs are in use and should be frequently logged for expiration dates.

With regards to training, current training standards for echocardiography are described in detail in the COCATS 4 Task Force 5 document published in 2015.[44] This document states that the ability to supervise and interpret echocardiography with UEAs (contrast echocardiography) should be considered part of Level II training, but that training is best performed under the supervision of a Level III echocardiographer trained in contrast imaging.

Traditionally, in the majority of centers in North America, IV catheter placement and contrast administration is performed by a registered nurse, medicine technician/phlebotomist, or fellow in training, whereas some sites have extended this responsibility to sonographers. The 2014 ASE Guidelines for the Cardiac Sonographer in the Performance of Contrast Echocardiography support sonographer training in intravenous (IV) insertions for the purpose of UEA administration in hospitals and clinic settings, in order to improve echocardiographic quality with increased efficiency.[3] The training of sonographers in IV line insertion and contrast administration requires hospital approval, knowledge of sterile technique and venous anatomy, and associated risks. While serious side effects are exceedingly rare, there should always be a physician present on site when contrast is administered. Efficiency of implementing UEAs is improved when standing orders are allowed and sonographers can independently select patients for contrast echocardiography, thereby reducing the time to decision for contrast use and resulting in potential cost savings.[45]

Key Points:

1. There are abundant data regarding the safety of UEAs for LVO in a wide variety of adult patients.
2. UEAs can safely be used in patients with pulmonary hypertension and right-to-left shunts.
3. No safety data exist for pregnant patients or children <5 years of age.
4. Efficiency in clinical contrast echocardiography is improved with standing orders that give sonographers the freedom to identify patients who should receive UEAs.

Recommendations for Imaging:

1. Although pseudoanaphylactic reactions are rare (1 in 10,000), laboratories that routinely use UEAs should have policies and resources for emergent resuscitation of patients who may experience serious side effects.
2. Physicians wishing to perform contrast echocardiography should receive supervised training in the implementation of UEAs and interpretation by a Level III echocardiographer.
3. Operational efficiency in the echocardiography laboratory can be improved by training of sonographers in the placement of IV lines and contrast administration.
4. Sonographers should be trained in the recognition of the side effects of UEAs.

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