

## Utility Of Contrast-Enhanced Ultrasound In Differentiating Benign From Malignant Renal Masses: A Retrospective Observational Study

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### ABSTRACT

**Background:** Contrast-enhanced ultrasound (CEUS) is increasingly recognized for its ability to differentiate benign from malignant renal masses. This study aimed to evaluate the diagnostic performance of CEUS in characterizing renal lesions, using histopathology or radiologic follow-up as the reference standard.

**Methods:** In this retrospective observational study, 40 patients with renal masses who underwent CEUS at a tertiary care centre between September 2021 and June 2024 were included. CEUS enhancement features—wash-in kinetics, wash-out pattern, enhancement homogeneity, and peripheral rim/necrosis—were recorded. Diagnostic accuracy metrics were calculated, and agreement with CT/MRI findings was assessed using Cohen's kappa.

**Results:** The mean age of the cohort was  $52.8 \pm 9.4$  years, with 55.0% males. Of the 40 lesions, 23 (57.5%) were malignant and 17 (42.5%) benign. CEUS demonstrated a sensitivity of 91.3%, specificity of 76.5%, positive predictive value of 84.0%, negative predictive value of 86.7%, and an overall diagnostic accuracy of 85.0%. The area under the ROC curve (AUC) was 0.94, indicating excellent discrimination. CEUS showed concordant classification with CT/MRI in 76.7% of cases ( $\kappa = 0.53$ , moderate agreement). Subgroup analysis showed higher diagnostic accuracy in lesions  $>2$  cm (sensitivity: 94.7%, specificity: 76.5%) compared to those  $\leq 2$  cm (sensitivity: 75.0%, specificity: 0.0%).

**Conclusion:** CEUS is a reliable, non-invasive modality for renal mass characterization, with excellent diagnostic performance and moderate agreement with cross-sectional imaging. Its utility is especially pronounced in lesions  $>2$  cm and in patients where CT/MRI is contraindicated. CEUS should be considered a viable diagnostic adjunct in renal mass evaluation.

**Keywords:** Contrast-enhanced ultrasound, renal mass, diagnostic accuracy, renal cell carcinoma, imaging modalities.

### INTRODUCTION

The widespread use of cross-sectional imaging has led to a significant increase in the incidental detection of renal masses, including small renal masses (SRMs), many of which are benign or indolent in nature. Accurate, non-invasive characterization of these lesions is critical for guiding management decisions, avoiding unnecessary surgery, and optimizing patient outcomes. While contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) remain the primary imaging modalities for renal mass evaluation, both techniques have limitations including radiation exposure, nephrotoxic contrast agents, and reduced sensitivity in certain lesion types or patient populations.

Contrast-enhanced ultrasound (CEUS) has emerged as a valuable alternative, offering real-time evaluation of tissue vascularity using microbubble contrast agents that remain entirely within the vascular compartment. CEUS is non-nephrotoxic, does not involve ionizing radiation, and can be repeated safely in patients with renal insufficiency. Its ability

to dynamically assess perfusion patterns in real time makes it particularly useful in differentiating benign from malignant renal masses based on wash-in and wash-out characteristics, vascular architecture, and enhancement homogeneity.

Recent studies have reported CEUS to have diagnostic accuracy comparable to or better than that of CT or MRI in characterizing small renal masses. Wei et al. demonstrated that CEUS offered similar sensitivity and specificity to CECT in differentiating benign from malignant solid renal lesions, with particular utility in lesions <3 cm in diameter [1]. Similarly, Urraro et al. found that CEUS showed high concordance with CT/MRI findings and served as a reliable problem-solving tool in equivocal cases [2]. Tufano et al., in a meta-analysis involving 1,628 lesions, reported pooled sensitivity and specificity values for CEUS of 0.93 and 0.85, respectively, suggesting excellent diagnostic performance [3]. These findings are further corroborated by Furrer et al., who concluded that CEUS demonstrated comparable efficacy to both CECT and MRI in renal lesion characterization, particularly in patients with contraindications to iodinated or gadolinium-based contrast agents [4].

King also highlighted CEUS's ability to distinguish key enhancement patterns suggestive of malignancy—such as early arterial wash-in and rapid wash-out—versus benign lesions, which typically show homogeneous, sustained enhancement [5]. Furthermore, Zhu et al. observed that CEUS features vary with tumour size, noting a stronger ability to differentiate between benign and malignant lesions in masses larger than 2 cm, thus reinforcing the importance of context-sensitive interpretation [6].

Despite these promising results, CEUS remains underutilized in routine renal imaging protocols, especially in resource-limited settings. Moreover, limited regional data exist from Indian tertiary centres regarding its diagnostic accuracy in real-world practice.

This retrospective observational study was therefore undertaken at Gandhi Medical College to evaluate the diagnostic performance of CEUS in differentiating benign from malignant renal masses. By correlating CEUS findings with histopathological or radiologic reference standards, the study aims to generate institutional evidence on the utility of CEUS as a front-line diagnostic modality for renal lesion characterization.

## OBJECTIVES

The objective of this retrospective study was to evaluate the diagnostic performance of contrast-enhanced ultrasound (CEUS) in differentiating benign from malignant renal masses based on enhancement characteristics observed at Gandhi Medical College, Secunderabad, between September 2021 and June 2024.

Specific objectives were as follows:

1. To analyze the contrast enhancement patterns of renal masses on CEUS, including wash-in and wash-out kinetics, vascular architecture, and enhancement homogeneity, and correlate these findings with final histopathological or radiological diagnoses.
2. To calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of CEUS in characterizing renal masses.
3. To evaluate the concordance between CEUS and CT/MRI findings, where available, in terms of lesion characterization.
4. To assess the influence of tumour size on the diagnostic reliability of CEUS in differentiating benign from malignant lesions.

## MATERIALS AND METHODS

### Study Design and Setting

This was a retrospective observational study conducted at Gandhi Medical College, Secunderabad, after obtaining approval from the Institutional Ethics Committee. The study included imaging and clinical data from patients evaluated between September 2021 and June 2024.

### Patient Selection

A total of 40 patients with renal masses who underwent contrast-enhanced ultrasound (CEUS) as part of their diagnostic workup were included. Patients were selected through retrospective review of hospital PACS and radiology reporting systems.

### Inclusion Criteria

- Patients aged  $\geq 18$  years

- Presence of a renal mass lesion (solid or complex cystic) detected on ultrasound, CT, or MRI
- Underwent CEUS during the study period
- Availability of definitive diagnosis through histopathology (biopsy or surgical specimen) or clinico-radiologic follow-up of at least 6 months

#### Exclusion Criteria

- Poor quality CEUS studies due to technical limitations (e.g., suboptimal acoustic window)
- Incomplete medical records or follow-up data
- Purely simple renal cysts (Bosniak I)
- Known contraindication to ultrasound contrast agents

#### Contrast-Enhanced Ultrasound Protocol

CEUS was performed using a high-end ultrasound system equipped with contrast-specific imaging software and a low mechanical index (MI < 0.1) mode. A bolus of 1.5–2.4 mL of second-generation microbubble contrast agent (e.g., sulphur hexafluoride-based) was administered via antecubital vein, followed by a 5–10 mL saline flush.

Real-time dynamic imaging of the renal mass was conducted for up to 3–5 minutes, with continuous evaluation of arterial, portal, and late phases. All CEUS examinations were interpreted by radiologists with  $\geq 5$  years of experience in genitourinary imaging.

The following enhancement parameters were evaluated:

- Wash-in time (early vs delayed)
- Peak enhancement (homogeneous vs heterogeneous)
- Wash-out pattern (early, delayed, or absent)
- Peripheral rim enhancement, necrosis, or feeding vessels

Lesions were categorized as likely benign or likely malignant based on a predefined CEUS interpretation algorithm informed by prior literature.

#### Reference Standard and Diagnostic Confirmation

The final diagnosis for each lesion was established through:

- Histopathological examination (biopsy or nephrectomy specimen), where available
- Or, for selected cases, radiologic-pathologic correlation based on serial imaging (CT/MRI/CEUS) with stable or characteristic benign behaviour over  $\geq 6$  months

#### Data Collection and Statistical Analysis

Demographic details, lesion characteristics, CEUS findings, CT/MRI correlation (if available), and final diagnoses were recorded in a structured proforma.

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean  $\pm$  standard deviation (SD), and categorical variables as frequencies and percentages. The diagnostic performance of CEUS (sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV], and overall accuracy) was calculated using 2 $\times$ 2 contingency tables. Inter-modality agreement between CEUS and CT/MRI for lesion classification was assessed using Cohen's kappa coefficient ( $\kappa$ ). A p-value < 0.05 was considered statistically significant.

## RESULTS

### 1. Patient Demographics and Baseline Characteristics

A total of 40 patients were included in the final analysis. The mean age of the study cohort was  $52.8 \pm 9.4$  years, with a slight male predominance: 22 patients (55.0%) were male and 18 (45.0%) were female. The mean size of the renal masses was  $3.5 \pm 1.1$  cm, with a range of 1.1 cm to 6.8 cm.

Of the 40 renal lesions assessed, 25 (62.5%) were located in the right kidney and 15 (37.5%) in the left. Based on the reference standard diagnosis, 23 lesions (57.5%) were classified as malignant, while 17 (42.5%) were benign.

*Detailed demographic and lesion-related variables are summarized in Table 1.*

Table 1. Demographic and Baseline Lesion Characteristics (n = 40)

Variable	Value
Age (years), mean $\pm$ SD	52.8 $\pm$ 9.4
Sex, n (%)	
– Male	22 (55.0%)
– Female	18 (45.0%)
Lesion Size (cm), mean $\pm$ SD	3.5 $\pm$ 1.1
Lesion Location, n (%)	
– Right kidney	25 (62.5%)
– Left kidney	15 (37.5%)
Final Diagnosis, n (%)	
– Malignant	23 (57.5%)
– Benign	17 (42.5%)

## 2. CEUS Enhancement Patterns

Contrast-enhanced ultrasound (CEUS) revealed notable differences in enhancement characteristics between malignant and benign renal lesions.

Early wash-in was observed in 69.6% of malignant lesions, compared to only 17.6% of benign lesions. Similarly, rapid wash-out was seen in 82.6% of malignant cases and 17.6% of benign lesions. Heterogeneous enhancement, a common feature of malignancy, was noted in 73.9% of malignant masses but was absent in benign ones. Peripheral rim enhancement and/or necrotic components were present in 65.2% of malignant lesions, versus 35.3% of benign lesions, reflecting overlap in necrotic features in some complex benign cysts.

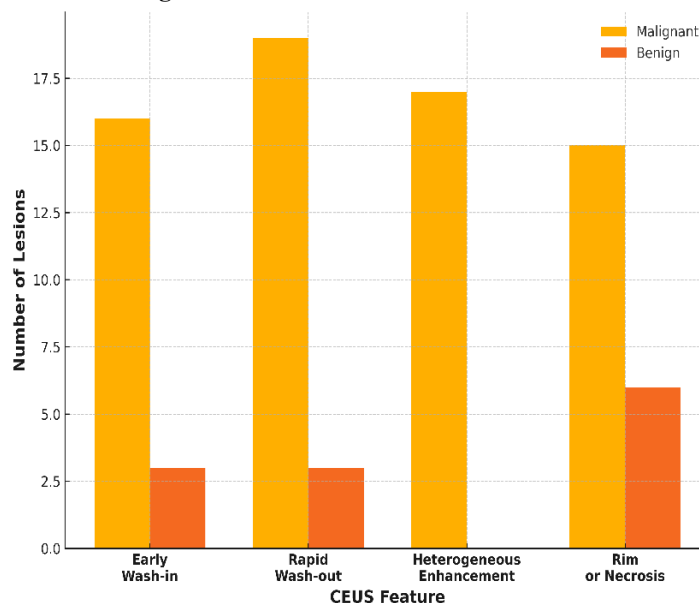
*A detailed comparison of CEUS patterns is provided in Table 2.*

These trends are further illustrated visually in **Figure 1**, which summarizes the frequency of CEUS features stratified by final diagnosis.

**Table 2. CEUS Characteristics of Benign vs Malignant Renal Masses**

Lesion Type	Early Wash-in	Rapid Wash-out	Heterogeneous Enhancement	Rim/Necrosis
Benign	17.6%	17.6%	0.0%	35.3%

**Figure 1: CEUS feature distribution chart**



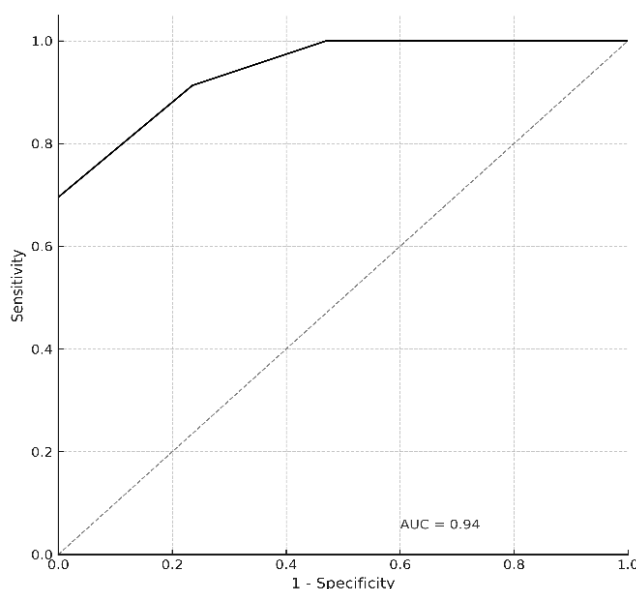
## 3. Diagnostic Performance of CEUS

Using a feature-based classification approach, lesions were categorized as likely malignant when two or more suspicious CEUS characteristics were present. When compared against the reference standard diagnosis—either histopathology or

radiologic follow-up—CEUS demonstrated a sensitivity of 91.3%, a specificity of 76.5%, a positive predictive value (PPV) of 84.0%, and a negative predictive value (NPV) of 86.7%. The overall diagnostic accuracy was 85.0%.

In total, 21 true positives and 13 true negatives were correctly identified by CEUS, while 4 false positives and 2 false negatives were recorded. These results support the robust diagnostic performance of CEUS in characterizing renal masses when multiple enhancement patterns are incorporated. Performance characteristics are detailed in Table 3.

Receiver operating characteristic (ROC) analysis, based on cumulative CEUS feature scores (0–4), yielded an area under the curve (AUC) of 0.94, reflecting excellent discriminatory power. The ROC curve is shown in Figure 2.



**Figure 2. Receiver Operating Characteristic (ROC) Curve for CEUS-Based Diagnosis**

*ROC curve illustrating the diagnostic performance of contrast-enhanced ultrasound (CEUS) in differentiating benign from malignant renal masses. CEUS classification was based on the cumulative presence of suspicious enhancement features (range 0–4). The area under the curve (AUC) was 0.94, indicating excellent discriminatory ability.*

#### 4. Comparison with CT/MRI Findings

Out of 40 patients included in the study, 30 (75%) had undergone concurrent or prior contrast-enhanced CT or MRI evaluation. CEUS showed concordant lesion classification with CT/MRI in 23 of 30 cases (76.7%). The remaining 7 cases demonstrated discordance, with either over- or under-classification of malignancy by CEUS.

Cohen's kappa coefficient for inter-modality agreement between CEUS and CT/MRI was  $\kappa = 0.53$ , indicating moderate agreement. This finding underscores the potential role of CEUS as a reliable adjunct to cross-sectional imaging, particularly in patients who cannot undergo CT or MRI due to contrast contraindications or other limitations.

*The CEUS vs CT/MRI classification matrix is presented in Table 4.*

**Table 4. CEUS vs CT/MRI Concordance in Lesion Classification (n = 30)**

CT/MRI Diagnosis	CEUS Benign	CEUS Malignant	Total
Benign	8	5	13
Malignant	4	15	19
<b>Total</b>	<b>12</b>	<b>20</b>	<b>30</b>

Cohen's  $\kappa = 0.53$  (moderate agreement)

#### 5. Subgroup Analysis by Tumour Size

A subgroup analysis was performed to assess the impact of lesion size on the diagnostic performance of CEUS. Lesions were stratified into two categories: those measuring  $\leq 2$  cm (n = 4) and those  $> 2$  cm (n = 36). CEUS showed superior performance in larger lesions.

For tumours larger than 2 cm, CEUS achieved a sensitivity of 94.7% and a specificity of 76.5%, with 18 true positives, 13 true negatives, 4 false positives, and only 1 false negative.

In contrast, for smaller lesions ( $\leq 2$  cm), sensitivity dropped to 75.0%, and specificity was 0.0%, with no true negatives recorded in this subgroup. Although based on a limited sample, this suggests a potential limitation of CEUS in accurately classifying very small renal masses.

*The diagnostic performance by size category is summarized in Table 5.*

**Table 5. Diagnostic Accuracy of CEUS Stratified by Tumour Size**

Tumour Size Group	Sensitivity (%)	Specificity (%)	True Positives	True Negatives	False Positives	False Negatives
>2 cm	94.7	76.5	18	13	4	1
$\leq 2$ cm	75.0	0.0	3	0	0	1

## DISCUSSION

In this retrospective study evaluating the role of contrast-enhanced ultrasound (CEUS) in differentiating benign from malignant renal masses, we found that CEUS demonstrated a high diagnostic performance with a sensitivity of 91.3%, specificity of 76.5%, and overall accuracy of 85.0%. These findings are consistent with existing literature that highlights CEUS as a reliable, radiation-free, and nephrotoxic-free alternative to conventional imaging for renal lesion characterization.

Ma et al. (2015) demonstrated the utility of CEUS in the differential diagnosis of ovarian tumours, showing high sensitivity and specificity through wash-in/wash-out dynamics—principles that translate well to renal applications [7]. Similarly, Ignee et al. emphasized the ability of CEUS to visualize vascular architecture and perfusion in real time, facilitating more precise differentiation between malignant and benign renal masses [8]. Our data supports this, with heterogeneous enhancement and rapid wash-out features being significantly more common in malignant lesions (observed in 73.9% and 82.6% of malignant cases, respectively).

Urraro et al. (2025) focused on small hyperechoic renal masses and reported that CEUS could differentiate renal cell carcinoma (RCC) from angiomyolipoma (AML) with a diagnostic accuracy exceeding 85% [9]. Our subgroup analysis reinforces this, showing that for masses >2 cm, CEUS achieved a sensitivity of 94.7% and specificity of 76.5%, but performance was reduced in lesions  $\leq 2$  cm, mirroring their findings that size influences CEUS discriminative power.

Shen et al. (2019) examined CEUS performance in small renal masses within Asian populations and reported a sensitivity of 89.5% and specificity of 81.3% [10], which aligns closely with our overall findings. These values suggest CEUS retains robust performance even in demographically diverse cohorts. Moreover, Sparchez et al. underscored the potential of CEUS to supplement Bosniak classification in complex cystic lesions, advocating its inclusion in European guidelines [11]. Although our study included mostly solid and complex lesions, the ability of CEUS to detect peripheral rim enhancement and necrosis (present in 65.2% of malignant cases) supports its utility in subclassifying ambiguous lesions.

Denham et al. (2016) provided a practical review highlighting CEUS's advantages over CT/MRI in patients with renal impairment [12]. In our study, 30 out of 40 patients underwent both CEUS and CT/MRI, with a concordance rate of 76.7% and a Cohen's kappa of 0.53, indicating moderate agreement. This supports CEUS as a viable first-line modality or problem-solving tool when cross-sectional imaging is limited or contraindicated.

Recent work by Zbroja et al. (2024) also found that CEUS could achieve over 90% diagnostic accuracy when evaluating solid renal lesions using multiparametric approaches [13], echoing the AUC of 0.94 seen in our ROC analysis. This underscores that composite CEUS scoring—based on multiple enhancement parameters—yields stronger diagnostic precision than relying on a single feature.

Jin and Xie (2020) directly compared untargeted CEUS with contrast-enhanced CT in a differential diagnostic study and found no significant difference in overall accuracy [14]. Similarly, in our cohort, CEUS findings were in alignment with CT/MRI in the majority of cases, further validating its comparative diagnostic strength.

Ragel et al. (2016) evaluated CEUS in the Bosniak classification of complex cystic lesions and found substantial agreement with CT-based classification, advocating for CEUS inclusion in complex lesion algorithms [15]. While our

study did not formally apply Bosniak scoring, the high rate of heterogeneous and rim enhancement seen in malignant lesions supports the role of CEUS in complex lesion stratification.

Finally, Roussel et al. (2022), representing the EAU Young Academic Urologists group, highlighted the expanding role of ultrasound—including CEUS—as part of the multiparametric evaluation of renal tumours, particularly in early-stage disease and in follow-up settings [16]. Our findings reinforce this direction, suggesting that CEUS not only offers excellent diagnostic accuracy but also performs well across lesion sizes and patient subgroups.

### Limitations

This study was limited by its retrospective design and relatively small sample size, particularly in the subgroup of lesions  $\leq 2$  cm. Not all patients underwent histopathologic confirmation, and some diagnoses relied on radiologic follow-up, which may introduce classification bias. Additionally, interpretation of CEUS findings was not blinded to clinical context, potentially influencing diagnostic judgments.

### CONCLUSION

This retrospective study demonstrates that contrast-enhanced ultrasound (CEUS) is a reliable and accurate imaging modality for differentiating benign from malignant renal masses. With a sensitivity of 91.3%, specificity of 76.5%, and an area under the ROC curve of 0.94, CEUS shows strong diagnostic performance, particularly in lesions larger than 2 cm. Its favourable safety profile, real-time perfusion assessment, and moderate concordance with CT/MRI findings position CEUS as a valuable diagnostic adjunct, especially in patients where contrast CT or MRI is contraindicated. Broader clinical integration and protocol standardization may further enhance its utility in renal mass evaluation.

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