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How does contrast-enhanced ultrasonography influence Bosniak classification for complex cystic renal mass compared with conventional ultrasonography?

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Abstract

To analyze the degree and pattern of influence of contrast-enhanced ultrasonography (CEUS) on the Bosniak classification system for complex renal cystic mass as compared with conventional ultrasonography (US). One hundred two consecutive patients with complex renal cystic masses were retrospectively analyzed. The diagnostic performance of the Conventional US and CEUS were evaluated separately for malignant and benign lesions. The diagnostic concordance rates were calculated according to pathologic diagnoses. ROC curve analysis determined the confidence in the diagnostic accuracy by calculating the area under each ROC curve. Compared to the Conventional US, septae number, wall and/or septae thickness, solid component and the Bosniak classification changed in 17 (16.7%), 39 (38.2%), 31 (30.4%), and 67 (65.7%) patients as compared with 0 (0.0%), 21 (20.6%), 31 (30.4%), and 37 (36.3%) of the treatment strategy that changed after CEUS respectively. The diagnostic performance of CEUS showed overall higher in terms of sensitivity (100.0 vs 97.2%); specificity (90.9 vs 62.1%); positive predictive value (PPV) (85.7 vs 58.3%); negative predictive value (NPV) (100.0 vs 97.6%); and the concordance with pathology (kappa = 0.876 vs 0.515). CEUS had a higher diagnostic confidence ($P < .05$) according to the area under the ROC curve (AUC = 0.968 vs 0.799).CEUS performed better than the Conventional US in the diagnosis of complex renal cystic mass, and it might be considered as the first tool to evaluate a complex cystic renal mass, especially for these Bosniak III masses displaying the presence of hemorrhage or infection.

Abbreviations: AUC = area under curve, CECT = contrast-enhanced computed tomography, CEUS = contrast-enhanced ultrasonography, CPS = contrast pulse sequencing, CT = computed tomography, DCE-MRI = dynamic contrast-enhanced magnetic resonance imaging, MI = low mechanical index, MRI = magnetic resonance imaging, NPV = negative predictive value, PPV = positive predictive value, ROC = receiver operating characteristic, SEN = sensitivity, SPE= specificity, US = ultrasonography.

Keywords: Bosniak classification system, complex cystic renal mass, contrast-enhanced ultrasonography, conventional ultrasonography, ultrasonography

1. Introduction

Most renal cell carcinomas are solid; however, up to 8% appear as complex cystic lesions.[1,2] The ability to accurately identify those complex renal cystic masses requiring surgical intervention or continuous surveillance still represents a major challenge to the clinician, especially in the presence of hemorrhage or infection.

The Bosniak classification of complex cystic renal masses has been applied in the evaluation of complex cystic renal mass, and has helped decide subsequent clinical management.[3–5] The Bosniak classification system is now accepted as a familiar effective tool by urologists and radiologists in clinical practice, and there has been general inter-observer agreement in most cases where the system has been adopted.[6,7]

The Bosniak classification system was initially designed to analyze the morphology of a complex cystic renal mass simply based on computed tomography (CT); however, this approach might provide a useful framework when evaluating by contrast-enhanced computed tomography (CECT), magnetic resonance imaging (MRI), dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), conventional ultrasonography (US) and contrast-enhanced ultrasonography (CEUS). Several research studies have demonstrated that CEUS was even better at detecting enhanced septea and tumor vascularity in complex cystic renal masses than contrast-enhanced CT.[8–11] In addition, CEUS has many advantages, including safety, real-time analysis, simplicity, patient tolerance of the procedure, lack of radiation and nephrotoxicity, an ability to provide perfect presentation of blood distribution and flow, as well as being able to provide a prompt diagnosis, so that it is much more acceptable by patients.[12] CEUS evaluation is a highly sensitive and specific method for characterization of indeterminate renal masses.[13] In addition, it has the potential to markedly change the workup and management of cystic renal masses, decreasing the need for unnecessary biopsies and surgery, and selecting patients for surgery that would otherwise be monitored.[14]

In our routine clinical practice, CEUS was used to reassess complex cystic renal mass that was initially found by Conventional US or other imaging modalities. In this study, we present data on a retrospectively identified cohort of patients with complex cystic renal mass. The purpose of this study was to evaluate the influence of the grade of complex renal cystic mass by CEUS with reference to the Bosniak classification system, and to determine the clinical value of CEUS in the diagnosis of a complex cystic renal mass as compared to Conventional US.

2. Patients

We retrospectively reviewed 102 consecutive patients (63 males and 39 females; age range 21–86 years; and a median age of 55.5 years) with newly diagnosed complex renal cystic mass by Conventional US at our hospital between January 2013 and August 2016. The study was approved by the institutional review board of our hospital, and written informed consent was obtained from each participant in our study. All predominantly solid or frankly solid masses were excluded. All patients had undergone both Conventional US and CEUS for the mass assessment before treatment. Both the degree and pattern of influence of CEUS on staging with reference to the Bosniak classification system[3,15] were analyzed as compared to the Conventional US approach.

2.1. Imaging protocol

All Conventional US and CEUS images were acquired by the same experienced doctor who had more than 10 years of working experience, using the Siemens Acuson Sequoia platform (Siemens, Issaquah, WA, USA) with a curved array multifrequency transducer (2–4.5 MHz, a curved array 4 MHz multifrequency transducer). In the contrast-enhanced study, a low mechanical index (MI) of 0.05 to 0.08, a real-time tissue harmonic imaging system (Cadence contrast pulse sequencing (CPS) imaging) and a one-image display mode were used. The examination started with a Conventional US and was followed by CEUS.

Informed consent was signed after the procedure had been fully explained. After Conventional US, a bolus intravenous injection of 1.2 ml of SonoVue (Bracco Imaging, Milan, Italy) consisting of stabilized microbubbles of sulfur hexafluoride was administered into the antecubital vein through an 18 G needle, which was followed by a flush of 5 ml of normal saline solution (0.9% NaCl). A single injection was essential for a lesion for most patients, unless secondary observation was required due to poor imaging quality. No adverse reactions occurred. The timer was activated at the beginning of contrast agent administration. Static images and video files over a span of 2 minutes were stored in a picture archiving and communication system.

2.2. Image assessment

Two doctors with 10 years of experience and who were blinded to the pathologic findings undertook to retrospectively and independently review the ultrasound images. A consensus interpretation was reached for ambiguous cases. Each lesion was respectively categorized into 5 groups (Bosniak I, II, IIF, III, and IV; Table 1) based on the morphology of the lesion and enhanced characteristics with reference to the Bosniak classification system, which was ordered with increasing probability of malignancy by both CEUS and Conventional US.

For both imaging techniques, imaging features of the number of septae, wall and/or septae thickness, solid component, and enhancement were all evaluated. The method that determined septae number, and septae and/or wall thickness was previously described by Israel et al,[15] in which, cystic renal masses were evaluated with the Bosniak classification system in comparison to imaging by CT and MRI. Lesions were categorized based on number of septae into 4 groups: Group 1, no septae; Group 2, between 1 and 4 septae; Group 3, between 5 and 9 septae; and Group 4, more than 9 septae. Thickness of the wall and/or septae was subjectively determined as follows: Category I, hairline thin wall only (≤1 mm); Category II, hairline thin (≤1 mm); Category IIF, minimally thickened (>1 mm and <2 mm); and Category III

Table 1

Bosniak classification system for renal complex cystic mass.

	Conventional US	CEUS
Bosniak I	a hairline thin wall that does not contain septae or solid component;	enhancement involving a hairline thin wall with no septae and solid component;
Bosniak II	a hairline thin wall with less than 4 hairline thin septae;	enhancement involving both the hairline thin wall and less than 4 hairline thin septae;
Bosniak IIF	increased number of septae with minimally thickened wall and/or septae;	enhancement involving increased number of septae with minimally thickened wall and/or septae;
Bosniak III	grossly thickened and irregular wall and/or septae; solid endocystic component with no vascular signals;	enhancement involving grossly thickened and irregular wall and/or septae;
Bosniak IV	solid endocystic component with vascular signals independent of wall and/or septae.	enhancement involving solid endocystic component independent of wall and/or septae.

or IV, grossly thickened and irregular (≥2 mm). On conventional US, a solid component was defined as hypo-iso or hyperechoic solid matter in the cyst with or without color Doppler signal. On CEUS, a solid component was defined as intralesional hyperechoic signal matter in the cyst during real-time observations. The presence of vascularization by color Doppler flow imaging on Conventional US was considered enhancement. By contrast, the presence of enhancement was considered once intralesional hyper-echoic signals were visualized during real-time observations on CEUS images.[9] If the mass did not change significantly in size (10% of the mean diameter per year) and had an appearance similar to that in the prior study, it was considered unchanged. If there was a change in size of more than 10% mean diameter per year, a change in enhancement pattern, or a change in overall appearance, it was considered substantially changed.[13] In addition, any lesion that was resolved, or was decreased in size, or was indeed stable at a follow-up study of greater than 1 year was considered benign.[16] If the patient was diagnosed as a Bosniak III or IV renal mass on CEUS, then the patient was recommended to have surgery. In addition, there were still some patients with benign lesions that also had a strong desire to have surgery, and we tried to meet their requirements under conditions of a fully informed consent procedure. The interval time between CEUS and surgery was less than 2 weeks for all patients.

Findings of Conventional US and CEUS were compared with the pathological findings. A lesion was classified as malignant if it was Bosniak III or IV for surgery, and benign if it was Bosniak I or II, but likely benign if it was Bosniak IIF in need of follow-up. Diagnostic performance, such as sensitivity (SEN), specificity (SPE), and positive predictive value (PPV), and negative predictive value (NPV) of Conventional US and CEUS were evaluated separately for malignant or benign lesions. The diagnostic concordance rates of both Conventional US and CEUS procedures were calculated according to pathological diagnosis.

2.3. Statistical analysis

Chi-Squared analysis was used to determine the SEN, SPE, PPV, NPV of Conventional US and CEUS. ROC curve analysis was used to determine the confidence of the diagnostic accuracy by calculating the area under each ROC curve. The degree of concordance with pathology for Conventional US and CEUS was determined by calculating kappa statistics. Further, the concordances were considered slight if the kappa coefficient values were less than 0.2; fair if the values were 0.21 to 0.40; moderate if the values were, 0.41 to 0.60; substantial if the values were 0.61 to 0.80; or almost perfect, if the scores were 0.80 to 1.00. And $P < .05$ was considered as a statistically significant difference.

3. Results

The maximum diameter of the 102 complex cystic renal masses ranged from 0.8 to 12.2 cm (median diameter of 4.0 cm). The surgery was done in 56 patients, including partial nephrectomy in 17 cases and total nephrectomy in 24 cases when a mass was classified as malignant if it was classified as Bosniak III or IV. Partial nephrectomy was conducted in 12 cases and unroofing of the renal cyst in 3 cases when the patients were diagnosed as benign if it was classified as Bosniak I or II or likely benign if it was Bosniak IIF who refused follow-up and chose surgery. The

main reason was that they were worried about the impact of the mass on their health.

Final pathological diagnoses revealed 36 malignant lesions and 20 benign lesions. In 36 renal malignant lesions, 33 masses (Conventional US: Bosniak IIF, n 1; Bosniak III, n 19; Bosniak IV, n 13; CEUS: Bosniak III, n 2; Bosniak IV, n 31) were cystic renal cell carcinomas, 1 was renal squamous cell carcinoma (Conventional US: Bosniak IV; CEUS: Bosniak IV), 1 was renal small round cell carcinoma (Conventional US: Bosniak III; CEUS: Bosniak IV) and 1 was low grade papillary epithelial carcinoma (Conventional US: Bosniak IV; CEUS: Bosniak IV). The final diagnoses of 20 renal benign lesions included 19 renal cysts and 1 renal papillary adenoma (Conventional US: Bosniak III; CEUS: Bosniak IV). Nineteen renal cysts included 8 simple cysts (Conventional US: Bosniak II, n 2; Bosniak IIF, n 3; Bosniak III n 3; CEUS: Bosniak II, n 5; Bosniak IIF, n 2; Bosniak III, n 1), 5 cysts with an infection (Conventional US: Bosniak III, n 5; CEUS: Bosniak IIF, n 5), 3 cysts with hemorrhage (Conventional US: Bosniak III, n 3; CEUS: Bosniak I, n 2; Bosniak II, n 1), 2 cysts with lipomatoid hyperplasia and 1 cyst with suppurative inflammation - all with Bosniak classification of Bosniak III on Conventional US imaging and Bosniak IV on CEUS imaging. The patients without surgery underwent follow-up for at least 24 months (range, 24–61 months), and there was no evidence of significant progression. Per-mass flowcharts are presented in Figure 1.

3.1. Number of septae

In these lesions, septae number was observed on Conventional US images as follows: 14 lesions in group 1; 52 lesions in group 2; 21 lesions in group 3; and 15 lesions in group 4. After CEUS, it changed in 17 (16.7%) patients, which included 1 lesion from group 4 to group 1, 1 lesion from group 3 to group 4, 2 lesions from group 3 to group 2, 2 lesions from group 3 to group 1, 4 lesions from group 2 to group 3, 5 lesions from group 2 to group 1, and 2 lesions from group 1 to group 2 (Table 2). No patient of treatment strategy changed because of number of septae.

3.2. Septae and/or wall thickness

As seen in Table 3, wall and/or septae thickness were depicted on Conventional US images including wall only (n = 3); hairline thin (n = 9); minimally thickened (n = 34), and grossly thickened and irregular (n = 56). It changed in 39 (38.2%) lesions after CEUS as follows: 14 lesions from grossly thickened and irregular to minimally thickened; 12 lesions from minimally thickened to hairline thin; 3 lesions from grossly thickened and irregular to hairline thin; 3 lesions from minimally thickened to the wall only; 2 lesions from the hairline thin to wall only; and 2 lesions from grossly thickened and irregular to wall only. By contrast, 2 lesions from minimally thickened to grossly thickened and irregular; 1 lesion from hairline thin to minimally thickened, and 1 lesion from wall only to hairline thin were identified. In 21 (20.6%) patients, the treatment strategy changed because of the wall and/or septae thickness.

3.3. Solid component and enhancement

Due to the poor sensitivity of the Conventional US blood flow detection, only a few lesions could be detected with blood flow signals. However, enhancement was shown on all lesions on
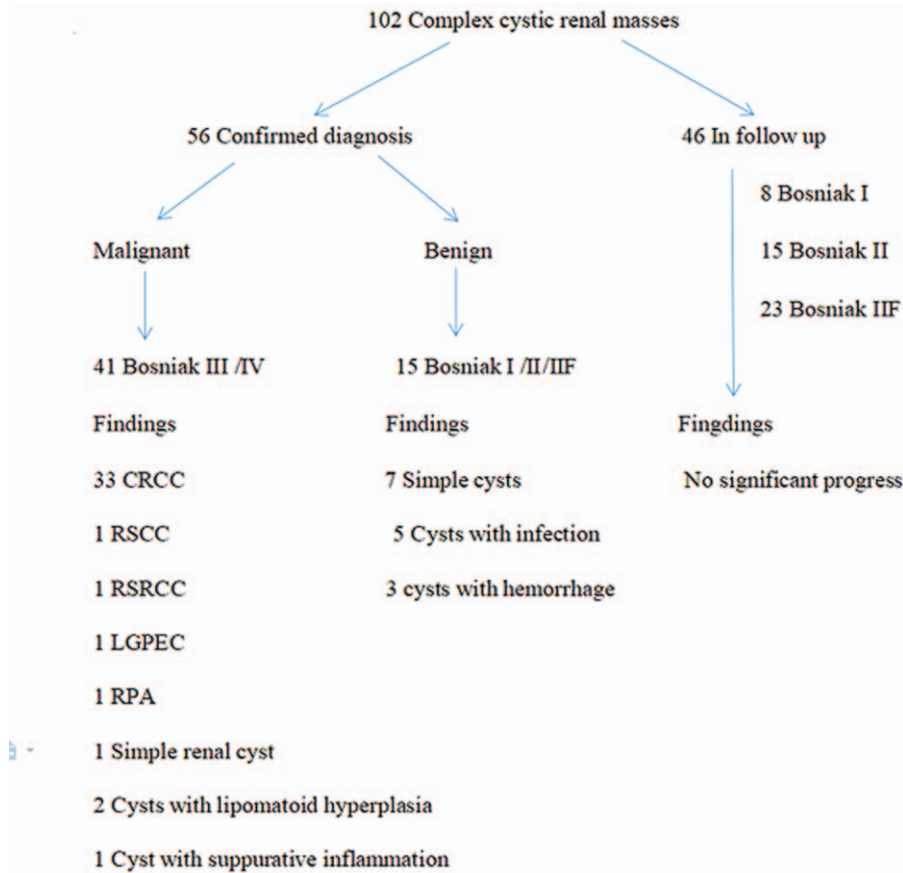
Figure 1. Flowchart shows per-mass analysis of CEUS. CRCC = cystic renal cell carcinoma, LGPEC = low grade papillary epithelial carcinoma, RPA = renal papillary adenoma, RSCC = renal squamous cell carcinoma.

CEUS images. Solid components within 6 lesions were not seen on the Conventional US, although they were seen on CEUS images, which resulted in an upgraded Bosniak classification (Fig. 2). However, solid components within 25 lesions were recognized as a benign cyst with intracapsular hemorrhage or an infection as visualized by Conventional US, but not by CEUS imaging, which resulted in a downgraded Bosniak classification (Figs. 3 and 4). In total, the solid component changed in 31 (30.4%) patients by CEUS (Table 4), leading to changes in their treatment strategies.

3.4. Bosniak category

Table 5 showed that the Bosniak classification category changed when comparing the CEUS and Conventional US. It was changed

in 67 (65.7%) patients after CEUS as compared the Conventional US. Upgrade occurred in 22 (21.6%) patients, including 1 case of Bosniak IIF that was upgraded to Bosniak IV, and 21 (20.6%) cases of Bosniak III that were upgraded to Bosniak IV. Downgrade occurred in 45 patients (44.1%), of which, 19 were downgraded from Bosniak III to Bosniak IIF, 10 were downgraded from Bosniak III to Bosniak II, 7 were downgraded from Bosniak III to Bosniak I, 6 were downgraded from Bosniak IIF to Bosniak II, 2 were downgraded from Bosniak IIF to Bosniak I, and 1 was downgraded from Bosniak II to Bosniak I. Changed cases accounted for 65.7% of the number of diseases, and 37 cases (36.3%) of changed treatment strategies, of which only 1 case was upgraded from Bosniak IIF to Bosniak IV for CEUS

Table 2

Differences between conventional US and CEUS in detecting septae number.

	CEUS				
Conventional US	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Total**
Group 1	12	2	0	0	14
Group 2	5	43	4	0	52
Group 3	2	2	16	1	21
Group 4	1	0	0	14	15
Total	20	47	20	15	102

Table 3

Differences between Conventional US and CEUS in detecting septae and/or wall thickness.

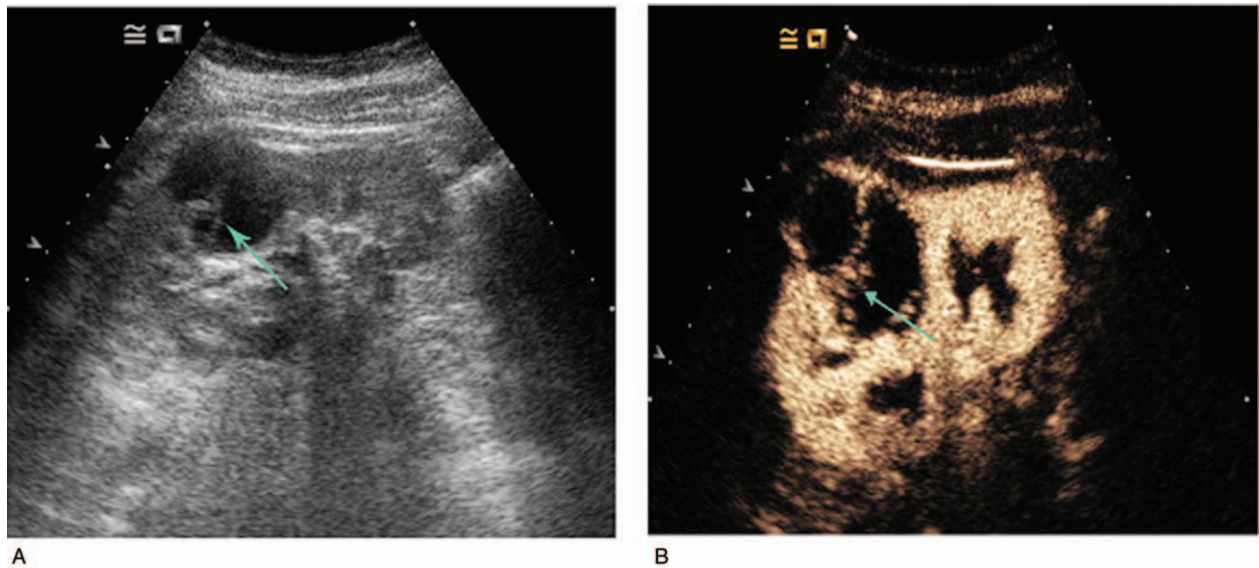|	CEUS				
Conventional US	**Category I**	**Category II**	**Category IIF**	**Category III or IV**	**Total**
Category I	2	1	0	0	3
Category II	2	6	1	0	9
Category IIF	3	12	17	2	34
Category III or IV	2	3	14	37	56
Total	9	22	32	39	102

Figure 2. A 46-year-old man with left renal cell carcinoma revealed an upgraded Bosniak classification. (a) Conventional US showed a complex cystic renal mass containing grossly thickened and irregular septae (blue arrow), ranging from one to 4 in number (group2), Bosniak III. (b) CEUS demonstrated a mural nodule (blue arrow) adhering to the septea as compared to Conventional US, Bosniak IV.

detection of a solid component within the lesion, which supported a diagnostic suspicion of malignant cystic tumor and acceptance of surgical intervention, and 36 patients that were downgraded from Bosniak III to Bosniak IIF/II/I that refused surgery.

The diagnostic performance of CEUS in the differentiation of benign and malignant cystic masses was overall superior to the Conventional US approach (SEN 100.0 vs 97.2%, SPE 90.9 vs 62.1%, PPV 85.7 vs 58.3%, and NPV 100.0 vs 97.6%). CEUS also had a higher diagnostic confidence ($P < .05$) with the area under the ROC curve compared to the Conventional US (AUC = 0.968 vs 0.799, Fig. 5). The concordance with pathology performed almost perfectly for CEUS but moderately well for Conventional US (kappa = 0.876 vs 0.515).

4. Discussion

The Bosniak classification system is the most widely accepted diagnostic classification of complex renal cystic masses, which provides criteria for deciding whether a complex cystic mass

Figure 3. A 34-year-old man with a right renal complex cystic mass revealed a downgraded Bosniak classification. (a) On Conventional US, a complex cystic renal that was mass mainly occupied by echogenic material with an intracystic solid lesion (blue arrow), which suggested Bosniak III. (b) Using CEUS, there were no solid lesions (blue arrow), but an exclusively peripheral enhancing regular wall was identified, which was compatible with a benign Cyst with intracapsular hemorrhage, Bosniak I.
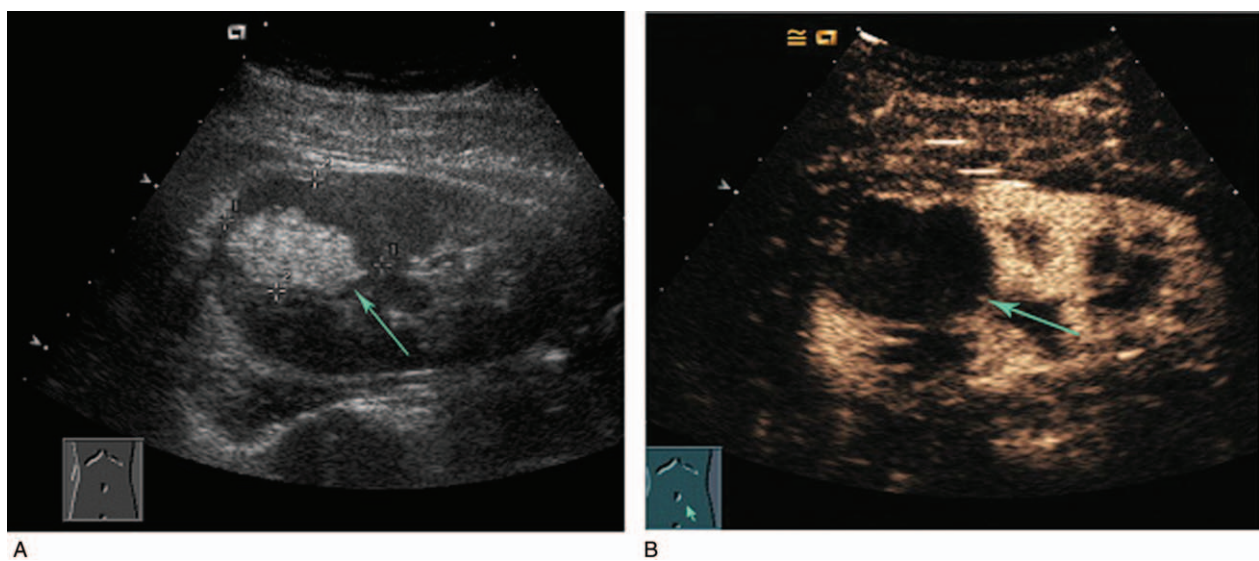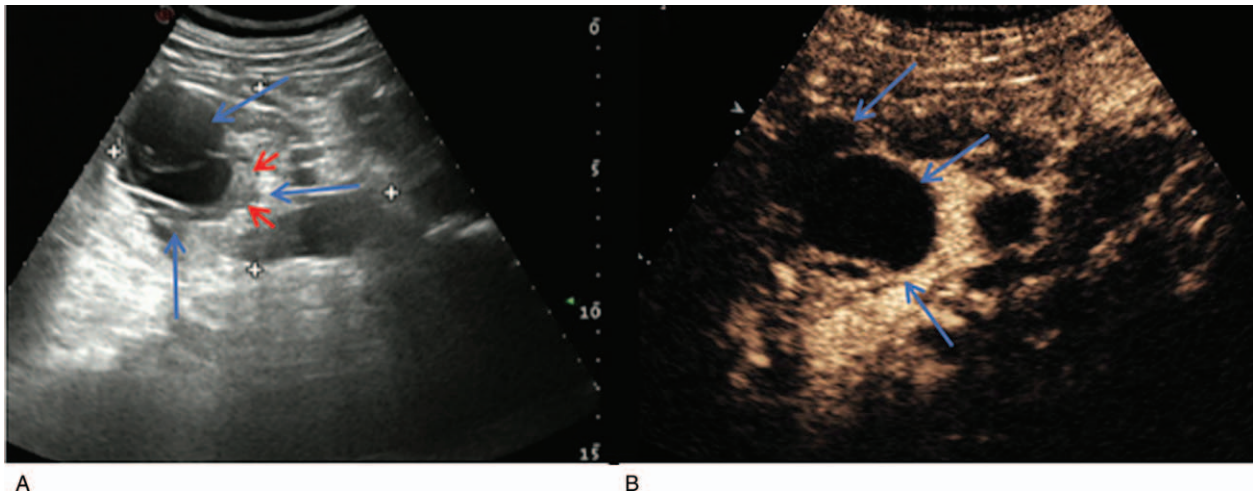
Figure 4. A 55-year-old man with a left renal complex cystic mass revealed a downgraded Bosniak classification. (a) On Conventional US, a complex cystic renal mass (blue arrow) with hair-thin septae and a hypoechoic material that adhered to the wall was seen (red arrow) that suggested Bosniak III. (b) Using CEUS, no solid lesion was seen, but a peripheral enhancing regular wall with hair-thin septae (blue arrow) was found, which was compatible with a benign cyst with intracapsular infection, Bosniak IIF.

should be removed by surgery. Some benign renal cysts can not be differentiated from malignant ones based on their Conventional US appearance, mainly because it is difficult to detect the blood signal in the wall, septae and solid endocystic component by color Doppler flow imaging.[17]CEUS is a micro-bubble specific harmonic US. Microbubbles are used to enter into capillaries, increasing the acoustic impedance difference and the reflectivity of the interface, so as to display the blood supply inside the tumor. It can provide a better assessment of vascular morphology and enhanced patterns to demonstrate delicate internal structures of cystic renal masses more sensitively, and obviously improve the display rate of low-speed small blood vessels. Compared with contrast-enhanced CT, CEUS is characterized by continuous real-time multi angle imaging, so as to observe the enhancement characteristics of target lesion and organ perfusion characteristics more carefully. In addition, the higher contrast and temporal resolution of CEUS allows fine septations and subtle mural nodules to be better displayed than on CT. It has recently developed as a promising modality for detecting cystic mass vascularity with higher resolution even than CT imaging.[9,17,18] The results of our study revealed that benign and malignant complex renal cysts present typical enhancement patterns at CEUS,[9,10,18] on which malignant cystic renal masses revealed specific signs of grossly thickened and irregular wall and/or septae and solid component enhancement after micro-bubble injection, while benign cystic renal masses lacked these characteristics.

The thickness of the wall and/or septae in a complex cystic renal mass is an important factor in the evaluation. In our study,

CEUS demonstrated increased thickness of the wall and/or septae in the lesions when compared with the Conventional US, which accounted for a higher classification at CEUS in 4 lesions, of which, 2 lesions were noteworthy in that the CEUS findings indicated category III or IV, but the Conventional US findings suggested category IIF, which were upgraded by the Bosniak classification and proved to be cancer following surgery. The possible reason for this was that CEUS could detect even very small levels of the microbubbles. While 35 lesions showed reduced thickness of the wall or septae, this might be due to interference from intracapsular hemorrhage or infection attached to the septae and wall.

The more important factor is the presence or absence of enhancement of the solid component in the evaluation of a complex cystic renal mass, as it is a key feature differentiating Bosniak III from Bosniak IV. The lesion is considered a malignant neoplasm if there is an enhancing solid component within the lesion. According to Israel and Bosniak,[19,20] in most cases one should not rely on Conventional US in the differentiation of a surgical complex cystic renal mass from non-surgical, because Conventional US cannot be used to accurately evaluate the presence of blood signal. However, CEUS can even detect very small amounts of micro-bubbles, and it is especially useful in suspected cases of "solid component" at Conventional US. It can

Table 4

Differences between conventional US and CEUS in detecting the solid endocystic component.

	CEUS		
Conventional US	**No**	**Yes**	**Total**
No	40	6	46
Yes	25	31	56
Total	65	37	102

Table 5

Differences between Conventional US and CEUS in Bosniak classification.

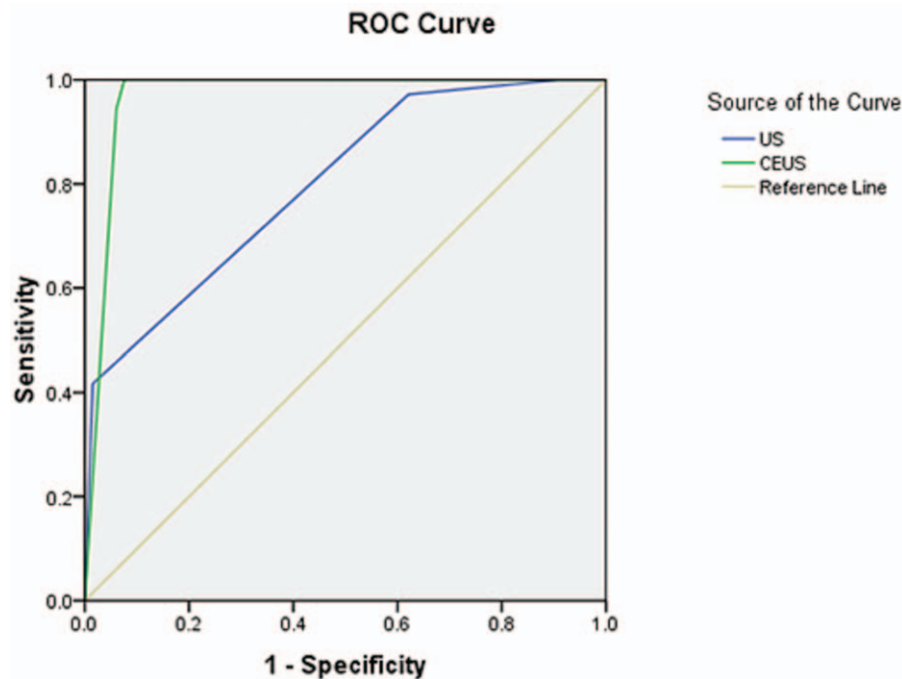|	CEUS					
Conventional US	**Bosniak I**	**Bosniak II**	**Bosniak IIF**	**Bosniak III**	**Bosniak IV**	**Total**
Bosniak I	0	0	0	0	0	0
Bosniak II	1	5	0	0	0	6
Bosniak IIF	2	6	11	0	1	20
Bosniak III	7	10	19	3	21	60
Bosniak IV	0	0	0	0	16	16
Total	10	21	30	3	38	102

ROC Curve

Figure 5. Receiver operating characteristic (ROC) curve analyses for the diagnostic accuracy of CEUS and Conventional US. Graph shows that the area under the ROC curve of CEUS (green line) is larger than Conventional US (blue line). Diagonal brown line represents a hypothetical technique that is unable to distinguish malignant from benign complex cystic renal masses.

downgrade the suspected category if no enhancement of solid components is detected, or upgrade if detection of solid area enhancement is present. As in our study, solid component within a total of 25 lesions by Conventional US were not enhanced by CEUS, which resulted in a downgraded Bosniak classification, and was a strong predictor of benignity. Meanwhile, enhancement of the solid component in 6 lesions by CEUS resulted in upgrading of the Bosniak classification was highly predictive of malignancy.

Bosniak category I lesions represent a simple cyst that does not require additional follow-up, with a malignancy rate of essentially zero. Most Bosniak category II lesions, as stated by Barr[13,14] shows that a thin septae with even relatively brisk enhancement, are reliably considered benign with an estimated 0% probability of malignancy. It was unlikely to be clinically significant, and with no follow-up. On the basis of our results, Bosniak category II lesions were confirmed by surgery as being benign, and those with no significant progression in at least a 24 month follow-up period were also considered benign. Our results were also consistent with this. Therefore, CEUS could provide increased confidence that Bosniak category II lesions are indeed benign.

Conversely, surgical resection is recommended for Bosniak III and IV, because of the high risk of malignancy. A multi-institutional analysis that included 22,204 patients over 16 years, analyzed the rate of synchronous metastases, and the results do not favor a conservative approach to small renal masses.[21] In the study, the synchronous metastasis rate was 9.6%, including 5.6 vs 14.2% for T1a vs T1b. Stratification by intervals of 1 cm for the size of the tumor revealed that the rate increased with increasing tumor size, which was 4.8% at 1.0 cm or less; 4.2% at 1.1 to 2.0 cm; 4.9% at 2.1 to 3.0 cm; 7.1% at 3.1 to 4.0 cm;

12.1% at 4.1 to 5.0 cm; 13.3% at 5.1 to 6.0 cm; and 18.4% at 6.1 to 7.0 cm. It was observed that even patients with small renal masses were at risk for synchronous metastasis. Thus, size is not a component of the Bosniak classification system. At our institution, a lesion was classified as malignant if it was classified as Bosniak III or IV for surgery regardless of size.

Whereas Bosniak IIF means follow-up of lesions that present insufficient features to be considered benign, unless a follow-up confirms that the lesion remains stable,[22] this has implications for the choice of treatment strategy. The ability to accurately identify those complex cystic renal masses that are malignant still represents a major challenge. CEUS is a very sensitive imaging technique aimed at detecting microvascularity of a lesion, especially with a solid component. Our study showed that 1 case had an upgraded Bosniak IIF to Bosniak IV for CEUS detection of a solid component within the lesion.

Conventional US is a very good technique to diagnose simple cysts, but it is very difficult in differentiating some benign hemorrhagic and inflammatory cysts showed a complex appearance from malignant cysts and solid lesions that require surgical management to obtain a final diagnosis. There were 25 cases down-graded from Bosniak III for no detection of a solid component and strongly predicting a benign cyst with intra-capsular hemorrhage or infection that might have benefited from an adjustment in the treatment strategy. In pathologically confirmed 8 cases, there were 3 cysts with hemorrhage that showed hyperechoic solid matter in the cyst, and 5 cysts with infection that showed hypoechoic solid matter on Conventional US, while these echoes disappeared after CEUS. It could be seen that CEUS, especially in the accurate identification of Bosniak III nodules with presence of hemorrhage or infection but without no color blood signal of solid components on Conventional US,

could improve the detection rate of false positive lesions and greatly reduce unnecessary surgery. Therefore, CEUS would be beneficial to develop a modification of the Bosniak classification to aid in future studies for prospectively determining whether CEUS can appropriately change clinical management, especially in Bosniak III lesions, which is the same view as Barr et al.[14]

Furthermore, CEUS was not only found to be useful for evaluating a complex cystic renal mass using the Bosniak classification system, but was also superior to Conventional US in both diagnostic performance and confidence by statistical assessments. In a review of the evidence for detecting malignant cystic kidney lesions, CEUS displayed SEN (89%–100%), SPE (71%–99%) and an NPV (86%–100%).[23] We showed better results in terms of SEN, SPE, PPV and NPV. We had an improved diagnostic accuracy when CEUS was used, and the agreement with pathology was moderate to almost perfect when using CEUS. It could help classify masses with a high degree of certainty, convert cases that seemingly required surgical removal, to necessitating follow-up instead, and could discover malignant lesions that might otherwise be followed up. These findings were similar to the results of several retrospective studies.[13,24–29]

CEUS characterized by dynamic and real-time microvascular profusion imaging of lesion is accepted as a potent diagnostic tool. Our investigation proved CEUS's value in complex cystic renal mass diagnoses. Nonetheless,CEUS can be influenced by poor sonic window due to obesity or bowel gas and operator experience-dependent for optimum quality of image, while CT is more objective and reliable for urologists. In addition, CEUS takes more time for radiologists on image acquisition and analysis than CT. So, in clinical practice, we usually use CT for Bosniak classification for complex renal cystic lesion, not rely on US, also not performed CEUS. CEUS is often a valuable alternative means of evaluate complex renal cystic lesion in patient whose iodinated CT contrast is contraindicated.

Our research also had some limitations. There was a potential for selection bias due to the retrospective design of the study. As well as not all diagnoses were confirmed pathologically, even with a lengthy follow-up (minimum of 24 months in this study). In addition, the number of cases was small, and further studies are needed to confirm our results.

5. Conclusion

The results of our study showed that thicker wall and/or septae, or more solid components in malignant cystic renal masses were found by CEUS as compared to Conventional US that could not find them. These findings might result in a higher-grade category. While a lower-grade category in benign lesions was chiefly due to absence of enhancement of solid component. Consequently, up to 65.7% of the Bosniak classification categories were changed, and 36.3% of the patients would have benefited from CEUS as compared to Conventional US. Besides, the diagnostic performance of CEUS for cystic renal lesions was higher than that of Conventional US by statistical means. Therefore, CEUS performed better than Conventional US in diagnosing a complex cystic renal mass. Since CEUS is safe, well tolerated, is not associated with any obvious nephrotoxicity, and does not expose the patient to radiation, it might be considered as the first tool to evaluate a complex cystic renal mass, especially for these Bosniak

III masses with hemorrhage or infection without blood signal of solid components by Conventional US.

Author contributions

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Investigation: Zhengdu Ye.
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Project administration: Tian-An Jiang.
Software: Chunhong Yan.
Writing – original draft: Xiaoying Qiu.
Writing – review & editing: Qiyu Zhao, Tian-An Jiang.

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