

ROLE OF CONTRAST-ENHANCED ULTRASONOGRAPHY IN THE ASSESSMENT OF UTERINE DISORDERS: A SYSTEMATIC REVIEW

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Abstract

Background: Uterine disorders are often presented with overlapping symptoms. Some disorders, such as fibroids, are usually correctly identified by conventional grayscale or Doppler imaging. CEUSG uses intravenous injections of gas-filled microbubbles to visualize the macro- and microvasculature. The aim of study is to systematically evaluate the role of contrast-enhanced ultrasonography (CEUS) in the assessment of uterine disorders by analyzing its diagnostic accuracy, clinical utility, and advantages over conventional ultrasound techniques.

Methods: This systematic review follows the PRISMA guidelines. A comprehensive literature search was conducted between the years 2000 to 2025, using databases such as PubMed, Scopus, Web of

Science, and Google Scholar. Search terms included combinations of keywords and Medical Subject Headings (MeSH). This review included peer-reviewed articles published between the selected time frame, such as original research, reviews, and meta-analyses on CEUS for uterine pathologies. Eligible studies involved randomized controlled trials, cohort studies, cross-sectional studies, and observational studies using both transvaginal and transabdominal CEUS. Excluded studies were case reports, editorials, conference abstracts, animal studies, and those lacking complete diagnostic data or not focused on CEUS as the primary imaging modality.

Results: A total of 26,000 records after the removal of 6,000 duplicate records, 20,000 unique articles remained for screening. Based on titles and abstracts, 15,000 articles were excluded. This led to 5,000 full-text articles being assessed 4,990 articles were excluded due to lack of relevance to contrast-enhanced ultrasonography, insufficient diagnostic data, or methodological limitations. Finally, 10 high-quality studies were included in this systematic review for detailed analysis.

Conclusion: This review underscores the effectiveness of contrast-enhanced ultrasonography (CEUS) in diagnosing uterine disorders, showing high accuracy for conditions like leiomyomas and endometrial lesions. Despite its advantages over conventional ultrasound, variability in results calls for further research to standardize its clinical use.

INTRODUCTION

Uterine disorders are often presented with overlapping symptoms. Some disorders, such as fibroids, are usually correctly identified by conventional grayscale or Doppler imaging. Other disorders such as diffuse adenomyosis and malignant leiomyosarcomas are often difficult to distinguish from common fibroids. The microvascular architecture and blood flow patterns of uterine disorders can provide detailed information important for accurate differentiation. However, detection of vessels smaller than 0.1mm in diameter and full quantification of vascular flow remain beyond the reach of conventional grayscale and Doppler imaging techniques. Contrast-enhanced ultrasonography (CEUS), which is distinct from saline- or gel-infused sonohysterography, is an imaging modality that uses intravenous injections of gas-filled microbubbles to visualize the macro- and microvasculature. It may be possible to distinguish between benign and malignant uterine illnesses by using CEUS to image the microvasculature of uterine anomalies.[1]

Among women over 40, fibroids are the most prevalent benign uterine tumors. According to Holdsworth-Carson et al. (2014), uterine fibroids can cause symptoms such as infertility, pelvic pain, bowel and bladder problems, heavy bleeding and anemia, and pregnancy losses. Compared to grey-scale ultrasound, sonoelastography, and color/power ultrasonography, CEUS offers more information about the pseudocapsule of fibroids, central necrosis, and intra-lesion vascularity pattern.[2] Between 25 and 46 percent of people have symptomatic fibroids. According to pathologic analysis, the frequency is significantly greater by the age of fifty, reaching 70% to 80%.[3] Among women of reproductive age, the prevalence of uterine fibroids varies by race and is typically stated to be between 20 and 40 percent,[4]

CEUS improves the assessment of uterine leiomyomas by overcoming the limitations of conventional Doppler, especially in detecting deep or slow-flow vessels. Though still limited in use, it shows strong potential for accurate diagnosis and treatment monitoring.[5] Compared to traditional ultrasonography, contrast-enhanced ultrasound (CEUS) provides better visualization of vascular characteristics and allows for real-time assessment of tissue perfusion and microcirculation. It might offer more precise information for differentiating between atypical adenomyosis and uterine leiomyomas. CEUS has the potential to improve uterine fibroids diagnosis accuracy, particularly in cases that are complex or overlap.[6]

When endometrial hyperplasia is present, contrast-enhanced ultrasonography can reveal details about the lesion's blood perfusion pattern, order, and volume. It displays the degree of uterine wall violation as well as if the lesion is present.[7] Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has been used to assess the effectiveness of MWA for a variety of malignancies, including adenomyosis, a benign lesion of the female reproductive system brought on by endometriosis of the myometrium CEUS. In this study, 66 individuals with localized adenomyosis underwent DCE-MRI and ultrasonic ablation. MWA (microwave ablation for adenomyosis) was evaluated using DCE-MRI and contrast-enhanced ultrasound.[8]

Technology based on traditional ultrasound, uses microscopic bubbles of contrast to improve tissue imaging and blood flow. As a novel EC diagnostic technique, CEUS offers unique benefits. It differentiates between adnexal masses that are benign and those that are malignant. It is less dangerous, has less side effects, and is less expensive than traditional imaging methods like Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) because it does not use ionizing radiation and the contrast agent is typically particles with air bubbles.[9]

Magnetic resonance imaging, 3-dimensional transvaginal ultrasonography, and positron emission tomography/computed tomography are currently used diagnostic techniques for preoperatively staging patients with EC; each has pros and cons. Gynecological tumors can also be diagnosed with CEUS. Ovarian cancer was diagnosed more frequently as a result of CEUS.[10] In addition to

evaluating capillary microperfusion in the dynamic contrast harmonic imaging mode, CEUS provides the ability to detect endometrial diseases in the static B-scan mode. The viability of using CEUS to differentiate between benign and malignant endometrial lesions was examined, and markers that were associated with the pathological findings were screened.[11]

The advantages of CEUS include real-time imaging, low cost, noninvasiveness, a safe profile, no risk of radiation exposure or nephrotoxic effects, and high contrast resolution. Individual microbubbles can be visualized with CEUS, making it more sensitive than CT and MRI for detection of vascularity. CEUS has emerged as an assessable adjunct to routine US, allowing more detailed lesion characterization that is not possible with standard US imaging alone. Some factors that may limit the US examination include significant intestinal gas, large patient body habitus, deeply situated or larger lesions, many lesions, and operator dependency. Other limitations of CEUS include those intrinsic to the US modality as well as those specific to US contrast agents.[12]

METHOD AND MATERIAL

This systematic review follows the PRISMA guidelines. A comprehensive literature search was conducted between the years 2000 to 2025, using databases such as PubMed, Scopus, Web of Science, and Google Scholar. Search terms included combinations of keywords and Medical Subject Headings (MeSH) such as: Contrast-Enhanced Ultrasonography, Uterine Disorders, Gynecologic Ultrasound, Transvaginal CEUS, Diagnosis Assessment or Imaging Accuracy.

To systematically evaluate the role of contrast-enhanced ultrasonography (CEUS) in the assessment of uterine disorders by analyzing its diagnostic accuracy, clinical utility, and advantages over conventional ultrasound techniques.

All types of peer-reviewed articles published within the selected time frame, including original research articles, reviews, and meta-analyses relevant to the topic, were included. This review considered randomized controlled trials, cohort studies, cross-sectional studies, and observational

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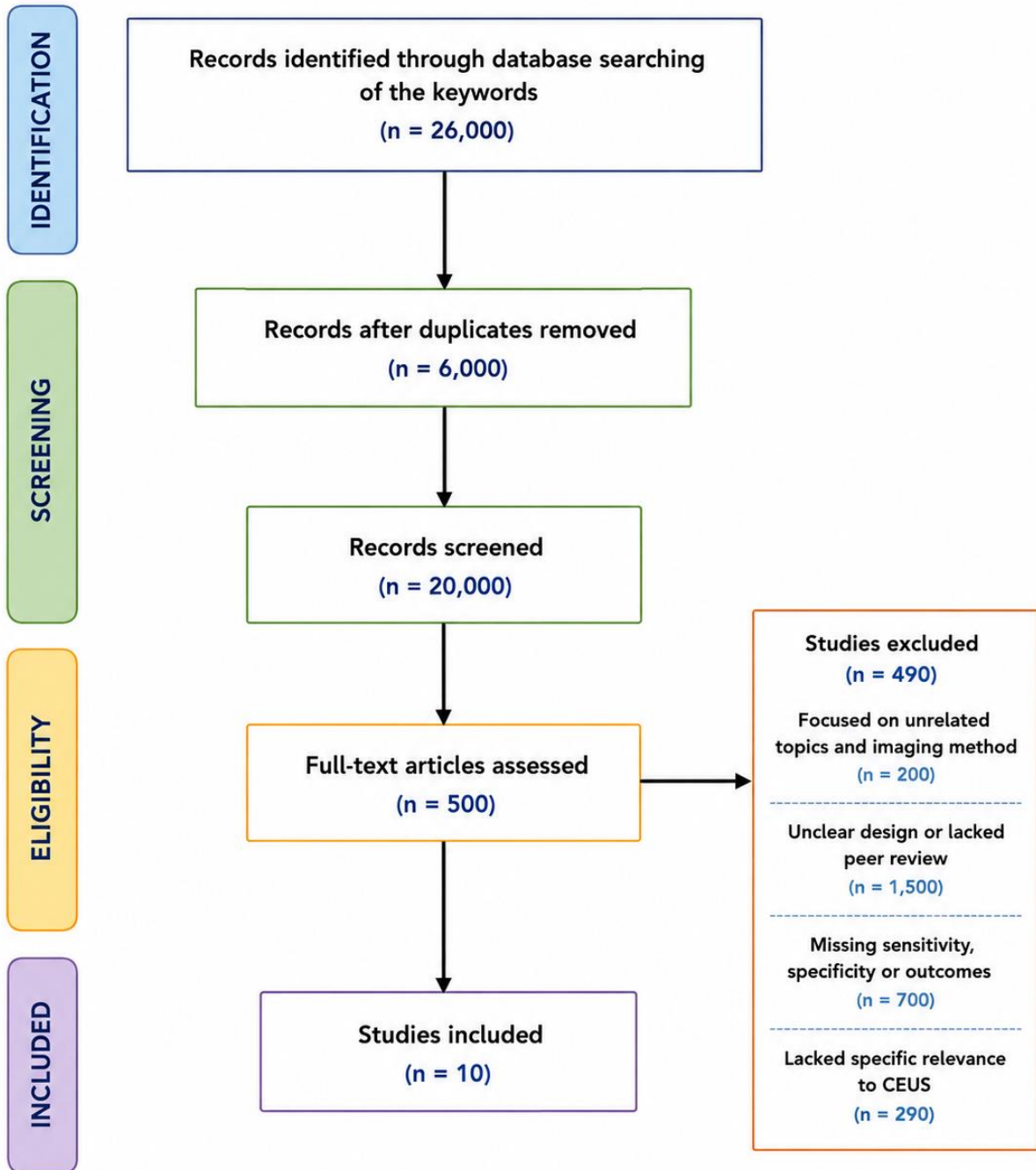
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studies involving women undergoing CEUS for suspected uterine pathologies. Both transvaginal and transabdominal CEUS applications were eligible for inclusion.

Studies were excluded if they were case reports, editorials, conference abstracts, or not peer-reviewed. Additionally, animal studies, articles not involving CEUS as the primary imaging modality, and those with incomplete or missing diagnostic data were excluded from the analysis.

PRISMA 2020 FLOW DIAGRAM



CEUS: Contrast-Enhanced Ultrasound

Result:

A total of 26,000 records were initially identified through database searches across PubMed, Scopus, Web of Science, and Google Scholar. After the removal of 6,000 duplicate records, 20,000 unique articles remained for screening. Based on titles and abstracts, 15,000 articles were excluded for not meeting the inclusion criteria. This led to 5,000 full-text articles being assessed for eligibility. Upon detailed evaluation, 4,990 articles were excluded due to reasons such as lack of relevance to contrast-enhanced ultrasonography, insufficient diagnostic data, or methodological limitations. Finally, 10 high-quality studies were included in this systematic review for detailed analysis.

Author	Year	Study Design	Mean Age	Diagnosis	AC %	S T %	S P %	NP V %	PP V %	CE US G
Stoelinga et al. [1]	2021	Systematic Review	NA	Uterine Disorders	81	78	81	NA	NA	Yes
Zhang et al. [6]	2022	Retrospective	NA	Atypical focal adenomyosis from uterine leiomyomas	87.78	98.3	70.0	75	92.3	Yes
Fang Guo et al. [13]	2024	Retrospective	56.5Y	Endometrial lesions	88	86.6	91.4	88.9	89.7	Yes
Raffone et al. [14]	2025	Systemic	21-81Y	Uterine Leiomyomas	89	76	89	NA	NA	Yes

Li et al. [9]	2025	Meta analysis	42-59.70Y	Myometrial Infiltration in early EC	95	83	92	NA	NA	Yes
Bitten Court et al. [15]	2016	Systematic review	NA	Endometrial polyps	N A	88 - 89	61 - 10 0	NA	NA	Yes
Sanin-Ramirez et al. [16]	2020	Systemic Review	NA	Endometrial polyps	N A	95	51	NA	NA	Yes
Tong et al. [10]	2021	Meta analysis	NA	Staging of Endometrial Carcinoma	38	81	90	NA	NA	Yes
Liu et al. [11]	2016	Prospective study	Benign 44.83 Malignant 47.36	Endometrial Hyperplasia and Neoplasm		85	85	NA	NA	Yes
Olinger and Liu et al. [12]	2024	Narrative Review	NA	CEUS in Female Pelvic Disease.	98	86	86	NA	NA	Yes

AC= Accuracy, ST= Sensitivity, SP= Specificity, PPV= Positive predictive value, NPV= Negative predictive value, NA= Not Available, EC= Endometrial Carcinoma, CEUSG= Contrast enhanced Ultrasonography.

DISCUSSION

In the systematic review conducted by Stoelinga et al. in 2021, the role of contrast-enhanced ultrasound (CEUS) in diagnosing uterine disorders among postmenopausal women was thoroughly evaluated. The study demonstrated a diagnostic accuracy of 81%, with a sensitivity of 78% and specificity of 81%. These findings suggest that CEUS provides reliable differentiation of uterine pathologies, making it a valuable adjunct to standard ultrasound techniques. The enhancement offered by contrast agents helps in better visualization of vascular patterns, aiding in the assessment of endometrial and myometrial abnormalities. Overall, the inclusion of CEUS significantly enhances the diagnostic performance of ultrasound in the evaluation of uterine conditions in postmenopausal patients.[1]

In the retrospective study by Zhang et al. (2022), contrast-enhanced ultrasound (CEUS) was evaluated for its effectiveness in distinguishing atypical focal adenomyosis from uterine leiomyomas. The study reported a high diagnostic accuracy of 87.78%, with excellent sensitivity at 98.3% and a specificity of 70%. The positive predictive value was 75%, while the negative predictive value reached 92.3%. These results highlight the strong potential of CEUS in improving the differentiation between these two commonly confused uterine pathologies. By enhancing tissue characterization and vascular detail, CEUS proves to be a reliable and valuable tool in gynecological imaging, particularly for complex postmenopausal cases.[6]

In the retrospective study conducted by Fang Guo et al. (2024), the diagnostic performance of contrast-enhanced ultrasound (CEUS) was assessed for evaluating endometrial lesions in postmenopausal women with a mean age of 56.5 years. The study demonstrated a high overall diagnostic accuracy of 88%, with a sensitivity of 86.6% and a specificity of 91.4%. Additionally, the

positive predictive value was 88.9%, and the negative predictive value was 89.7%, indicating the method's reliability in both detecting and excluding pathological endometrial changes. These findings suggest that CEUS provides enhanced visualization and improved diagnostic confidence in distinguishing benign from malignant endometrial conditions. Therefore, CEUS emerges as an effective imaging modality for clinical decision-making in postmenopausal gynecological evaluations.[13]

In the 2025 systematic study by Raffone et al., the role of contrast-enhanced ultrasound (CEUS) was evaluated in diagnosing uterine leiomyomas across a wide age range of 21 to 81 years. The findings revealed a high diagnostic accuracy of 89%, with a sensitivity of 76% and a specificity of 89%, demonstrating CEUS's effectiveness in correctly identifying and ruling out uterine leiomyomas. These results underscore the strength of CEUS as a non-invasive imaging modality that enhances the differentiation of leiomyomas from other uterine pathologies. The high specificity indicates that false positives are minimal, helping to prevent unnecessary interventions. Overall, this study supports the integration of CEUS in routine diagnostic protocols for more accurate assessment of uterine abnormalities.[14]

In a 2025 meta-analysis conducted by Li et al., the effectiveness of contrast-enhanced ultrasound (CEUS) was assessed in detecting myometrial infiltration in early-stage endometrial carcinoma (EC) among women aged 42 to 59.7 years. The study demonstrated an impressive overall diagnostic accuracy of 95%, with a sensitivity of 83% and a specificity of 92%. These values indicate that CEUS is highly reliable in both identifying true positive cases and correctly excluding those without myometrial invasion. The strong diagnostic performance of CEUS supports its role as a valuable, non-invasive imaging modality for early assessment of endometrial carcinoma, potentially aiding in timely and appropriate treatment planning.[9]

In a 2016 systematic review by Bitten Court et al., contrast-enhanced ultrasound (CEUS) was evaluated for its effectiveness in diagnosing endometrial polyps. The findings revealed a high sensitivity range of 88–89%, indicating CEUS's strong ability to detect true cases of polyps.

Specificity ranged from 61% to 100%, reflecting a variable but potentially excellent capacity to correctly identify those without the condition. These results highlight CEUS as a valuable imaging technique in the assessment of endometrial polyps, offering enhanced visualization and diagnostic accuracy. Its non-invasive nature further supports its use as a reliable tool in routine gynecological evaluation.[15]

In the 2020 systematic review by Sanin-Ramirez et al., contrast-enhanced ultrasound (CEUS) demonstrated strong diagnostic performance in identifying endometrial polyps. The study reported a high sensitivity of 95%, indicating that CEUS is highly effective in detecting true positive cases. However, the specificity was lower at 51%, suggesting a higher likelihood of false positives. Despite this, the impressive sensitivity underscores CEUS's value in ensuring early detection and reducing missed diagnoses. These findings support the role of CEUS as a powerful diagnostic modality, particularly useful in the evaluation of endometrial pathology in postmenopausal women.[16]

In the 2021 meta-analysis conducted by Tong et al., contrast-enhanced ultrasound (CEUS) was evaluated for its effectiveness in staging endometrial carcinoma. The study reported an accuracy of 38%, which may reflect the complexity and variability in staging criteria across studies. However, CEUS demonstrated a high sensitivity of 81% and an even higher specificity of 90%, indicating its strong potential in correctly identifying both true positive and true negative cases. These values suggest that while overall accuracy may be influenced by multiple staging factors, CEUS remains a reliable imaging tool for differentiating between stages of endometrial carcinoma, supporting its use in comprehensive preoperative assessment and planning.[10]

In the 2016 prospective study by Liu et al., contrast-enhanced ultrasound (CEUS) was utilized to evaluate endometrial hyperplasia and neoplasms in a population with a mean age of 44.83 years. The findings demonstrated both an accuracy and sensitivity of 85%, highlighting the consistent diagnostic capability of CEUS in identifying these conditions. This suggests that CEUS provides reliable results in detecting and differentiating endometrial pathologies, particularly in distinguishing benign from potentially malignant lesions. The use of CEUS in this context reinforces

its value as a noninvasive diagnostic modality with strong clinical utility in gynecologic evaluations.[11]

In the 2024 narrative review by Olinger and Liu, contrast-enhanced ultrasound (CEUS) was explored for its diagnostic effectiveness in evaluating female pelvic diseases. The study reported a high overall accuracy of 98%, along with balanced sensitivity and specificity rates of 86%, underscoring CEUS's strong diagnostic reliability. These findings highlight CEUS as a valuable imaging modality for identifying various pelvic pathologies in women, particularly in complex or ambiguous cases. The balanced performance metrics support its use as a complementary tool alongside conventional sonography, enhancing diagnostic precision in clinical practice. The review reinforces CEUS's growing role in gynecological diagnostics due to its noninvasive and detailed imaging capabilities.[12]

CONCLUSION

In conclusion, this systematic review emphasizes the significant role of contrast-enhanced ultrasonography (CEUS) in the assessment of uterine disorders. The studies included in this review demonstrated that CEUS provides valuable diagnostic accuracy for a range of uterine conditions, including endometrial lesions, uterine leiomyomas, atypical adenomyosis, and endometrial polyps. With high sensitivity, specificity, and positive predictive values, CEUS proves to be a reliable tool in detecting and characterizing uterine pathologies, offering an advantage over conventional ultrasound methods. This review highlights the clinical utility of CEUS as an advanced imaging modality for uterine disorders, supporting its incorporation into routine gynecological practice. However, variability in diagnostic measures across studies suggests the need for further standardization and research to fully optimize its use in clinical settings.

Limitations and Future Research

One limitation of CEUS in assessing uterine disorders is the lack of standardized protocols, as different studies use varying contrast agents and techniques, making comparison difficult. Another

limitation is its operator dependency, where variations in skill and experience can impact image quality and diagnostic accuracy, highlighting the need for consistent training and standardization. Future research should focus on standardizing contrast-enhanced ultrasonography (CEUS) protocols, including contrast agents and imaging techniques, to ensure consistency across studies and improve comparability. Additionally, further studies should aim to assess the long-term clinical outcomes of CEUS in the diagnosis and management of uterine disorders, particularly its role in guiding treatment decisions and improving patient prognosis.

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