Diagnostic Accuracy of Contrast-Enhanced Ultrasonography for the Assessment of Small Renal Mass: A Prospective Study

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Purpose: We prospectively compared the diagnostic accuracy of kidney dynamic computed tomography (KDCT), magnetic resonance imaging (MRI), and contrast-enhanced ultrasonography (CEUS) for the assessment of small renal mass (SRM) (≤4 cm).

Materials and Methods: Seventy-six patients with SRM (mean age, 58.4±13.1 years) who underwent renal biopsy (n=11) or nephrectomy (partial or radical) (n=65) were enrolled. All patients underwent KDCT, MRI, and CEUS before renal biopsy or nephrectomy.

Results: The mean maximal tumor size was 21.0±9.8 mm. The mean R.E.N.A.L nephrometry score was 7.0±1.7. Fifty-six patients had renal cell carcinoma (RCC) (clear cell, 42; papillary, 7; chromophobe, 5; succinate dehydrogenase deficient, 1; unspecified RCC, 1). Twenty patients had a benign tumor (angiomyolipoma, 11; oncocytoma, 3; others, 6). Clinicopathologic variables were comparable in RCC and benign groups. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of KDCT were 89.3%, 10.0%, 73.5%, and 25.0%, respectively. The sensitivity, specificity, PPV, and NPV of MRI were 89.3%, 10.0%, 73.5%, and 25.0%, respectively. The sensitivity, specificity, PPV, and NPV of CEUS were 85.7%, 50.0%, 82.8%, and 55.6%, respectively. The diagnostic accuracy of KDCT, MRI, and CEUS were 68.4%, 68.4%, and 76.3%, respectively. In a subgroup analysis based on clinical tumor size of 10 mm and 20 mm, CEUS also showed the highest diagnostic accuracy.

Conclusions: CEUS had the highest specificity, PPV, and NPV and may help improve the assessment of SRM.

Key Words: Small renal mass, Computed tomography, Magnetic resonance imaging, Contrast-enhanced ultrasonography

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Research Ethics: This study was approved by the Institutional Review Board (IRB) of Kyungpook National University, School of Medicine, Daegu, Republic of Korea (IRB No. 2022-06-038). The study complied with the applicable laws and regulations, good clinical practices, and the ethical principles enshrined in the Declaration of Helsinki. The board exempted the requirement for informed consent because it was a retrospective study.
Conflicts of Interest: The authors have nothing to disclose.
INTRODUCTION

Renal cancer is the third most frequent urogenital tumor worldwide after prostate and bladder cancers [1]. In the United States, an estimated 81,800 new cases of renal cancer were diagnosed in 2023 and around 14,890 deaths due to renal cancer occur every year [2]. Likewise, in South Korea, renal cancer is the second most frequent urogenital tumor after prostate cancer, with an estimated 6,823 new cases diagnosed in 2023 and approximately 1,071 deaths occurring every year [3]. Renal cell carcinoma (RCC) accounts for nearly 80%–85% of all renal cancers [4]. Clear cell RCC is the most common pathologic subtype of RCC, accounting for 70%–80% of all newly diagnosed cases of RCC [1].

The widespread use of cross-sectional imaging for diagnostic workup, such as computed tomography (CT), has contributed to the increased incidence of RCC over the past decade, especially low-grade RCC [5]. The increased incidence is in large part attributable to the increased detection of small renal mass (SRM), defined as a renal mass of ≤4 cm in maximum diameter [6]. Not all SRMs are RCC and 15%–20% of SRMs are benign. SRM is potentially aggressive in only 10% of cases [7]. While some SRMs may be malignant, many exhibit an indolent biological behavior [8].

Therefore, the ability to determine whether SRM is malignant or benign can offer a distinct leverage in clinical settings. However, there is a paucity of studies that have correlated the findings of kidney dynamic CT (KDCT), magnetic resonance imaging (MRI), and contrast-enhanced ultrasonography (CEUS) with histopathological diagnosis. In 2018, our center published a unique experience with the use of CEUS as a diagnostic modality for cystic renal mass for the first time in South Korea [9].

In the present study, we compared the diagnostic accuracy of KDCT, MRI, and CEUS for the assessment of SRMs.

MATERIALS AND METHODS

1. Study Population

This was a prospective single-center study conducted from January 2021 to July 2023. Eighty-seven patients were enrolled in this study. All eligible patients were counseled regarding the aim and protocol of the study, and only patients who consented to participate were enrolled. The inclusion criteria were: (1) patients in whom SRM was detected in initial KDCT and who were willing to undergo MRI and CEUS; (2) patients who were scheduled to undergo partial/radical nephrectomy or renal biopsy. Patients with chronic kidney disease (estimated glomerular filtration rate <60 mL/min/body surface area) and those who refused to undergo nephrectomy or renal biopsy were excluded. The Eastern Cooperative Oncology Group performance status of all patients was 0 or 1. The clinical data, including demographic characteristics, radiologic findings, and pathologic outcomes were analyzed.

2. Study Design

A schematic illustration of the study design is presented in Fig. 1. A total of 102 patients were screened, of which 15 patients refused additional imaging study (n=11) or tissue confirmation (n=4). Therefore, 87 patients were enrolled. Of these, 11 patients withdrew informed consent. Finally, 76 patients who satisfied the study eligibility criteria were included. Sixty-five patients underwent nephrectomy (partial, 64; radical, 1) and 11 patients underwent renal biopsy.

A partial or radical nephrectomy was performed by the same urologist (JWC). Renal biopsy and interpretation of KDCT/MRI/CEUS were performed by 2 expert uro-radiologists (SYP and SHK). Two uro-radiologists were blinded to the patients’ previous KDCT and MRI findings at the time of CEUS. The urologic research nurses (SHW, YAK) only informed them about the laterality of SRM.

Pathologic tissue confirmation was done by the same uropathologist (GSY). Data pertaining to clinical information, radiological results, and pathological results were maintained by 2 urologic specialist research nurses who were blinded to the investigators. None of the patients in this study required repeat renal biopsy or had an uncertain diagnosis.

3. Statistical Analysis

Student t-test was used for the analysis of continuous variables. The chi-square test or Fisher exact test was used for categorical variables. Statistical analyses were performed
using IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA). A p-value of <0.05 was considered indicative of statistical significance.

**RESULTS**

The clinical characteristics of patients are summarized in Table 1 (n=76). Fifty-six patients were diagnosed as having RCC and 20 patients had a benign renal tumor. Males accounted for 55.3% (42 of 76) of patients. The mean age of patients was 58.4±13.1 years and the mean body mass index was 26.2±4.8 kg/m$^2$. The mean maximal tumor size was 21.0±9.8 mm. The RCC group showed a significantly higher R.E.N.A.L nephrometry score than the benign group (7.2±1.6 vs. 6.3±1.9, p=0.032). There was no significant difference between the 2 groups regarding tumor laterality (right vs. left) or location (anterior vs. posterior). Nephrectomy was performed more frequently in the RCC group (91.1%, 70.0%, p=0.031).

Table 2 shows the final pathologic outcomes. In the RCC group (n=56), 42 patients had clear cell RCC, 7 had papillary RCC, 5 had chromophobe RCC, 1 had succinate dehydrogenase deficient RCC, and 1 had unclassified RCC. In the benign group (n=20), 11 patients had angiomyolipoma, 3 had oncocytoma, and 6 had other benign tumors.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each imaging modality are listed in Table 3 and 4. The sensitivity, specificity, PPV, and NPV of KDCT were 89.3%, 10.0%, 73.5%, and 25.0%, respectively. The sensitivity, specificity, PPV, and NPV of MRI were 89.3%, 10.0%, 73.5%, and 25.0%, respectively. The sensitivity, specificity, PPV, and NPV of CEUS were 85.7%, 50.0%, 82.8%, and 55.6%, respectively. The diagnostic accuracy of KDCT, MRI, and CEUS were 68.4%, 68.4%, and 76.3%, respectively.

Table 5 shows a subgroup analysis based on clinical tumor size of 10 mm and 20 cm. The results were same. CEUS showed the highest specificity, PPV, NPV, and diagnostic accuracy in all 3 subgroups.

**DISCUSSION**

This study compared the diagnostic performance of KDCT, MRI, and CEUS for the assessment of SRM. CEUS showed the highest specificity, PPV and NPV.

The increasing incidence of RCC over the past 3 decades is mainly due to the increasing use of cross-sectional abdominal imaging for unrelated symptoms. In cross-sectional imaging, renal masses are often identified as incidental findings. These lesions need to be discerned by follow-up or pathologic confirmation, which has considerable cost implications [6].

SRMs account for the largest proportion of incidentally detected renal masses [10]. Not all SRMs are RCC, and
incidentally detected SRMs are more likely to be benign [11].
The size of SRM correlates with the risk of malignancy. In
a large series of 2,770 renal tumors, 46.3% of renal masses
smaller than 1 cm were benign [11]. In the same series,
increasing mass size was associated with a higher risk of
RCC.

Owing to the widespread utilization of imaging, the
median age at RCC diagnosis has also increased. The greatest
increase in incidence has been seen in patients aged >70
years [12]. Therefore, active surveillance is currently the
initial management option for these patients [5]. In this
context, identification of methods that can increase the
diagnostic accuracy of SRM is of much clinical importance.

Characterization of indeterminate renal masses, especially
SRM, is a common clinical challenge for both urologists and
radiologists [13]. SRMs are often discovered incidentally on
ultrasonography (USG) or on a CT or MRI performed for
another purpose. Often, no unenhanced images are available
for some patients, or only unenhanced images have been

### Table 1. Demographic and clinical characteristics of the study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=76)</th>
<th>RCC (n=56)</th>
<th>Benign (n=20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>42 (55.3)</td>
<td>34 (60.7)</td>
<td>8 (40.0)</td>
<td>0.110</td>
</tr>
<tr>
<td>Female</td>
<td>34 (44.7)</td>
<td>22 (39.3)</td>
<td>12 (60.0)</td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>58.4±13.1</td>
<td>58.7±12.4</td>
<td>54.3±14.6</td>
<td>0.138</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.2±4.8</td>
<td>26.5±4.1</td>
<td>25.4±6.5</td>
<td>0.520</td>
</tr>
<tr>
<td>Maximal tumor size (mm)</td>
<td>21.0±9.8</td>
<td>21.5±9.7</td>
<td>19.7±10.2</td>
<td>0.472</td>
</tr>
<tr>
<td>Maximal tumor size (mm) ≤10</td>
<td>9 (11.8)</td>
<td>5 (8.9)</td>
<td>4 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Maximal tumor size (mm) &gt;10, ≤20</td>
<td>36 (47.4)</td>
<td>27 (48.2)</td>
<td>9 (45.0)</td>
<td></td>
</tr>
<tr>
<td>Maximal tumor size (mm) &gt;20, ≤40</td>
<td>31 (40.8)</td>
<td>24 (42.9)</td>
<td>7 (35.0)</td>
<td></td>
</tr>
<tr>
<td>R.E.N.A.L nephrometry score</td>
<td>7.0±1.7</td>
<td>7.2±1.6</td>
<td>6.3±1.9</td>
<td>0.032</td>
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<tr>
<td>Laterality</td>
<td></td>
<td></td>
<td></td>
<td>0.426</td>
</tr>
<tr>
<td>Right</td>
<td>40 (52.6)</td>
<td>31 (55.4)</td>
<td>9 (45.0)</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>36 (47.4)</td>
<td>25 (44.6)</td>
<td>11 (55.0)</td>
<td></td>
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<tr>
<td>Tumor location</td>
<td></td>
<td></td>
<td></td>
<td>0.329</td>
</tr>
<tr>
<td>Anterior</td>
<td>45 (59.2)</td>
<td>35 (62.5)</td>
<td>10 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>31 (40.8)</td>
<td>21 (37.5)</td>
<td>10 (50.0)</td>
<td></td>
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<tr>
<td>Methods of tissue confirmation</td>
<td></td>
<td></td>
<td></td>
<td>0.031*</td>
</tr>
<tr>
<td>Nephrectomy</td>
<td>65 (85.5)</td>
<td>51 (91.1)</td>
<td>14 (70.0)</td>
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<tr>
<td>Renal biopsy</td>
<td>11 (14.5)</td>
<td>5 (8.9)</td>
<td>6 (30.0)</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as number (%) or mean±standard deviation.
RCC, renal cell carcinoma.
*Fisher exact test.

### Table 2. Pathologic outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCC (n=56)</td>
<td></td>
</tr>
<tr>
<td>Clear cell RCC</td>
<td>42</td>
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<tr>
<td>Papillary RCC</td>
<td>7</td>
</tr>
<tr>
<td>Chromophobe RCC</td>
<td>5</td>
</tr>
<tr>
<td>Succinate dehydrogenase deficient RCC</td>
<td>1</td>
</tr>
<tr>
<td>Unclassified</td>
<td>1</td>
</tr>
<tr>
<td>Benign (n=20)</td>
<td></td>
</tr>
<tr>
<td>Angiomyolipoma</td>
<td>11</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>3</td>
</tr>
<tr>
<td>Other benign tumor</td>
<td>6</td>
</tr>
</tbody>
</table>

RCC, renal cell carcinoma.

### Table 3. Diagnostic performance of various imaging modalities

<table>
<thead>
<tr>
<th>Imaging modality type</th>
<th>Pathologic outcomes</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benign</td>
<td>RCC</td>
</tr>
<tr>
<td>KDCT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>RCC</td>
<td>18</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>56</td>
</tr>
<tr>
<td>MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>RCC</td>
<td>18</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>56</td>
</tr>
<tr>
<td>CEUS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>RCC</td>
<td>10</td>
<td>48</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>56</td>
</tr>
</tbody>
</table>

KDCT, kidney dynamic computed tomography; RCC, renal cell carcinoma; MRI, magnetic resonance imaging; CEUS, contrast-enhanced ultrasound.
obtained due to contraindications for the use of contrast media, such as impaired renal function. Standard USG has a low contrast resolution and high acoustic disturbance, and Doppler offers limited value for the detection of microvessels [14]. This explains the need to use CT and MRI to assess or characterize the nature of SRM [15]. However, in case of subtle septations or nodular lesions within renal masses, discerning enhancement on CT or MRI can be challenging due to factors such as image noise, partial volume effects, and the phenomenon of pseudoenhancement.

To overcome these limitations of CT or MRI, CEUS is increasingly used for the investigation of renal masses. The use of CEUS for assessing renal masses may reduce the need for CT, minimizing radiation risks, or the more expensive MRI. Furthermore, in the absence of renal or hepatic limitations, CEUS is invaluable for patients with renal insufficiency.

Our center’s previous study in 2018 [9] introduced our ‘novel experience of CEUS to differentiate between renal cysts and RCC’. CEUS is the newest diagnostic tool to detect vascularization using intravenous contrast agents containing microbubbles [16]. Contrast agents used in CEUS are intravascular agents and do not extravasate from blood vessels, unlike many contrast agents used for CT and MRI. The CEUS contrast materials are neither nephrotoxic nor hepatotoxic and have a short half-life of approximately 5 minutes, facilitating multiple inspections within a single session. Software specific to contrast material facilitates the subtraction of background tissue from the image, thereby enhancing the detection of even subtle ultrasonic contrast enhancement. Such minimal enhancements might not be detectable in contrast-enhanced CT or MRI due to the potential blending of the contrast agent with the surrounding tissue [13]. Furthermore, the narrow ultrasonic beam width enhances the clarity of microvasculature in minute structures, such as septations or diminutive mural nodules. The renal vascular enhancement patterns observed in CEUS are similar to the arterial phase of CT and MRI. However, in the delayed phase, the enhancement pattern is quite different between them due to the nonextravasative nature of the
CEUS agent.

Benign solid tumors such as oncocyotoma and malignant tumors such as RCC exhibit similar enhancement patterns in CT and MRI. The central stellate scar and spoke-wheel pattern of feeding arteries in oncocyotoma are unreliable diagnostic signs for preoperative differential diagnosis and have poor predictive value [17]. Therefore, enhancing solid renal lesions should be managed as RCC with curative intent based on the clinical context. However, due to the strength of suppression of background parenchymal tissue, CEUS is superior in revealing the blood flow within hypovascular lesions compared to CT. It is challenging to distinguish angiomyolipoma from echogenic RCC. In our study, the enhancement of angiomyolipoma was inferior to that of the renal cortex during the arterial phase, often manifesting a peripheral distribution (Fig. 2). In contrast, echogenic RCCs consistently display a diffuse and intense enhancement followed by a washout phase.

Two previous studies are similar to our study. In 2015, Bertolotto et al. [18] retrospectively analyzed the role of CEUS in the characterization of renal masses with equivocal enhancement on CT. Forty-seven renal lesions with equivocal enhancement at CT were evaluated by CEUS. Although histologic results were available only for 30 of 47 lesions (64%), they concluded that CEUS is effective for characterizing renal lesions presenting with equivocal enhancement at CT.

In 2017, Defortescu et al. [14] prospectively investigated the diagnostic performance of CEUS and MRI for the assessment of complex renal cysts. They evaluated 47 patients with Bosniak category 2F or 3 renal cysts detected on CT, MRI, or CEUS. CT showed the lowest sensitivity (36%) and specificity (76%; k=0.11). MRI showed 71% sensitivity and 91% specificity (k=0.64). CEUS showed the highest sensitivity (100%) and specificity (97%), and a 100% NPV (k=0.95). In this study, CEUS showed superior sensitivity, specificity, PPV, and NPV in the characterization of renal masses. Although our study did not demonstrate the overwhelming superiority of CEUS in all aspects compared to this previous study, our results were similar in all aspects except for sensitivity. Based on the author’s experience, SRMs frequently present as endophytic lesions. The inherent challenges in detecting these cases with CEUS explain the lower sensitivity of CEUS for such presentations (Fig. 3).

Furthermore, since washout can be directly confirmed

![Fig. 2. Distinguishing angiomyolipoma from echogenic renal cell carcinoma using contrast-enhanced ultrasonography. (A) Angiomyolipoma exhibited enhancement inferior to the renal cortex during the arterial phase, often manifesting a peripheral distribution. The mean regions of interest value of contrast-enhanced ultrasound were 231.05 in mass lesion and 249.48 in renal parenchyma. (B) In ultrasound, it shows an oval echogenic and exophytic mass in medial pole of right kidney.](image)

![Fig. 3. Preoperative contrast-enhanced ultrasound contrast-enhanced ultrasonography of a 63-year-old woman who confirmed as clear cell renal cell carcinoma after robotic partial nephrectomy. Radiologist’s opinion was the intraparenchymal mass lesion suspicious for angiomyolipoma. (A) Magnetic resonance imaging T2-weighted axial scan shows a 15-mm cystic mass lesion in left kidney. (B) In ultrasound, it shows echogenic nodular lesion in gray scale image. (C) In contrast-enhancement ultrasonography, it is difficult to detect due to endophytic lesion.](image)
during CEUS, it would likely be easy to differentiate RCC from angiomyolipoma, which shows relatively gradual enhancement. However, the slightly lower sensitivity in our study was likely attributable to the very high incidence of RCC compared to fat-poor angiomyolipoma. In the previous study, histological confirmation was available only for 19 patients (40.4%) [14]. However, our study had a much larger sample size (n=76) and histological confirmation was available for all patients (100%), which is a strength of our study. Furthermore, we included only SRMs of <4 cm, while the previous study also included neoplasms larger than 4 cm.

The limitations of the present study include the relatively small number of patients (n=76), especially in the benign cohort (n=20). Due to the study design, which required comparison of these 3 imaging modalities with histological confirmation, the proportion of benign patients may have been high. Nevertheless, to the best of our knowledge, this is the first study to compare CT, MRI, and CEUS findings as well as histological confirmation in all patients with SRM. Our findings suggest that CEUS may offer a significant advantage in delineating renal masses in patients in whom the use of CT or MRI contrast agents is contraindicated. Beyond evaluating cystic renal entities, CEUS may also provide invaluable insights into solid renal masses where traditional imaging modalities might not offer conclusive diagnostic clarity.

CONCLUSIONS

CEUS may help improve the assessment of SRM. In this study, CEUS showed the highest specificity, PPV, and NPV. Therefore, CEUS can provide invaluable information for counseling patients who are scheduled to undergo nephrectomy or biopsy.

NOTES

• Author Contribution: Conceptualization: JWC, SYP; Data curation: SW, YAK, JKK; Formal analysis: JKK, JWC, HSY; Funding acquisition: JWC, YSH, JNL, BSK; Methodology: JWC, SYP; Project administration: TGK, SHK, HSY; Visualization: JWC, SW, YAK; Writing - original draft: JWC, SYP; Writing - review & editing: TGK, SHK, THK.

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