

# **Contrast-enhanced Ultrasound (CEUS) vs contrast-enhanced computed tomography for multilocular cystic renal neoplasm of low malignant potential**

# A retrospective analysis for diagnostic performance study

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#### Abstract

Multilocular cystic renal neoplasm of low malignant potential (MCRNLMP) might be benefited from nephron-sparing surgery. Contrast-enhanced computed tomography is used for the diagnosis of MCRNLMP but contrast-enhanced ultrasound has lack of nephrotoxicity and several advantages over contrast-enhanced computed tomography and contrast-enhanced magnetic resonance. The purpose of the study was to compare diagnostic parameters of preoperative contrast-enhanced ultrasound against contrast-enhanced computed tomography for the detection of MCRNLMP in patients who faced curative surgery for complex cystic renal mass.

Data regarding contrast-enhanced ultrasound, contrast-enhanced computed tomography, and clinicopathological results of 219 patients who underwent curative surgery for complex cystic renal mass (Bosniak classification III or IV) were retrospectively collected and analyzed. Bosniak classification for imaging modality and the 2016 WHO criteria for clinic pathology were used for detection of MCRNLMP.

Contrast-enhanced ultrasound, contrast-enhanced computed tomography, and clinicopathology were detected 68, 66, and 67 as a MCRNLMP respectively. Contrast-enhanced ultrasound and contrast-enhanced computed tomography had 30.37% and 29.27% sensitivities for the detection of MCRNLMP. While 60% and 50% specificities respectively. Bosniak classification III (P=.045) and lower mean Hounsfield unit (P=.049) were associated with the prevalence of MCRNLMP. Contrast-enhanced computed tomography was detected 6 and 7, while contrast-enhanced ultrasound detected 3 and 2 complex cystic renal mass as false positive and false negative MCRNLMP respectively. A contrast-enhanced ultrasound had 0.011 to 1.0 diagnostic confidence and contrast-enhanced computed tomography had 0.045 to 0.983 diagnostic confidence for decision making of nephron-sparing surgeries.

Contrast-enhanced ultrasound may have better visualization of MCRNLMP than contrast-enhanced computed tomography. Level of Evidence: III.

**Abbreviations:** ANOVA = analysis of variance, q = Critical value, HU = hounsfield unit, MCRNLMP = multilocular cystic renal neoplasm of low malignant potential, TNM = tumor, nodes, and metastases, WHO = World Health Organization.

Keywords: Bosniak classification, contrast-enhanced computed tomography, contrast-enhanced ultrasound, hounsfield unit, multilocular cystic renal neoplasm of low malignant potential, nephron-sparing surgery

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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# 1. Introduction

Multilocular cystic renal neoplasm of low malignant potential (MCRNLMP) are accounted for only 2% to 4% of clear renal cell carcinoma <sup>[1]</sup> with an excellent prognosis.<sup>[2]</sup> The 2016 World Health Organization (WHO) defined it as a renal tumor that is composed entirely of numerous cysts, the septa of which consist of small groups of clear cells without extensive growth, and are morphologically inseparable from low-grade clear renal cell carcinoma.<sup>[3]</sup> In MCRNLMP, patients cannot be affected by large tumor size or advanced stage. Therefore, patients of MCRNLMP might be benefited from nephron-sparing surgery.<sup>[4]</sup>

Imaging methods like magnetic resonance imaging and computed tomography are used frequently for the diagnosis of MCRNLMP.<sup>[5]</sup> Contrast-enhanced ultrasound is a new technique for the diagnosis of renal cell carcinoma.<sup>[6]</sup> Unlike magnetic resonance imaging and computed tomography, contrast-enhanced ultrasound provides real-time images, zero-radiation, and cost-effective<sup>[7]</sup> with high accuracy even at bedside.<sup>[8]</sup> Contrastenhanced ultrasound has lack of nephrotoxicity and has several advantages over contrast-enhanced computed tomography and contrast-enhanced magnetic resonance.<sup>[9]</sup> The Bosniak classification system is preoperatively used for the differentiation of MCRNLMP from the other cystic renal cell carcinoma.<sup>[4]</sup> A new proposal for the Bosniak classification is for contrast-enhanced computed tomography and contrast-enhanced magnetic reso-nance imaging only.<sup>[10]</sup> Ultrasound is generally used for detection of renal masses.<sup>[9]</sup> Bosniak classification was not developed for contrast-enhanced ultrasound.<sup>[10]</sup> Contrast-enhanced ultrasound grading of Bosniak classification can appropriately change clinical management of renal masses by changing the probability of malignancy compared to Bosniak classification for contrastenhanced computed tomography and contrast-enhanced magnetic resonance.<sup>[9]</sup>

The objectives of a non-randomized retrospective analysis of the cross-sectional study were to compare the diagnostic parameters of preoperative contrast-enhanced ultrasound against those of contrast-enhanced computed tomography for the detection of MCRNLMP in patients who faced curative surgery for complex cystic renal mass (Bosniak classification III or IV) considering the clinicopathological results as the reference standard. Also, to determine the preoperative factors differentiating MCRNLMP from the other cystic renal cell carcinoma.

#### 2. Materials and methods

#### 2.1. Ethics approval and consent to participant

The designed protocol of the study (Reg. No. ZXMFSY00060, dated May 7, 2020) was approved by the Second Hospital of Tianjin Medical University review board. All enrolled patients have signed prior informed consent before enrollment in the study regarding diagnosis, radiology, surgery, and pathology, and publication of anonymized information of patients in the article form. Written approval was taken before collection of data from competing authority.

#### 2.2. Study population

From January 12, 2018 to April 15, 2020, a total of 5469 patients underwent curative surgery for renal cell carcinoma at the Second Hospital of Tianjin Medical University, Tianjin, Hebei, China. Of these, on contrast-enhanced ultrasound and contrast-enhanced computed tomography evaluation basis, 287 patients had complex cystic renal mass (Bosniak classification III (suspicious for malignancy) or IV (malignant)). Of 287 patients, 61 patients had not performed contrast-enhanced ultrasonographic images, 5 patients had von Hippel–Lindau disease, and 2 patients had dialysis-related renal cell carcinoma. Therefore, data of these patients were excluded from the analysis. Data regarding contrast-enhanced ultrasound, contrast-enhanced computed tomography, and the clinicopathological results of 219 patients ( $18 \ge$  years) who underwent curative surgery for renal cell carcinoma, and had complex cystic renal mass (Bosniak classification III or IV) were retrospectively collected and analyzed (Fig. 1).

#### 2.3. Contrast-enhanced ultrasound

Patients were injected with 1.2 ml bolus microbubble (SonoVue; Bracco Imaging France, Léonard de Vinci, Massy, France) by a 20-G intravenous cannula (BD Venflon, BD, Franklin Lakes, NJ, USA), followed by a 10-ml normal saline flush (Baxter Pharmaceuticals, Deerfield, IL, USA). Both kidneys were examined under LOGIQ E10 (GE Healthcare, Chicago, IL, USA). After injection of contrast agent cine loops were acquired under continuous scanning and images were stored. Lesions were evaluated qualitatively (Fig. 2). Image analyses were performed as per the Bosniak classification.<sup>[11]</sup> Contrast ultrasound was performed and analyzed by ultrasound technologists of the institute. All have minimum of 3years of experience in renal images.

#### 2.4. Contrast-enhanced computed tomography

Corticomedullary-phase, nephrographic phase, and excretoryphase contrast-enhanced computed tomographic images were performed using a 64-channel single-source, dual-energy helical computed tomography scanner (SOMATOM Definition Edge, Siemens Healthineers Malvern, PA, USA), acquiring 128 slices/ rotation through the double sampling of the detector rows, 0.384 mm spatial resolution, 100 kw generator power at 100 kv, and 384 reconstructing slices after intravenous administration of 1 mm/ml Gadovist (Bayer, Reading, Berkshire, United Kingdom). The region of interest was drawn outside of cystic renal mass and mean Hounsfield unit (HU) of each region of interest was measured (Fig. 3). Image analyses were performed as per the Bosniak classification.<sup>[10]</sup> Contrast-enhanced computed tomography was performed and analyzed by radiologists of the institute. All have minimum of 3-years of experience.

#### 2.5. Clinic pathology

Pathology of surgically removed cystic renal mass was performed by pathologists of the institute. All have minimum of 3-years of experience in genitourinary pathology. The 2016 WHO criteria used to define MCRNLMP.<sup>[3]</sup> Gross and microscopic features of cystic renal mass were defined as per Fuhrman nuclear grade (Fuhrman grades 1 and 2: low grade, Fuhrman grades 3 and 4: high grade) and TNM (tumor, nodes, and metastases) staging.<sup>[12]</sup>

#### 2.6. Diagnostic parameters

The diagnostic criteria for MCRNLMP and another cystic renal cell carcinoma on contrast-enhanced ultrasound and contrastenhanced computed tomography was just the existence of

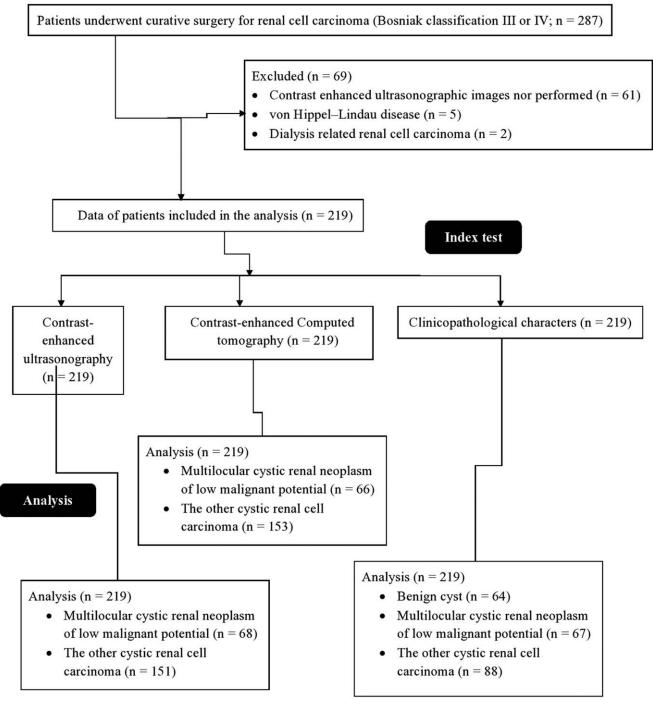


Figure 1. Flow diagram of retrospective analysis.

enhancement. The enhancement was judged by visual inspection. The ratio of true positive MCRNLMP detected by imaging modality to total true characterization of complex cystic renal mass by that imaging modality was considered as sensitivity and the ratio of false-positive MCRNLMP detected by imaging modality to the total false characterization of complex cystic renal mass by that imaging modality was considered as specificity.

#### 2.7. Beneficial score analysis

Beneficial score analysis for each imaging method was calculated as per Eq. (1) <sup>[13]</sup>:

Beneficial score =	True positive MCRNLMP detected Data of cysts included in the analysis	- ((False - positive MCRNLMP detected Data of cysts included in the analysis	× ))
Leve of diagn	ostic confidence above which decision	of nephron - sparing surgery was made	))
1 – Level of dia	gnostic confidence above which decision	on of nephron – sparing surgery was made	
			(1)



Figure 2. Ultrasound images of complex cystic renal mass (Bosniak classification IV) in the interpolar area of the right kidney.

True positive MCRNLMP: Complex cystic renal mass was defined as a MCRNLMP by Bosniak classification<sup>[10,11]</sup> and 2016 WHO criteria.<sup>[3]</sup>

False-positive MCRNLMP: Complex cystic renal mass was defined as a MCRNLMP by Bosniak classification<sup>[10,11]</sup> but failed in the definition of the 2016 WHO criteria.<sup>[3]</sup>

#### 2.8. Statistical analysis

SPSS V25.0 IBM Corporation, Chicago, IL, USA was used for statistical analysis purposes. Univariate following multivariate linear regression analysis was performed to determine the preoperative factors differentiating MCRNLMP from the other cystic renal cell carcinoma.<sup>[4]</sup> One-way analysis of variance (ANOVA) or unpaired *t*-test was performed for continuous

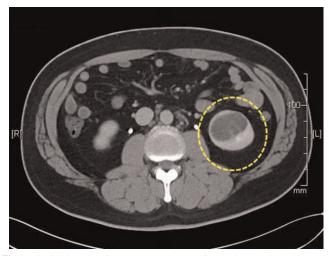


Figure 3. Axial magnetic resonance image of complex cystic renal mass (Bosniak classification III) in the interpolar area of the left kidney. The yellow circle indicates the region of interest.

parameters. The Tukey test (considering critical value (q) > 3.345 as significant) was performed for post hoc analysis. The Fischer exact test or the Chi-Squared independence test was performed for constant parameters. All results considered significant if P value was reported less than.05.

## 3. Results

#### 3.1. Contrast-enhanced ultrasound

Contrast-enhanced ultrasound detected 68 cysts as a MCRNLMP and 151 cysts as the other cystic renal cell carcinoma. The results of contrast-enhanced ultrasound reported no difference for Bosniak classification (P=.051) and diameter (P=.663) between MCRNLMP and the other cystic renal cell carcinoma but MCRNLMP were more calcified (P=.003). The detailed contrast-enhanced ultrasonographic characteristics of complex renal cysts before curative surgery are reported in Table 1.

#### 3.2. Contrast-enhanced computed tomography

Contrast-enhanced computed tomography was detected 66 cysts as a MCRNLMP and 153 cysts as the other cystic renal cell carcinoma. The results of contrast-enhanced computed tomography reported that MCRNLMP was more in class III Bosniak classification type (P < .0001) and calcified (P = .001). HUs during the pre-contrast phase (P = .021), corticomedullary phase (P < .0001), and early excretory phase (P < .0001) were lower for MCRNLMP than the other cystic renal cell carcinoma. The detailed of contrast-enhanced computed tomography characteristics of complex renal cysts before curative surgery are reported in Table 2.

#### 3.3. Clinic pathological characters

Clinic pathological study was characterized complex cystic renal mass as 64 benign cysts, 67 MCRNLMP, and 88 as the other cystic renal cell carcinoma. Age was higher in patients with

# Table 1

Contrast-enhanced ultrasonographic	characteristics of co	omplex renal cysts	before curative surgery
		JIIIPIER I Ellai Cysis	before curative surgery.

Characters		Multilocular cystic renal neoplasm of low malignant potential	The other cystic renal cell carcinoma	Comparisons between group
Data of cysts included in	the analysis	68	151	P value
Bosniak classification		33 (49)	51 (34)	.051
	IV	35 (51)	100 (66)	
Calcification	Yes*	20 (29)	18 (12)	.003
	No	48 (71)	133 (88)	
Diameter (cm)	Minimum	2.10	1.35	.663
	Maximum	10.10	9.89	
	Mean $\pm$ SD	$4.08 \pm 1.24$	4.17±1.48	

\* Significant difference.

Descriptive data are presented as number (frequency) and continuous data are presented as mean  $\pm$  SD.

Fischer exact test for constant parameters and unpaired t-test for continuous parameters were used for statistical analysis.

A P<.05 was considered significant.

Contrast ultrasonography was performed and analyzed by ultrasound technologists of the institute. All have minimum of 3-years of experience in renal images.

benign cyst. Hemorrhagic/necrotic nature of cysts was fewer reported in the MCRNLMP. The other clinic pathological characteristics are summarized in Table 3.

#### 3.4. Diagnostic parameters

Contrast-enhanced computed tomography had significant numbers of false positive (P=.039) and false negative (P=.022) MCRNLMP detected as compared to clinic pathology results (Table 4).

Contrast-enhanced ultrasound and contrast-enhanced computed tomography had 30.37% and 29.27% sensitivities for the detection of MCRNLMP. While 60% and 50% accuracies respectively (Table 5).

#### 3.5. Beneficial score analysis

A contrast-enhanced ultrasound had 0.011 to 1.0 diagnostic confidence and below 0.011 diagnostic confidence, it had a risk of overdiagnosis for detection of MCRNLMP. Contrast-enhanced computed tomography had 0.045 to 0.983 diagnostic confidence,

below 0.045 it had the risk of over diagnosis, and above 0.983 it had the risk of under diagnosis for detection of MCRNLMP (Fig. 4).

# 3.6. MCRNLMP risk assessment

Univariate following multivariate analysis reported that Bosniak classification III (odd ratio 2.441; 95% confidence limit: 1.111–2.431; P=.045) and lower mean HU (odd ratio 1.345; 95% confidence limit: 1.012–1.41; P=.049) were associated with prevalence of a MCRNLMP.

#### 4. Discussion

The study was reported 1.23% (67/5, 467) prevalence of MCRNLMP. The 2004 WHO criteria suggested the prevalence of a MCRNLMP in the range of 1.0% to 1.5%.<sup>[4]</sup> The results of the current study were within the limit of the 2004 WHO criteria for complex cystic renal mass.

The study reported that contrast-enhanced ultrasound had the same sensitivity but high specificity than contrast-enhanced

#### Table 2

Contrast-enhanced computed tomography characteristics of complex renal cysts before curative surgery.

Characters		Multilocular cystic renal neoplasm of low malignant potential	The other cystic renal cell carcinoma	Comparisons between group
Data of cysts included i	in the analysis	66	153	P value
Bosniak classification	∭*	39 (59)	45 (29)	<.0001
	IV	27 (41)	108 (71)	
Calcification	Yes*	21 (32)	17 (11)	.001
	No	45 (68)	136 (89)	
Diameter (cm)	Minimum	2.11	1.33	.851
	Maximum	10.12	9.91	
	$Mean \pm SD$	$4.11 \pm 1.25$	$4.15 \pm 1.52$	
Mean HU	During pre-contrast phase*	25.12±6.15	$27.81 \pm 8.45$	.021
	During corticomedullary phase*	$32.91 \pm 7.16$	$48.18 \pm 9.15$	<.0001
	During early excretory phase*	$40.15 \pm 6.45$	$52.11 \pm 8.81$	<.0001

\* Significant difference.

Descriptive data are presented as number (frequency) and continuous data are presented as mean ± SD.

Fischer exact test for constant parameters and unpaired t-test for continuous parameters were used for statistical analysis.

A P<.05 was considered significant.

HU = hounsfield unit.

Contrast-enhanced computed tomography was performed and analyzed by radiologists of the institute. All have minimum of 3-years of experience.

Antional cyclic real     Antional cyclic real     Antional cyclic real       Currance     Banga     Banga of low     Banga of low     Banga of low       Currance     Banga     Banga of low     Banga of low     Banga of low     Banga of low       Currance     Banga     Banga of low       Currance     Banda     Second     Second     Banga of low     Banga of low     Banga of low       Currance     Banda     Second     Banda     Second     Banda of low     Banda of l									
Image: constraint of the set of								q-value	
Image: constraint of the point of							Benion cvst vs. multilocular		Multilocular cystic renal neoplasm of low
systs included in the analysis     64     67     88     9     17     16     16     16     16     16     16     16     16     16     16     16     16     1	Characters		Benign cyst	Multilocular cystic renal neoplasm of low malignant potential		P value	cystic renal neoplasm of low malignant notential	Benign cyst vs. the other cystic renal cell carcinoma	malignant potential vs. the other cystic renal cell carcinoma
s)     Minimum     35     33     28     <.0001	Data of cysts included in	1 the analysis	64	67	88				
Meximum     70     65     70       Mean ± SD     58154-915     41513.88     4917±10.15       Mean ± SD     58154-915     41513.88     4917±10.15       Mean ± SD     58154-915     41513.88     4917±10.15       Female     24(37)     26(39)     30(34)     821     NrA       Female     24(37)     26(39)     30(34)     829     NrA     NrA       Symptoted     22(34)     19(28)     23(13)     20(57)     NrA     NrA       Symptoted     23(52)     23(64)     21(24)     NrA     NrA       Upper pole     23(52)     23(33)     23(25)     NrA     NrA       Upper pole     15(23)     23(53)     23(26)     NrA     NrA       Upper pole     15(23)     23(33)     23(26)     NrA     NrA       Tabut     NA     11(16)     14(16)     NrA     NrA       Tabut     NrA     23(33)     23(26)     NrA     NrA       Tabut     NrA     11(16)     14(	Age (years)	Minimum	35	33	28	<.0001	11.633	8.148	4.284
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		Maximum	70	65	70				
Male     40 (63)     41 (61)     58 (66)     821     NA     NA       Finale     21 (37)     26 (39)     30 (34)     829     NA     NA       Inclental     22 (63)     36 (31)     30 (34)     829     NA     NA       Symptomatic     22 (34)     31 (46)     27 (31)     369     27 (31)     NA     NA       Dominant side     22 (34)     31 (46)     21 (24)     NA     NA     NA       Upper pole     15 (23)     25 (31)     28 (54)     21 (24)     NA     NA       Upper pole     15 (23)     23 (51)     23 (25)     33 (25)     33 (25)     36 (4)     NA       Unper pole     15 (23)     24 (86)     23 (26)     36 (4)     23 (26)     NA     NA       Unper pole     15 (23)     24 (86)     23 (26)     33 (42)     MA     NA       Unper pole     16 (25)     23 (31)     23 (26)     23 (26)     MA     NA       T1a     NA     23 (31)     14 (65)     23 (26)		Mean ± SD	$58.15 \pm 9.15$	$44.51 \pm 8.88$	$49.17 \pm 10.15$				
Fenale     24 (3)     26 (3)     30 (34)       Nonclemati     24 (5)     48 (72)     0 (6)     829     N/A     N/A       Sympositic     22 (34)     19 (28)     27 (31)     0 (6)     829     N/A     N/A       Sympositic     22 (34)     19 (28)     27 (31)     0 (6)     N/A     N/A       Onimant side     22 (34)     31 (46)     27 (31)     0 (6)     N/A     N/A       Upper pole     33 (52)     21 (31)     28 (32)     0 (6)     N/A     N/A       Leature (T stage)     T1a     NA     24 (50)     23 (2)     0 (7)     N/A     N/A       Leature (T stage)     T1a     NA     24 (50)     23 (2)     0 (7)     N/A     N/A       T1D     NA     24 (50)     28 (32)     0 (7)     N/A     N/A       T1D     NA     21 (30)     21 (30)     21 (20)     0 (7)     N/A       T1D     NA     21 (30)     28 (3)     20 (5)     0 (7)     N/A     N/A  <	Gender	Male	40 (63)	41 (61)	58 (66)	.821	N/A	N/A	N/A
$ \begin{array}{llllllllllllllllllllllllllllllllllll$		Female	24 (37)						
Symptomatic     22 (34)     19 (28)     27 (31)       Non-dominant side     22 (34)     31 (46)     47 (53)     .067     N/A       Non-dominant side     22 (34)     31 (45)     21 (24)     N/A     N/A       Non-dominant side     22 (33)     33 (52)     21 (31)     28 (23)     .056     N/A     N/A       Interpoler     16 (25)     22 (33)     23 (26)     .056     N/A     N/A       Interpoler     15 (23)     24 (56)     23 (26)     .057     N/A     N/A       T11     N/A     34 (51)     46 (52)     .33 (25)     .067     N/A       T2     N/A     11 (16)     11 (16)     11 (16)     .073     N/A       T2     N/A     34 (51)     76 (53)     .074     N/A     N/A       T2     N/A     11 (15)     11 (15)     .073     N/A     N/A       T2     N/A     11 (12)     .073     .074     N/A     N/A       S a (high) grade     N/A     .074     .074	Detection	Incidental	42 (65)			.829	N/A	N/A	N/A
Dominant side     22 (34)     31 (46)     47 (53)     067     NA     NA       Non-dominant side     42 (66)     36 (54)     21 (24)     NA     22 (33)     23 (25)     .982     NA     NA     NA     NA     NA     NA     .097     NA     NA     NA     .097     NA     NA     .097     NA     NA     NA     .097     NA     NA     .097     NA     .011     .		Symptomatic	22 (34)						
Non-dominant side     42 (6)     36 (4)     21 (24)       Upper pole     33 (52)     21 (31)     28 (32)     056     N/A       Upper pole     33 (52)     21 (31)     28 (32)     056     N/A       Interpolar     16 (25)     22 (33)     37 (42)     N/A     N/A       Iterpolar     15 (23)     24 (56)     23 (26)     N/A     N/A       T10     N/A     34 (51)     46 (52)     38 (20)     N/A     N/A       T10     N/A     11 (16)     14 (16)     N/A     17 (88)     N/A     N/A       T2     N/A     11 (15)     14 (16)     N/A     17 (16)     N/A       Grade     1 & 2 (0w) grade     N/A     3 (4)     11 (12)     N/A     N/A       Grade     1 & 2 (0w) grade     N/A     3 (3)     11 (12)     N/A     N/A       statue     3 & 4 (high) grade     N/A     3 (3)     3 (3)     17 (3)     N/A       statue     3 & 4 (high) grade     N/A     13 (3)     3 (3)	Side	Dominant side	22 (34)	31 (46)		.067	N/A	N/A	N/A
Upper pole     33 (52)     21 (31)     28 (32)     .056     N/A     WA       Interpolar     16 (25)     22 (33)     37 (42)     .056     N/A     WA       Interpolar     16 (25)     22 (33)     37 (42)     .056     N/A     WA       Interpolar     15 (23)     24 (36)     23 (26)     .082     N/A     WA       T1b     N/A     34 (51)     46 (52)     .982     N/A     WA       T2     N/A     11 (16)     14 (16)     .097     N/A     WA       Clear     N/A     51 (16)     14 (16)     .097     N/A     WA       Non-clear     N/A     3 (3)     11 (12)     .074     N/A     WA       andure     3 & 4 (ngh) grade     N/A     3 (3)     .074     N/A     WA       s nature     Servus     23 (4)     .11 (12)     .074     N/A     WA       andure     Non-clear     N/A     14 (21)     .074     N/A     WA       s nature     Servus <td></td> <td>Non-dominant side</td> <td>42 (66)</td> <td>36 (54)</td> <td></td> <td></td> <td></td> <td></td> <td></td>		Non-dominant side	42 (66)	36 (54)					
Interpolar     16 (25)     22 (3)     37 (42)       Lower pole     15 (23)     24 (56)     23 (26)       Lower pole     15 (23)     24 (56)     23 (26)       T1b     N/A     34 (51)     46 (52)     382     N/A       T2     N/A     11 (16)     14 (16)     14 (16)     N/A       T2     N/A     11 (16)     14 (16)     097     N/A     N/A       T2     N/A     11 (16)     14 (16)     074     N/A     N/A       Non-clear     N/A     3 (4)     11 (12)     N/A     3 (3)     N/A     N/A       adde     1 & 2 (0w) grade     N/A     57 (65)     .074     N/A     N/A       s nature     Serous     42 (6)     63 (4)     25 (28)     <.0001	Location	Upper pole	33 (52)			.056	N/A	N/A	N/A
Lower pole     15 (23)     24 (36)     23 (26)		Interpolar	16 (25)						
Fleature (T stage)     T1a     N/A     34 (51)     46 (52)     .982     N/A     N/A       T1b     N/A     22 (33)     28 (32)		Lower pole	15 (23)	24 (36)					
T1b   N/A   22 (33)   28 (32)     T2   N/A   11 (16)   14 (16)     T2   N/A   11 (16)   14 (16)     Clear   N/A   64 (96)   77 (88)   .097   N/A   N/A     Non-clear   N/A   53 (79)   57 (65)   .074   N/A   N/A     atter   3 & 4 (high) grade   N/A   14 (21)   31 (35)   .074   N/A   N/A     atter   Serous   42 (66)   63 (94)   25 (28)   <.0001	Pathologic feature (T stage)		N/A	34 (51)	46 (52)	.982	N/A	N/A	N/A
T2     N/A     11 (16)     14 (16)       Clear     N/A     64 (96)     77 (88)     .097     N/A     N/A       Von-clear     N/A     64 (96)     77 (88)     .097     N/A     N/A       Von-clear     N/A     53 (79)     57 (65)     .074     N/A     N/A       3 & 4 (high) grade     N/A     14 (21)     31 (35)     .074     N/A     N/A       a ture     Serous     42 (66)     63 (94)     25 (28)     <.0001			N/A	22 (33)	28 (32)				
Clear     N/A     64 (96)     77 (88)     .097     N/A     N/A       Non-clear     N/A     3 (4)     11 (12)     N/A     N/A     N/A       grade     1 & 2 (ow) grade     N/A     57 (65)     .074     N/A     N/A       3 & 4 (high) grade     N/A     14 (21)     31 (35)     .074     N/A     N/A       a ture     Serous     42 (66)     63 (94)     25 (28)     <.0001		T2	N/A	11 (16)	14 (16)				
Non-clear     N/A     3 (4)     11 (12)       grade     1 & 2 (ow) grade     N/A     53 (79)     57 (65)     .074     N/A     N/A       3 & 4 (high) grade     N/A     14 (21)     31 (35)     .074     N/A     N/A       a ture     Serous     42 (66)     63 (94)     25 (28)     <.0001	Cell type	Clear	N/A	64 (96)	77 (88)	760.	N/A	N/A	N/A
1 & 2 (low) grade     NA     53 (79)     57 (65)     .074     NA     NA       3 & 4 (high) grade     NA     14 (21)     31 (35)     .074     NA     NA       3 & 4 (high) grade     NA     14 (21)     31 (35)     .074     NA     NA       Serous     42 (66)     63 (94)     25 (28)     <.0001		Non-clear	N/A	3 (4)	11 (12)				
3 & 4 (high) grade     NA     14 (21)     31 (35)       3 Serous     42 (66)     63 (94)     25 (28)     <.0001	Fuhrman grade	1 & 2 (low) grade	N/A		57 (65)	.074	N/A	N/A	N/A
Serous     42 (66)     63 (94)     25 (28)     <:0001     5.622     7.837       hemorrhagic/necrotic     22 (34)     4 (6)     63 (72)     7.83     7.837       Nephron-sparing surgery     39 (61)     28 (42)     41 (47)     .073     NA     NA       Radical nephrectomy     25 (39)     39 (58)     47 (53)     .073     NA     NA		3 & 4 (high) grade	N/A		31 (35)				
hemorrhagic/necrotic     22     (34)     4     (6)     63     (72)       Nephron-sparing surgery     39     (61)     28     (42)     41     (47)     .073     N/A     N/A       Radical nephrectomy     25     (39)     39     (58)     47     (53)	Cyst fluid's nature	Serous	42 (66)		25 (28)	<.0001	5.622	7.837	14.001
Nephron-sparing surgery 39 (61) 28 (42) 41 (47) .073 N/A N/A Radical nephrectomy 25 (39) 39 (58) 47 (53)		hemorrhagic/necrotic	22 (34)		63 (72)				
25 (39) 39 (58) 47	Type of surgery	Nephron-sparing surgery	39 (61)	28 (42)	41 (47)	.073	N/A	N/A	N/A
		Radical nephrectomy	25 (39)						

6

Clinical conditions of patients who underwent curative surgery and pathological features of surgically removed complex cystic renal mass.

Table 3

Numerical data are demonstrated as frequency (percentage) and continuous data are demonstrated as mean  $\pm$  SD. One-way ANOVA following Tukey post hoc test was used for statistical analysis.

NA = n of applicable. A P < .05 and q > 3.345 were considered significant. Pathology of surgically removed cystic renal mass was performed by pathologists of the institute. All have minimum of 3-years of experience in gentourinary pathology.

**Comparisons between group** 

renal cell carcinoma The other cystic

# Table 4

Results according to imaging methods and clinicopathology for complex cystic renal mass.

Parameters	Clinicopathology		enhanced ography		enhanced tomography
Data of cysts included in analysis	219	219	* P value	219	*P value
True positive multilocular cystic renal neoplasm of low malignant potential detected	67 (31)	65 (30)	.917	60 (27)	.528
True negative multilocular cystic renal neoplasm of low malignant potential detected	152 (69)	149 (68)	.837	145 (67)	.539
False positive multilocular cystic renal neoplasm of low malignant potential detected	0 (0)	03 (1)	.247	06 (3)**	.039
False negative multilocular cystic renal neoplasm of low malignant potential detected	0 (0)	02 (1)	.479	07 (3)**	.022

A Chi-Squared independence test was performed for statistical analysis.

\* With respect to clinicopathology.

A P<.05 was considered significant.

\*\* Significant difference with respect to clinicopathology.

Multilocular cystic renal neoplasm of low malignant potential by Bosniak classification for imaging modality and those were detected by the 2016 WHO criteria for clinicopathology.

Data are demonstrated as frequency (percentage).

computed tomography. For complex cystic renal mass contrastenhanced, computed tomography is superior to contrastenhanced ultrasound because contrast-enhanced ultrasound is defined as a type of kidney tumor only<sup>[14]</sup> but high sensitivity is required than high specificity in cases of a MCRNLMP for decision making of curative surgeries.<sup>[15]</sup> Contrast-enhanced ultrasound improved lesion detection rate and decreases the misdiagnosis rate for complex cystic renal mass.

Contrast-enhanced computed tomography had detected high false negative (7 vs 2) MCRNLMP than contrast-enhanced ultrasound. The computed tomography has difficulties in interpreting density values of complex cystic renal mass and sometimes it may detect convex protrusion as clear cell renal cell carcinoma,<sup>[16]</sup> detection of small cyst in the interpolar portion of the kidney is difficult (by both imaging methods), and computed tomography of obese patients are challenging,<sup>[16]</sup> leads to falsenegative results. The study reported that contrast-enhanced computed tomography had detected high false positive (6 vs 3) MCRNLMP than contrast-enhanced ultrasound. In the current study, a benign cyst and the other cystic renal cell carcinoma mostly had hemorrhagic/necrotic cyst fluids nature (60%; 85 out of 152), which was detected as obtusely margined convex protrusion<sup>[4]</sup> by contrast-enhanced computed tomography leads to false-positive results. The results of the current study were agreed with the results of retrospective studies,<sup>[16,17]</sup> a prospective study,<sup>[14,18,19]</sup> and a diagnostic evaluation study of contrastenhanced ultrasound against magnetic resonance imaging<sup>[20]</sup> for complex cystic renal masses. Contrast-enhanced ultrasound better visualized complex cystic renal mass than contrastenhanced computed tomography.

Contrast-enhanced computed tomography had reported fewer numbers of MCRNLMP with Bosniak classification IV than contrast-enhanced ultrasound. The distribution of vascularization into intracystic septa and intracystic nodules plays an

# Table 5

Diagnostic	performance	of	imaging	methods	for	multilocular
cystic rena	l neoplasm of	low	malignar	nt potentia	I.	

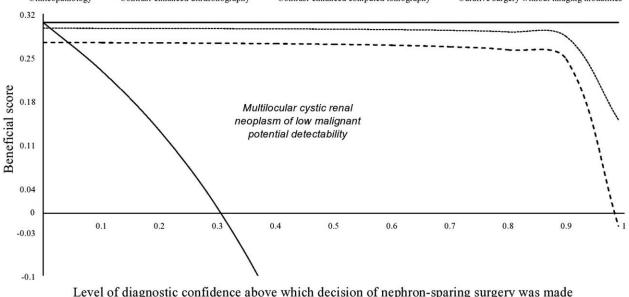
Parameters	Contrast-enhanced ultrasonography	Contrast-enhanced computed tomography
Sensitivity	30.37%	29.27%
Specificity	60.00%	50.00%
Positive predictive value	97.01%	89.55%
Negative predictive value	1.97%	4.61%
Likelihood ratio	75.93%	58.54%

important role in the diagnosis of complex cystic renal mass by imaging modalities.<sup>[21]</sup> Ultrasound is very sensitive to blood flow to judge complex cystic renal mass. The effect of separating blood supply within the lesion is very good, so it is more accurate to judge the Bosniak classification of complex cystic renal mass.<sup>[15]</sup> Contrast-enhanced computed tomography often underestimates the Bosniak classification of complex cystic renal mass.

The study reported that Bosniak classification III and lower mean HU were associated with the prevalence of MCRNLMP. The results of the study were agreed with the retrospective study.<sup>[4]</sup> HU value is associated with the density of tumor and MCRNLMP has low tumor density.<sup>[4]</sup> Contrast-enhanced computed tomography may indirectly helpful for the detection of MCRNLMP from the other cystic renal cell carcinoma.

A contrast-enhanced ultrasound had high diagnostic confidence for decision making of nephron-sparing surgeries than the contrast-enhanced computed tomography. The results of the study are agreed with the results of a retrospective study.<sup>[17]</sup> A prerequisite for reliable classification of renal lesions is the close collaboration of radiologists and urologists for their management.<sup>[22]</sup> An ideal treatment for MCRNLMP is nephron-sparing surgery while radical nephrectomy is preferred in case of the other cystic renal cell carcinoma for >5 cm diameter tumor.<sup>[23]</sup> If urologist makes the decision of radical nephrectomy then either of imaging modality will helpful for decision making of curative surgery but if urologist makes the decision of nephron-sparing surgery, in such condition contrast-enhanced ultrasound is required for decision making of nephron-sparing surgery to decrease the risk of another surgery (radical nephrectomy). Contrast-enhanced ultrasound is problem solving imaging method for curative surgeries of complex cystic renal mass.

There are several limitations of the study, for example, retrospective study and lack of control (enhanced nuclear magnetic resonance imaging) index test. Contrast-enhanced ultrasound is cost-effective than contrast-enhanced computed tomography<sup>[24]</sup> and magnetic resonance imaging<sup>[25]</sup> for the characterization of cystic renal lesions but the study did not evaluate cost parameters. The diagnostic accuracies did not compare for imaging modalities regarding the other cystic renal cell carcinoma. Large numbers of benign cyst detected in pathology after curative surgeries were misdiagnosed as the other cystic nephroma showed enhanced hairline-thin and thick septa by imaging modalities that are responsible for misdiagnosis.<sup>[15]</sup> An interrater reliability among readers did not evaluated. Contrast-enhanced ultrasound had 30.37% sensitivity and 60%



- Clinicopathology ------ Contrast-enhanced ultrasonography - - - Contrast-enhanced computed tomography ----- Curative surgery without imaging modalities

Figure 4. Beneficial score analysis. Multilocular cystic renal neoplasm of the low malignant potential detected by Bosniak classification for imaging modality and those were detected by the 2016 WHO criteria for clinicopathology.

accuracy for the detection of MCRNLMP, which are quite lower than the study would expect from other studies regarding cystic lesions.<sup>[17]</sup> The reasons for such lower diagnostic parameters are that the detection of MCRNLMP was on the basis of complex cystic renal mass (absolute sensitivity and specificity). The differentiation between MCRNLP and tubulocystic renal cell carcinoma might be difficult. The number of tubulocystic renal cell carcinoma did not report in the study.

# 5. Conclusions

Contrast-enhanced ultrasound may have the same sensitivity and high specificity as contrast-enhanced computed tomography for the detection of multilocular cystic renal neoplasm of low malignant potential. Contrast-enhanced ultrasound may be better visualized complex cystic renal mass than contrastenhanced computed tomography. Contrast-enhanced computed tomography underestimates the Bosniak classification of complex cystic renal mass. Contrast-enhanced ultrasound is required for decision making of nephron-sparing surgery for complex cystic renal mass (Bosniak classification III or IV).

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