Clinical applications of contrast-enhanced ultrasound in vascular surgery: State-of-the-art narrative and pictorial review

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ABSTRACT

Background: Contrast-enhanced ultrasound (CEUS) has emerged as a powerful, noninvasive imaging modality in vascular surgery. By using microbubble contrast agents, CEUS enhances vascular imaging, allowing for real-time, high-resolution visualization of blood flow and microvascular perfusion. Unlike other imaging techniques such as computed tomography angiography and magnetic resonance imaging, CEUS does not require ionizing radiation or nephrotoxic contrast agents, making it a safer option for patients with renal impairment.

Methods: This narrative review examines the state-of-the-art applications of CEUS in vascular surgery. A comprehensive literature search was conducted in PubMed, MEDLINE, Embase, Ovid, and Scopus for articles published between 2000 and 2024. Studies addressing CEUS applications in carotid artery disease, aortic aneurysms, peripheral arterial disease, and venous disorders were analyzed.

Results: CEUS has demonstrated significant advantages in multiple vascular conditions. In carotid artery disease, CEUS enhances the detection of vulnerable plaques, improving risk stratification for cerebrovascular events. In aortic aneurysms, CEUS aids in assessing aneurysm wall integrity, endoleak detection after endovascular repair, and monitoring growth rate. For peripheral arterial disease, CEUS provides insights into skeletal muscle microperfusion, aiding in disease severity stratification. In venous disorders, CEUS improves the visualization of deep vein thrombosis and incompetent perforator veins, optimizing diagnosis and treatment planning. Additionally, emerging applications of CEUS include artificial intelligence-assisted imaging and sonothrombolysis, which uses microbubbles for targeted thrombus dissolution.

Conclusions: CEUS represents a valuable imaging tool in vascular surgery, offering superior diagnostic accuracy while minimizing patient risk. Despite its advantages, CEUS remains underused in clinical practice, likely owing to operator dependency and limited standardization. Future research should focus on optimizing CEUS protocols, integrating artificial intelligence for automated analysis, and expanding its role in therapeutic applications. Increased awareness and training may further establish CEUS as a routine vascular imaging modality. (JVS-Vascular Insights 2025;3:100254.)

Keywords: Contrast-enhanced ultrasound; Vascular disease; Vascular surgery; Review

Noninvasive imaging methods such as duplex ultrasound (DUS), computed tomography angiography (CTA), and magnetic resonance imaging are routinely applied in the domain of vascular surgery for preoperative as well as postoperative purposes. The possibility of using contrast medium during ultrasonography has led to development of contrast-enhanced US (CEUS) for vascular imaging, whose use has increased exponentially during the last two decades. Indeed, CEUS is a powerful noninvasive imaging modality offering numerous potential diagnostic and therapeutic applications in vascular surgery. Because blood and the surrounding tissues are similar in echogenicity, the addition of microbubble contrast agents may be used to enhance the overall contrast and quality of US images, which represents the basic underlying physical

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concept of CEUS.[1] The main advantage of US-based contrast agents relies on their ability to enhance imaging without the limitations of radiation exposure or the risk for nephrotoxicity and hypersensitivity potentially linked with other contrast agents.[2] Although contraindicated in patients with right-to-left shunts and those with known hypersensitivity to the contrast material, microbubble contrast agents have a very low rate of serious adverse events mainly limited to allergic reactions (1 in 10,000). The rate of serious neurologic events is even lower (<0.006%).[3]

Numerous studies have addressed the potential clinical value of CEUS in different vascular beds including the carotid arteries, the abdominal aorta, and the lower extremity vessels.[4] Initially developed for assessing the proliferation of adventitial vasa vasorum, which is linked with the development and progression of atherosclerotic plaques, CEUS has found several other applications. US contrast agents have the potential to even further increase not only the diagnostic, but also the therapeutic capabilities of US technology in the cardiovascular field, with particular usefulness in some situations such as low-flow states.[5] A rare but serious adverse effect is an anaphylactic reaction to the US contrast agent, which is reported to occur in 1 of 100,000 cases.

In this review, we discuss the most contemporary evidence on the clinical usefulness of CEUS for clinical applications in vascular surgery as a tool to deliver high-resolution, real-time images of microvascular perfusion with a focus on the main areas of interest in vascular surgery including the carotid arteries, the abdominal or thoracic aorta, the visceral vasculature, lower extremity vessels, and venous disease.

METHODS

The aim of this narrative and pictorial review was to investigate the current state of the art for the use of CEUS for clinical applications in vascular surgery. A nonsystematic search of the literature was conducted from PubMed, MEDLINE, Embase, Ovid, and Scopus databases. These were searched to identify relevant English-language articles fully published in the period January 1, 2000, to December 31, 2024. The MeSH search terms used included contrast-enhanced, microbubble, US, carotid, aneurysm, peripheral, and arterial. These were adopted in combination with the Boolean operators AND or OR. Reference lists of selected articles were also searched. Editorials, case reports with fewer than five cases, conference abstracts, and non-English-language articles were excluded. Prior reviews were consulted as appropriate to identify potentially missing articles. The review was constructed following the Scale for the Assessment of Narrative Review Articles principles.[6]

BASIC CONCEPTS OF CEUS: PHYSICS AND MOLECULAR BACKGROUND, EQUIPMENT, AND TECHNIQUE

CEUS is performed with the intravenous administration of a bolus dose of the US contrast agent. It enables the real-time capture and assessment of the wash-in and wash-out dynamics of the US contrast agent over several minutes. Currently, most of the US contrast agents are microbubbles with a diameter like that of red blood cells, which means that they will never leave the vascular bed.

In more details, microbubble contrast agents used during CEUS have a diameter range of 1 to 7 μm and are composed of encapsulating shells surrounding an inert gas core, typically comprising denatured albumin, surfactants, or phospholipids. The composition of the gas core influences the stability and the echogenicity of the microbubbles. Gases with higher molecular weights and lower blood solubility, such as sulfur hexafluoride and perfluorocarbons, have a longer enhancement time compared with earlier agents like carbon dioxide bubbles.[4] When exposed to US waves emitted by the transducer, microbubbles undergo rapid volumetric oscillations in response to changes in acoustic pressure. These oscillations lead to the generation of nonlinear acoustic signals, different from those produced by the surrounding tissues. SonoVue (Bracco, Milano, Italy) is the most commonly used US contrast agent for vascular purposes in Europe, whereas Definity (Lantheus Medical Imaging, MA) is the more commonly used agent in the United States. The recommended dose for vascular applications, as per the manufacturer, is 2.4 mL of SonoVue. The recommended dose for Definity is 2.0 mL, which includes a bolus dose in addition to an infusion dose. Nevertheless, dose adjustments may be made based on patient characteristics and the scanning device used.[7]

The mechanical index (MI) of the US field influences the behavior of microbubbles. It is defined as the peak negative pressure divided by the square root of the US frequency. It provides an estimate of the potential for mechanical bioeffects, such as cavitation and tissue disruption, resulting from the interaction of US waves with human tissue and contrast agents. High MI imaging allows for high signal-to-noise ratios and increased microbubble sensitivity but may disrupt microbubble shells, whereas low MI imaging enables real-time imaging while maintaining microbubble preservation and facilitating the assessment of both perfusion and wall motion.[8]

For standard examinations, CEUS of the carotid arteries and lower extremity vessels typically uses linear probes operating within the 5- to 10-MHz range, while examinations of the abdominal aorta and visceral vessels use convex probes ranging from 2.5 to 5.0 MHz. US contrast agents are eliminated by exhalation, thereby avoiding any safety concerns related to renal accumulation and excretion. Moreover, the safety of microbubbles has been studied extensively, with no evidence of nephrotoxicity, hepatotoxicity, or cardiotoxicity reported in patients.[2]

Diagnostic applications for carotid artery disease

The accurate diagnosis and management of carotid artery disease is of utmost importance given the significant morbidity associated with strokes or transient ischemic attacks. The Society for Vascular Surgery and European Society for Vascular Surgery guidelines on carotid disease suggest DUS as the first-line imaging modality for the assessment of carotid artery disease.[9] It is a safe, economical, and reliable method to evaluate the degree of stenosis and the plaque morphology, as well as its composition. In this setting, CTA and magnetic resonance imaging are additional tools that can be used in combination with DUS to improve diagnostic accuracy and optimize preoperative planning.[10]

CEUS has been proposed as a tool to identify vulnerable plaques (ie, asymptomatic plaques with embolization potential and subsequent neurological complications).[11] Indeed, CEUS provides high-resolution imaging of the carotid arteries, allowing for detailed visualization of vascular structures including plaque morphology, surface ulcerations, and intraplaque neovessels. CEUS can help to differentiate between various components of carotid plaques, including calcifications, lipid-rich necrotic cores, and hemorrhagic regions, as well as irregularities and ulceration on the carotid plaque surface. This information can be highly helpful for risk stratification and treatment planning.[12]

Some authors have investigated whether intraplaque vessels observed through CEUS could predict the histological characteristics of carotid plaques. CEUS examinations were performed on patients scheduled for carotid endarterectomy and the CEUS findings were compared with the histological analysis of the removed plaques.[13] They found that the presence of intraplaque vessels detected by CEUS was associated significantly with specific histological features of the plaques, including intraplaque hemorrhage and neovascularization, suggesting CEUS as a valuable tool for predicting the histological composition of carotid plaques, which may help in assessing the risk of cerebrovascular events such as stroke. In fact, different studies have investigated the association between carotid intraplaque neovascularization and future vascular events, particularly in asymptomatic patients.[14,15] Intraplaque neovascularization refers to the growth of new blood vessels within the plaque, which is associated with plaque instability and an increased risk of stroke, transient ischemic attack, or other cardiovascular complications. These studies have highlighted the importance of assessing intraplaque neovascularization as a potential biomarker for identifying high-risk individuals with asymptomatic carotid stenosis who may benefit from closer monitoring and more aggressive management strategies to prevent future vascular events.[14] Similarly, intraplaque neovascularization observed through CEUS was used to predict the recurrence of ischemic stroke in patients with symptomatic carotid atherosclerotic plaque. All patients included in the study presented with extracranial carotid artery disease and a history of ischemic stroke. Their findings suggested that intraplaque neovascularization detected through CEUS was associated with an increased risk of recurrent ischemic stroke in patients with carotid atherosclerotic plaque.[15]

Regarding follow-up after carotid revascularization, the 2023 Recommendation Update for Vascular Ultrasound Evaluation of Carotid and Vertebral Artery Disease suggest that follow-up after carotid artery stenting can be performed using CEUS with improved intraluminal stent evaluation and detection of in-stent restenosis with reduction in terms of artifacts compared with DUS.[16,17] This factor is particularly important in light of the known difficulty in using conventional threshold values (as those used for de novo atherosclerotic lesions) for estimating the percentage of in-stent restenosis, given the stiffer nature of implanted devices that affect velocity waveforms.[10]

Diagnostic applications for thoracic and abdominal aortic aneurysms

CEUS can be a valuable diagnostic tool in evaluating abdominal aortic aneurysms (AAAs) (Figs 1-4). Like traditional US evaluation, CEUS can provide information regarding the size and extent of the aneurysm, and it can help with improved visualization of AAA, particularly in cases where traditional imaging modalities such as DUS or CTA scans might be inconclusive or carry additional safety risks. Compared with traditional US, it provides enhanced visualization of the arterial wall and real-time perfusion visualization of the flow lumen. Compared with CTA, it obviates the need for contrast or radiation exposure and is less costly.[1]

Assessment of growth rate and wall integrity. Serial microbubble studies can be used to monitor the growth rate of AAAs over time. Changes in the perfusion pattern within the aneurysm sac can indicate alterations in blood flow dynamics and potentially predict the risk of rupture. Microbubble studies can detect localized disruptions or areas of focal weakness in the aneurysm wall. In one series, CEUS was used for the detection of ruptured AAA, which correlated with CT scan findings without causing undue surgical delay.[18] They have also been used in the trauma setting to detect active bleeding, highlighting their potential role in the acute clinical setting.[19] As such, it is reasonable to consider the CEUS modality in unstable patients who cannot be transported to the CT scanner.

Assessment of aneurysm wall and intimal neovascularization. Microbubble studies can aid in detecting thrombus formation. In vivo animal studies have

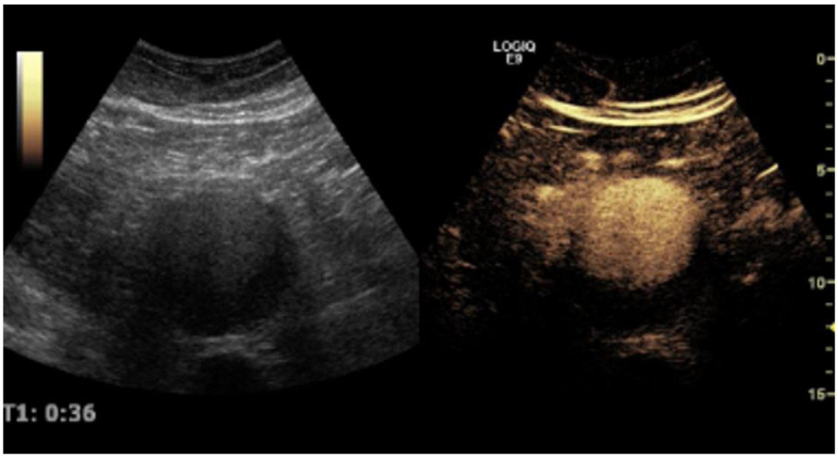

Fig 1. B-mode ultrasound (US) of an abdominal aortic aneurysm (AAA) (left). Contrast-enhanced visualization of the AAA before microbubble disruption by US waves (right). Microbubble disruption refers to the bursting of microbubbles when exposed to US at a certain frequency. After disruption, differential uptake of different areas of a blood vessel (aneurysm in this case) may indicate a stable vs. unstable aneurysm wall.

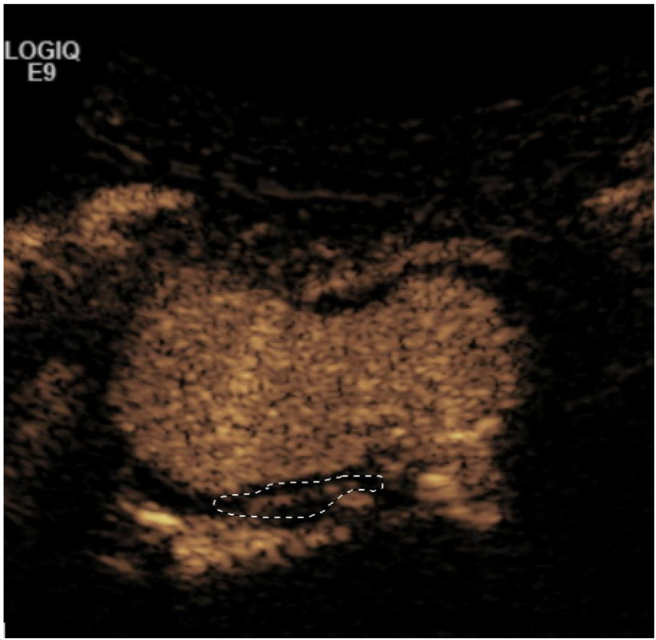

Fig 2. Microbubble uptake seen in the posterior aortic aneurysm wall vasa vasorum.

shown that targeted microbubbles toward activated platelets on the vascular endothelium allow the identification of early lesions of atherosclerosis. CEUS has been used to measure intraluminal thrombus and obtain aneurysm volumetric assessments, which can correlate with aneurysm growth behavior. Three-dimensional CEUS can be as accurate as CTA in intraluminal thrombus volume estimation while providing volumetric measurements without radiation exposure.[20] Although intraluminal thrombus evaluation has been reported with standard DUS, the heterogenous echogenicity of the thrombus on standard US can limit the differentiation between lumen and thrombus.[20] It also allows the study of the severity and the progression of atherosclerosis.[21] CEUS can in fact provide insights into the neovascularization within and around the aneurysm. Increased atherosclerotic plaque vascularity may indicate a higher risk of plaque or wall rupture.[22]

Evaluation of endoleaks after endovascular repair. After endovascular repair of AAAs, which is currently endorsed as first-line therapy in most AAA patients with suitable aortic anatomy, CEUS studies can be used to detect and characterize endoleaks.[23] Previous research has shown that CEUS can be comparable with CTA in the detection and characterization of endoleaks. In a meta-analysis of retrospective studies, CEUS had a pooled rate of endoleak detection of 96.7% (95% confidence interval, 88.7-100.0) compared with a detection rate of 92.8% (95% confidence interval, 77.4-100.0) with CTA.[24] Although the specificity of CEUS is similar to color Doppler ultrasound for the detection of endoleaks, CEUS has better sensitivity allowing for fewer missed endoleaks.[25] The ability to detect flow direction with CEUS helps with further characterization and mapping of these endoleaks. Although standard color duplex US can detect type II endoleaks, CEUS has a higher sensitivity for detecting low flow endoleaks, which are typically type II leaks. Both color and CEUS have high sensitivity in detecting high-velocity leaks such as type I endoleaks. Compared with CTA, CEUS can achieve high sensitivity rates, although the rates tend to drop with obese patients.[26] Similarly, with fenestrated endovascular aneurysm repairs, endoleak detections rates were comparable with the rates of CTA; it was as accurate as CTA in target vessel evaluation.[27] This allows for accurate diagnosis and prompt intervention to prevent further complications. Real-time CEUS evaluation has also been used as a part of preprocedural planning for endoleak embolization in

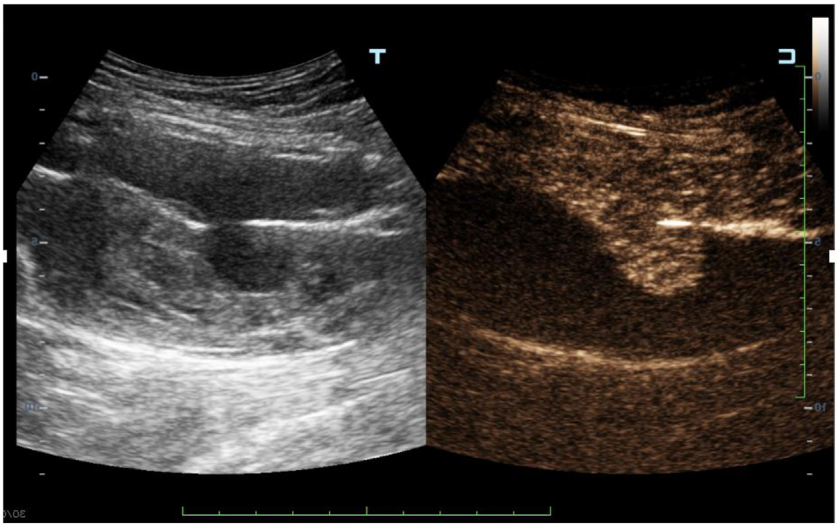

Fig 3. Detection of a type III endoleak on contrast enhanced imaging status post prior endovascular aneurysm repair.

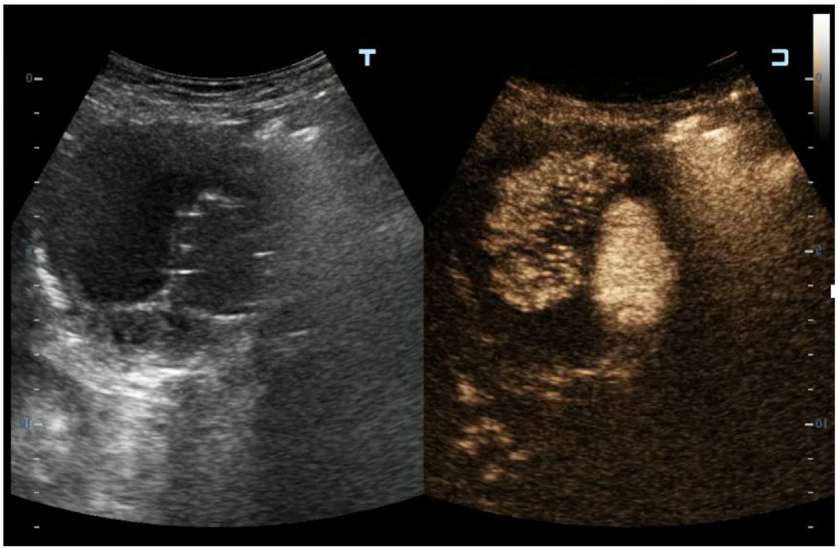

Fig 4. Detection of a type IA endoleak on contrast-enhanced imaging status post prior endovascular aneurysm repair.

clinical scenarios that necessitate minimum contrast exposure.[28]

The use of CEUS for the evaluation of the thoracic aorta is more limited as compared with the abdominal aorta given the anatomical location of the aorta in the chest. However, reports of utilizing CEUS with transesophageal echocardiography in the treatment of thoracic aortic aneurysms have been published.[29,30] The inherent requirement for invasive evaluation of the thoracic aorta with transesophageal echocardiogram (TEE) limits the diagnostic use of CEUS and its use for surveillance.

Diagnostic applications for visceral artery aneurysms

CEUS has been used for renal artery aneurysm diagnosis, although this approach has not been standardized. For visceral aneurysms in the postoperative follow-up period, CEUS has been implemented to determine malperfusion in organ microvasculature after open vs endovascular treatment of visceral artery aneurysms. This method can be critical and advantageous in the management of visceral aneurysms when the objective also involves concomitant preservation of end-organ function. Specifically for renal microvasculature evaluation, CEUS can provide details about organ function while avoiding the need for nephrotoxic contrast administration compared with CTA.[31] CEUS has been reported to be particularly useful after visceral aneurysm coil embolization, because it can observe contrast uptake within the visceral aneurysm while eliminating the artifact generated from the coils. CEUS has been used for diagnosing failing kidney transplants by identifying the time to peak contrast uptake in segmental renal arteries and mean renal medullary transit time. This provides improved diagnostic accuracy for detecting failing kidney grafts.[32] Whereas CEUS use is more established in evaluating liver and kidney tumors, its role in visceral aneurysm management remains limited.

Diagnostic applications for aortic dissections

CEUS can help to detect the presence of blood flow within the true and false lumens of the abdominal aorta and help to distinguish the true from the false lumen, which is crucial for treatment planning. True and false lumen distinction depends on the early and late phases of contrast enhancement, respectively. In this regard, notwithstanding the potential pitfalls related to poor visualization of the thoracic aorta (as mentioned), CEUS has been shown to have better sensitivity and specificity rates compared with B-mode and color-coded US for diagnosing abdominal aortic dissections. Indeed, differentiation between true and false lumens and the flow direction between the two lumens were better detected with CEUS compared with DUS.[33] Concomitantly, it can provide detailed imaging of the intimal flap of the dissection. By visualizing the flap and its movement during the cardiac cycle, CEUS can contribute to confirming the diagnosis. CEUS combined with TEE demonstrated better diagnostic capabilities compared with standard TEE for acute thoracic aortic syndromes with higher specificity rates.[30]

CEUS can also help to evaluate complications associated with aortic dissection, such as ischemia or infarction of organs supplied by aortic direct branches. By assessing perfusion in these organs, CEUS can provide valuable information about the extent and severity of complications.[34] The ability to identify intimal membranes gives CEUS a distinctive advantage to evaluate static and dynamic end-organ malperfusion.[34] This is of particular relevance when limiting contrast exposure is of important clinical significance, such as in aortic dissections causing kidney end-organ damage. CEUS can better detect the intimal membrane compared with DUS.[34] CEUS can provide dynamic assessment of the aortic dissection and the intimal flap and can therefore be used to monitor treatment response. This allows providers to evaluate the effectiveness of treatment and guide further medical or surgical interventions.[35]

Diagnostic applications for peripheral arterial disease

Although CEUS is not part of the standard diagnostic algorithm for peripheral arterial disease, the diagnostic applications have the potential to quantify skeletal microrevascularization. By analyzing the time-intensity curves of skeletal muscle regions, valuable input about the microvasculature can be obtained. The delayed transit time of contrast agents from the artery to the vein can suggest microvascular disease.[36] Time to peak intensity was found to be significantly higher in patients with peripheral arterial disease compared with control patients. The ankle-brachial index and pulse volume recordings are often unreliable in peripheral arterial disease patients with diabetes mellitus. In that subset, CEUS provides more diagnostic information about the severity of peripheral arterial disease compared with standard evaluation. It provides times to peak intensity, which are typically greater in patients with peripheral arterial disease. This quantification of tissue perfusion is faster and less costly than magnetic resonance imaging.[37] It also evaluates and quantifies the perfusion of the microvasculature, which is advantageous in diabetic patients given the limitations of standard modalities. Time to peak sensitivity was inversely correlated with the ankle-brachial index in some studies, suggesting that CEUS can be used for disease severity stratification.[38] CEUS was also used to differentiate peripheral arterial disease patients into those with adequate vs inadequate collateralization.[39] Despite these findings, the clinical usefulness of CEUS for patients with PAD remains limited.

Artificial intelligence and CEUS

Artificial intelligence (AI) is being implemented to improve the diagnostic accuracy of US imaging. The largest body of evidence comes from carotid plaque evaluation. AI has a role in standardizing plaque characteristics identified on CEUS to improve plaque vulnerability prediction.[40] Machine learning and segmentation methods for classifying carotid atherosclerotic plaques into low- and high-risk categories have been implemented with models reaching sensitivity and specificity rates of 98% and 99%, respectively.[41] Analyzing different feature extraction techniques on carotid US images has been shown to improve machine learning training and inference speed.[42] Machine learning algorithms have also been integrated with CEUS for the evaluation of failing kidney transplants to help improve the diagnostic accuracy by providing times for peak contrast uptake and mean times for renal medullary flow.[32] Although the integration of AI and CEUS is more established in oncology, it remains in its early phases in vascular disease. Future research focusing on the incorporation of AI in CEUS evaluation allows for the development of models and algorithms that incorporate more granular atherosclerotic plaque analysis in various vascular beds. The ability of CEUS to distinguish between stable and unstable plaque based on its composition has always been a critical goal in vascular imaging because it influences patient risk stratification and clinical decision-making.

Therapeutic applications

CEUS primally serves as a diagnostic imaging technique, but its therapeutic applications are emerging in several medical fields. Intravascular microbubbles used for CEUS can incorporate ligands or antibodies that target specific vascular receptors and provide precise spatial and temporal control over drug and gene delivery while minimizing side effects. In response to US waves, microbubbles can oscillate or collapse. Depending on the intensity of the ultrasonic waves, the release of the therapeutic agent can be induced by a thermal or a cavitation effect. High-intensity ultrasonic waves produce mechanical oscillations of the microbubble that are then converted into thermal energy; the increase in temperature of the area under treatment acts like a trigger to release the drug. The cavitation process is caused by variations in the size of the microbubbles that generate localized deformation of cell membranes, leading to the formation of temporary pores in the membrane structure, thereby increasing its permeability. This phenomenon is known as sonoporation and allows drugs to enter cells more efficiently.[43]

Sonothrombolysis is a therapeutic approach that combines US energy with thrombolytic drugs to dissolve thrombus in blood vessels. It can be used in myocardial infarction, ischemic stroke, peripheral arterial occlusions, and pulmonary embolism. Severe studies have demonstrated the potential of microbubbles combined with US in thrombolysis showing their ability to enhance clot lysis through mechanical and cavitational effects. In this setting, CEUS involves the use of intravenously administered microbubble contrast agents, which play a dual role in diagnostic imaging and the therapeutic process. Although sonothrombolysis typically combines US waves with thrombolytic drugs, in this approach, microbubbles serve as both a contrast agent to improve imaging precision and an active therapeutic tool to amplify the effects of US on thrombus disintegration. Sonoperfusion is another approach that combines US with microbubbles to enhance the permeability of blood vessels and improve tissue perfusion.[44] Its usefulness has been demonstrated the coronary literature, where microbubble infusion postpercutaneous coronary intervention was associated with improved recanalization rates and reduced infarct size compared with the absence of sonoperfusion.[45] For instance, sonothrombolysis was investigated in patients with ST-segment elevation myocardial infarction. It was shown that in combination with percutaneous coronary intervention, sonothrombolysis promoted clot dissolution, improved microvascular perfusion, and prevented left ventricular remodeling with a significant impact on the long-term prognosis of those patients compared with percutaneous coronary intervention alone.[46] Sonothrombolysis has also been studied in the management of acute ischemic stroke. A meta-analysis of randomized controlled clinical trials suggests that sonothrombolysis can be a treatment option for acute ischemic stroke, because it improves recanalization rates without increasing the risk of adverse events compared with non-sonothrombolysis interventions.[47] Also, MUST (Microbubbles and UltraSound accelerated Thrombolysis) showed promising safety and technical feasibility of contrast-enhanced sonothrombolysis for acute peripheral arterial occlusion of native arteries and bypass grafts without side effects related to the microbubbles.[48] Sonothrombolysis is emerging as a promising intervention for acute pulmonary embolism, offering targeted treatment with lower drug doses and minimized bleeding risks. Clinical studies and trials have provided encouraging evidence supporting the safety and efficacy of sonothrombolysis in patients with acute pulmonary embolism.[47] For instance, the combination of US-assisted catheter-directed thrombolysis and low-dose thrombolytic therapy has demonstrated improved pulmonary arterial perfusion, reduced right ventricular strain, and faster symptom resolution compared with systemic thrombolysis or anticoagulation alon.[48] Moreover, the targeted nature of the therapy allows for precise delivery at the site of the thrombus, mitigating the risks associated with systemic thrombolysis. Advancements in catheter-based systems and the promising potential of sonothrombolysis show improved outcomes, but further research is required to ensure safety, validate results, and compare its efficacy and cost effectiveness with alternative treatments.

Venous disease

DUS is widely considered the gold standard for diagnosing chronic venous disease (CVD) because it provides both anatomical and hemodynamic information about the venous system and enables the assessment of vessel compressibility, blood flow direction, and venous reflux.[49] However, in CVD applications, traditional DUS often struggles to clearly define veins with slow or stagnant blood flow, especially when they are small or situated deep within the body. CEUS may improve the visualization of small-caliber or perforating veins significantly, as well as areas of suspected venous insufficiency and thrombotic obstructions, by using microbubble contrast agents that act as effective blood markers, increasing the backscatter of US waves and enhancing the echogenicity of blood flow within the vascular system.

Recent studies have demonstrated the superior sensitivity of CEUS in detecting incompetent perforator veins compared with DUS (89.2% vs 70.2%).[50] Moreover, CEUS proved particularly useful in distinguishing competent from incompetent perforator veins, facilitating precise preoperative localization. This improved accuracy reduces the likelihood of missed diagnoses and postoperative recurrence, further underscoring the role of CEUS as a powerful tool in the management of CVD.

CEUS has also proven valuable in improving imaging for deep vein thrombosis (DVT), particularly in challenging cases, such as obese patients or those with peripheral edema. A study investigating CEUS for complex DVT detection found that although the common femoral vein did not show significant visualization gains, CEUS improved full visualization of the femoral vein and popliteal vein from 67% and 83% to 100%, respectively. The posterior tibial vein and peroneal vein also demonstrated statistically significant visualization improvements, with full visualization of the peroneal vein increasing from 25% to 58%. These results suggest that CEUS enhances DVT detection, particularly in patients with suboptimal traditional US imaging, potentially decreasing follow-up costs and diagnostic uncertainty.

These findings highlight the promising role of CEUS in the diagnosis and management of venous disease; however, further large-scale studies are necessary to validate its clinical utility and establish standardized guidelines for its widespread implementation.

Credentialing and training

In addition to the standard vascular US setup, vascular labs will require sonographers certified in intravenous contrast agent administration. While the cost of microbubble agents ranges between $100 and $200 per vial, personnel training is an additional investment on behalf of the vascular lab, particularly in the absence of trained nurses. There is also a learning curve associated with both the performance (by the ultrasonographers) and the interpretation (by the physicians) of microbubble enhanced images.

The credentialing and training of CEUS sonographers is largely dependent on regional and local institutional regulations. However, the European Federation of Societies for Ultrasound in Medicine and Biology has published minimum training requirements for the performance of CEUS.[35] Each sonographer should be familiar with the indications and contraindications of CEUS. In the United States, the American Registry for Diagnostic Medical Sonography credentials sonographers with certifications in their respective specialties. Although there is no specific credentialing for CEUS, vascular, abdominal, and cardiac proficiency is encouraged. Hands-on CEUS training is also required, which includes patient preparation, contrast agent administration, and postprocedure monitoring. However, it is worth noting that different states may have different credentialing requirements. Depending on institutional policies, training in intravascular cannulation and contrast administration may be required. Other than personnel training, the available equipment should be optimized to allow for the capture and the postprocessing of US images and videos.

CONCLUSIONS

The well-established technology of microbubbles and CEUS holds considerable interest for vascular surgery given its diagnostic and therapeutic usefulness. Although CEUS has been applied in different vascular fields, its current application as part of the routine vascular testing landscape is limited. Indeed, a recent survey has demonstrated that CEUS is still rarely used in current practice for many vascular diseases despite the availability of this tool in most centers.[51] Practically, CEUS can be considered as a supplement, if and when conventional DUS studies fail or are deemed insufficient to draw meaningful conclusions. However, it also shares the same limitations of conventional DUS including operator dependency as well as potential drawback in patients with hostile body habitus. This is especially true for deeply located structures, such as for diagnostic evaluation of AAA (both before and after treatment). The future use of targeted microbubbles could further enhance and expand the diagnostic capabilities of current vascular US imaging by detecting specific molecular processes that play a role in the pathophysiology of vascular disease.[49] The merging of vascular imaging with AI, radiomics, and machine learning may bring further advancements to the field and holds promises for the future. Future studies are needed, as well as enhanced guidance on the proper implementation of CEUS from guidelines to investigate optimal protocols and its integration with alternative imaging modalities.[50]

AUTHOR CONTRIBUTIONS

Conception and design: MDO, AAA
Analysis and interpretation: MDO, AF, JRN, BR, FB, ZAG, GS, SL, AAA
Data collection: MDO, AF, JRN, BR, FB, ZAG, GS, SL, AAA
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Critical revision of the article: MDO, AF, JRN, BR, FB, ZAG, GS, SL, AAA
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