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Development and prospective validation of a novel weighted quantitative scoring system aimed at predicting the pathological features of cystic renal masses

Yaohui Li[1] · Chenchen Dai[2] · Tingchang Bian[1] · Jianjun Zhou[2] · Zhuoyi Xiang[1] · Minke He[1] · Jiaqi Huang[1] · Yanjun Zhu[1] · Xiaoyi Hu[1] · Shuai Jiang[1] · Jianming Guo[1] · Hang Wang[1]

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Abstract

Objectives To develop and prospectively validate a novel weighted quantitative scoring system based on CT findings, namely, the renal cyst index (RCI), aimed at preoperatively predicting the pathological features of cystic renal masses (CRMs).

Methods The RCI was based on four critical features of CRMs: the cyst wall, septal, nodule, and cyst contents. These parameters were scored with 1, 2, or 3 points. Weight coefficients for these parameters were determined by the multivariable logistic regression. The odds ratio (OR) and 95% confidence interval (95% CI) were used to summarise the results. The RCI was defined as the sum of these four weight coefficients. Malignancy risk prediction models were built based on the retrospective evaluation of 441 patients. We also compared the prediction ability of the RCI with the Bosniak classification in the 441 patients and applied these novel models to 152 masses resected in our institution to prospectively validate the efficiency of the RCI.

Results The wall point (OR = 5.71 [95% CI = 1.734–18.808, $p = 0.004$, point = 2], OR = 12.665 [95% CI = 3.750–42.770, $p < 0.001$, point = 3]), septal point (OR = 3.325 [95% CI = 1.272–8.692, $p = 0.014$, point = 3]), nodule point (OR = 4.588 [95% CI = 1.429–14.729, $p < 0.001$, point = 2], OR = 17.032 [95% CI = 5.017–57.820, $p = 0.010$, point = 3]), content point (OR = 22.822 [95% CI = 1.041–495.995, $p = 0.047$, point = 2], OR = 2.723 [95% CI = 1.296–10.696, $p = 0.015$, point = 3]), and RCI (OR = 1.247 [95% CI = 1.197–1.299, $p < 0.001$]) were significantly associated with malignancy. Masses with an RCI < 6 were regarded as benign masses; masses with an RCI ≥ 10 were regarded as malignant masses. The malignancy risk of masses with an RCI > 6 but < 10 were determined by a nomogram. The prediction ability of the RCI was significantly superior to the Bosniak classification for Bosniak IIF and III masses (AUC: 0.912 vs. 0.753, $p = 0.001$). The RCI also accurately predicted the pathological features of 152 masses.

Conclusion The RCI is a reliable quantitative scoring system in predicting the malignancy risk of CRMs, and it outperformed the Bosniak classification system in some ways.

Key Points

- *The renal cyst index (RCI) is a useful weighted quantitative classification system based on CT findings for diagnosing cystic renal masses.*
- *The RCI outperforms the Bosniak classification system in some ways, especially for Bosniak IIF and III masses.*
- *Masses with an RCI < 6 can be regarded as a simple cyst, while those with an RCI > 10 can be regarded as malignant masses.*

Keywords Cystic kidney diseases · Renal cell carcinoma · Tomography, x-ray computed · ROC curve

Yaohui Li and Chenchen Dai contributed equally to this work.

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✉ Jianming Guo
guo.jianming@zs-hospital.sh.cn

✉ Hang Wang
wang.hang@zs-hospital.sh.cn

[1] Department of Urology, Zhongshan Hospital, Fudan University, 180th Fengling Rd, Xuhui District, Shanghai 200032, China

[2] Department of Radiology, Zhongshan Hospital, Fudan University, 180th Fengling Rd, Xuhui District, Shanghai, China

Abbreviations

AUC	Areas under the curve
ccRCC	Clear cell renal cell carcinoma
CIs	Confidence intervals
CMP	Corticomedullary phase
CRM	Cystic renal masses
CT	Computerised tomography
ORs	Odds ratios
PCP	Pre-contrast phases
RCI	Renal cyst index
ROC	Receiver-operating characteristic
ROI	Region of interest

Introduction

The incidence of cystic renal masses (CRM) is increasing rapidly because of the wide use of cross-sectional imaging in the past few decades [1]. A considerable number of CRMs are simple renal cysts that do not deserve any surgical procedures or follow-ups. However, some of them are difficult to diagnosis and manage, as they show a complex pattern, with a thickness of septations or a cyst wall, an enhancement of the mural nodule, calcifications, and so on [2, 3].

The primary issue in the decision-making process is determining the likely diagnosis [4]. To address the problem, Bosniak et al introduced a classification system [5] that categorised cystic renal masses into four groups of different malignancy risks on the basis of computerised tomography (CT) findings (such as the number of septa, nodular or solid components, smooth or irregular walls, and enhancement) in 1986 to help with the diagnosis of CRMs. A fifth group, called "IIF", was suggested for addition into this classification system to help distinguish between minimally complex and benign cystic renal masses [6] in 1993. In 2005, the classification system was updated by Bosniak et al and reached its current format.

The Bosniak classification has been widely used in the past decades. Many studies [7–13] have evaluated the reliability of the Bosniak classification and validated its efficiency in the diagnosis of CRM. However, the Bosniak classification has some limitations; interobserver variability cannot be avoided since the classification system is reader dependent and lacks strict definitions of some criteria. Thus, a Bosniak IIF mass may be misdiagnosed as a Bosniak III mass or vice versa; a substantial proportion of Bosniak III lesions are benign and undergo unnecessary resection [9]; additionally, the classification system is not a quantitative scoring system, which reduces its ability of a malignant risk successive assessment. Therefore, a quantitative scoring system with a nomogram, which can continuously assess the malignancy risk of a CRM, was needed to improve the interobserver variability and diagnostic efficiency.

Many indexes that may be helpful in the diagnosis of CRM, including the mass size, calcification, cyst wall, septum, nodule, cyst content, and some biomarkers, have been studied by radiologists and urologists [3, 14, 15]. Generally, the mass size was not regarded as a meaningful index that was significantly associated with malignancy [4, 16], while Han et al believed that the mass size may make a contribution to predicting a malignant mass with a reasonable partition [17]. It was widely agreed that there was not an inevitable connection between the calcification in the wall or septa of a CRM and malignancy [14, 18, 19]. However, the cyst wall, septum, nodule, and cyst contents were considered as significant indexes in the diagnosis of CRM [3, 11, 20, 21].

In this study, we developed a new quantitative scoring system based on CT findings, including the cyst wall, septum, nodule, and cyst contents, called the renal cyst index (RCI), aimed at preoperatively predicting the malignancy risk of CRMs. We also validated the outstanding ability of the RCI to predict the pathological features of CRM in an independent cohort. Furthermore, we compared the prediction accuracy of the RCI and Bosniak classification in different masses. A priori sample size and a post hoc power analysis were developed by G*POWER [22]. The results are listed in Supplemental Table 1.

Materials and methods

Inclusion and exclusion criteria

One thousand seven hundred fourteen patients were identified from the medical record system in our institute between August 2007 and June 2014 using various key words, including cysts, renal cysts, cystic renal masses, and cystic renal carcinoma. The inclusion criteria were as follows: (1) adults (18 years old or older); (2) those diagnosed with cystic renal masses by radiologists (cystic component > 70%); (3) those with masses resected in our institution. The exclusion criteria were as follows: essential data, including demographic data, contrast-enhanced CT images, and pathological data, were incomplete.

Techniques of CT imaging

CT examinations were performed at our institution with one of the following multidetector CT scanners: Siemens sensation 16 (Siemens Healthineers), Siemens definition 64 (Siemens Healthineers), and GE lightspeed 64 (Ge Healthcare). After a routine unenhanced scan, 1.5 ml/kg of contrast material (Ultravist 370, Bayer Schering Pharma) was injected into an antecubital vein at a rate of 3.0 ml/s to 3.5 ml/s via a pump injector. The corticomedullary CT images were obtained at 25 −30 s after the start of injection. The slice thickness was 5 mm in all scans. The tube voltage was 120 kVp.

Definition of RCI

RCI contained four parameters. The details of the four parameters are shown in Table 1, Figs. 1 and 2. These four parameters were all based on CT findings.

1. Cyst wall point. A cyst with a non-enhanced hairline thin cyst wall was assigned one point; a cyst with a non-enhanced thickened (> 1 mm) or irregular cyst wall was assigned two points; a cyst with an enhanced cyst wall was assigned three points.
2. Septum point. A cyst without septa was given one point; a cyst with non-enhanced septa was given two points; a cyst with enhanced septa was given three points.
3. Nodule point. A cyst without a nodule was given one point; a cyst with a non-enhanced nodule was given two points; a cyst with an enhanced nodule was given three points.
4. Cyst content point. A homogeneous cyst whose CT value was < 20 HU or > 70 HU was given one point; a homogeneous cyst whose CT value was > 20 HU but did not reach 70 HU was given two points; a heterogeneous cyst defined as the difference of HU values of random ROIs > 20 HU was given three points [23]. The CT values were assessed in pre-contrast phases (PCP).

Enhancement was routinely defined as the difference in the HU values of the same ROI between the corticomedullary phases (CMP, HU values were assessed on the highest enhancing area) and PCP (CMP minus PCP) > 20 HU [23]. Since the region of interest (ROI) measurement was not feasible in the cyst wall or septum, the cyst wall and septum were also deemed to be enhanced when they were not evident on the pre-contrast phases (PCP) but when they were seen as distinct structures on the corticomedullary phases (CMP) [24].

Weight coefficients for these for parameters were determined by the multivariable logistic regression. RCI was defined as the sum of the weight coefficients.

All CT images were interpreted as described above by two radiologists who were blind to the pathological diagnoses. (D.C.C. and Z.J.J. with 4 years and 18 years of experience in genitourinary imaging, respectively). Procedurally, there were two steps in interpreting the CT images. In the first step, two radiologists interpreted CT images independently. A kappa value was used to measure the interobserver agreement. In the second step, parameters whose points were different between the two radiologists reached a final consensus based on discussion between the two radiologists for each mass. The values of the final consensuses were used in the statistical analysis.

Data collection and statistical analysis

Demographic and clinical data, including age, gender, RCI, tumour size, and pathological results, were recorded. Quantitative data were shown as the means ± SD.

The statistical analysis in this study was divided into two parts. The first part consisted of the building of models aimed at predicting the malignancy risk of CRM, including a multivariable logistic regression model and a univariate model based on the threshold of RCI. In this part, a Pearson chi-square or Fisher exact tests, *t* test, or Mann-Whitney tests, and binary logistic regression were used to test the associations between the pathological results and gender, location of tumour, age, tumour size, or RCI, respectively. In the univariate binary logistic regression analysis, the wall, septal, nodule, and content points were enrolled in the model as factorial variables (point = 1 was served as reference). The results of the binary logistic regression were summarised with odds ratios (ORs) and 95% confidence intervals (95% CIs). In addition, wall, septum, nodule, and content points were involved in the multivariable logistic analysis after a univariate analysis with necessary adjustments. A nomogram for predicting the malignancy risk of cystic renal masses was developed using the results from the multivariable logistic regression model. The C-index was used to assess the predictive accuracy

Table 1 The standard for evaluation of the renal cyst index (RCI)

Points	1	2	3
Wall	≤ 1 mm, not enhanced	> 1 mm, not enhanced	Enhanced
Coefficient	1	5.711	12.665
Septum	None	One or more, not enhanced	Enhanced
Coefficient	1	1	3.325
Nodule	None	One or more, not enhanced	Enhanced
Coefficient	1	4.588	17.032
Content	Homogeneous, CT values < 20 HU or > 70 HU	Homogeneous, CT values > 20 HU and < 70 HU	Heterogeneous
Coefficient	1	22.822	2.723

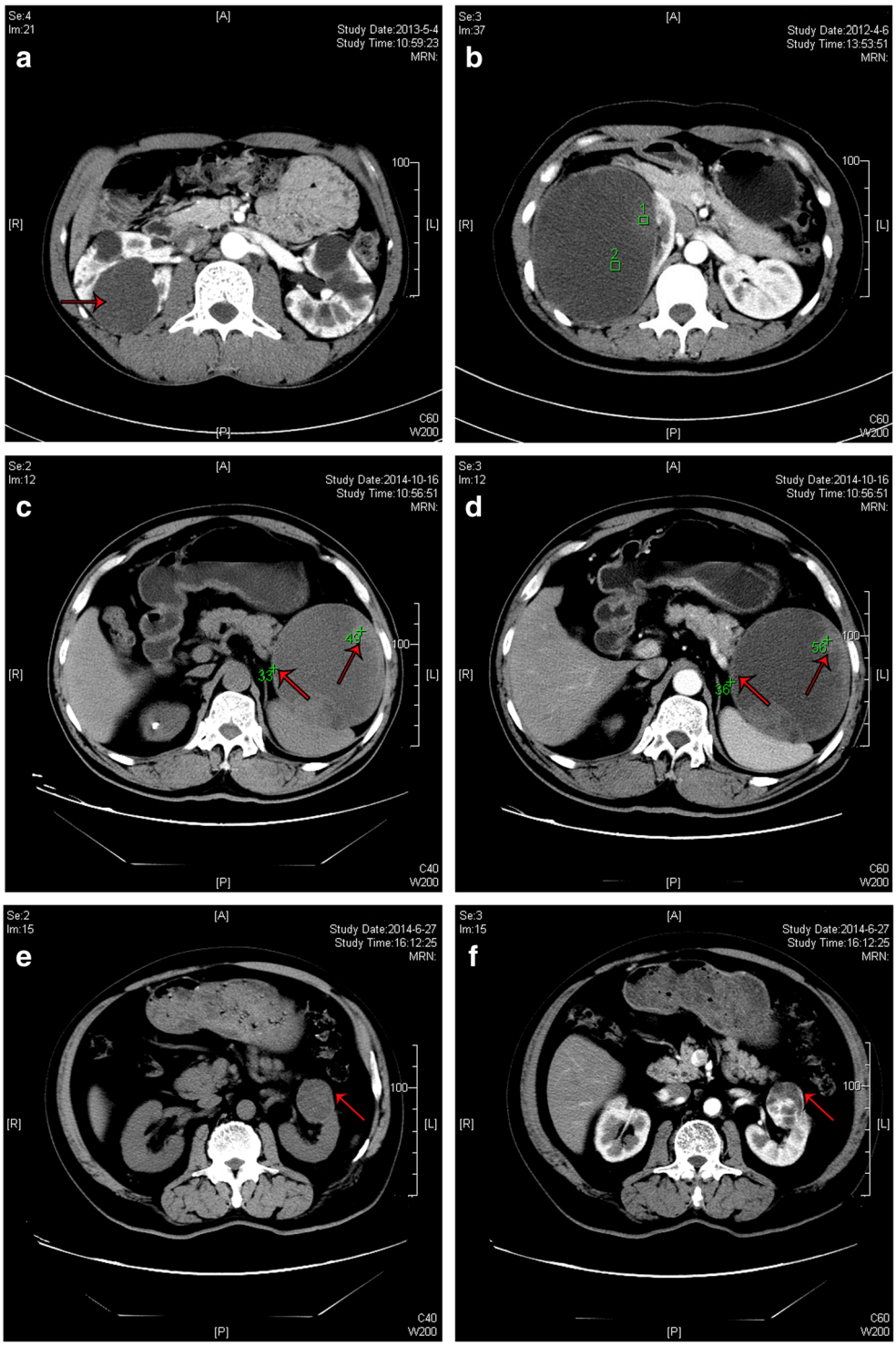

Fig. 1 **a** All four parameters are 1 point. This mass was proven to be a papillary renal cell carcinoma (male, 40 years). **b** Cyst content point = 3. The mean CT value of Box 1 is 33, while Box 2 is 12. This mass was proven to be a cystic clear cell renal cell carcinoma with haemorrhage (female, 33 years). **c** and **d** Wall point = 2; nodule point = 2. The CT values of the wall in the pre-contrast phase and the corticomedullary phase were 33 and 36, respectively. The CT values of the nodule in the pre-contrast phase and the corticomedullary phase were 49 and 56, respectively. This mass was proven to be a papillary renal cell carcinoma (male, 54 years). **e** and **f** Wall point = 3. As indicated by the arrows, the cyst wall was not evident in the pre-contrast phases (PCP) but was seen as a distinct structure in the corticomedullary phases (CMP). This mass was proven to be a cystic clear cell renal cell carcinoma (male, 75 years)

and the sufficiency of this model. The receiver-operating characteristic (ROC) was plotted, and the area under the curve (AUC) was calculated for the RCI to predict the malignancy risk of CRM; a cut-off value was further determined based on the ROC. A decision curve analysis was used to calculate the net benefit of the RCI and Bosniak classification as described by Vickers et al [25].

In the second part, we compared the malignancy prediction ability of the RCI with the Bosniak classification and validated the efficiency of these models. The Hanley & McNeil test

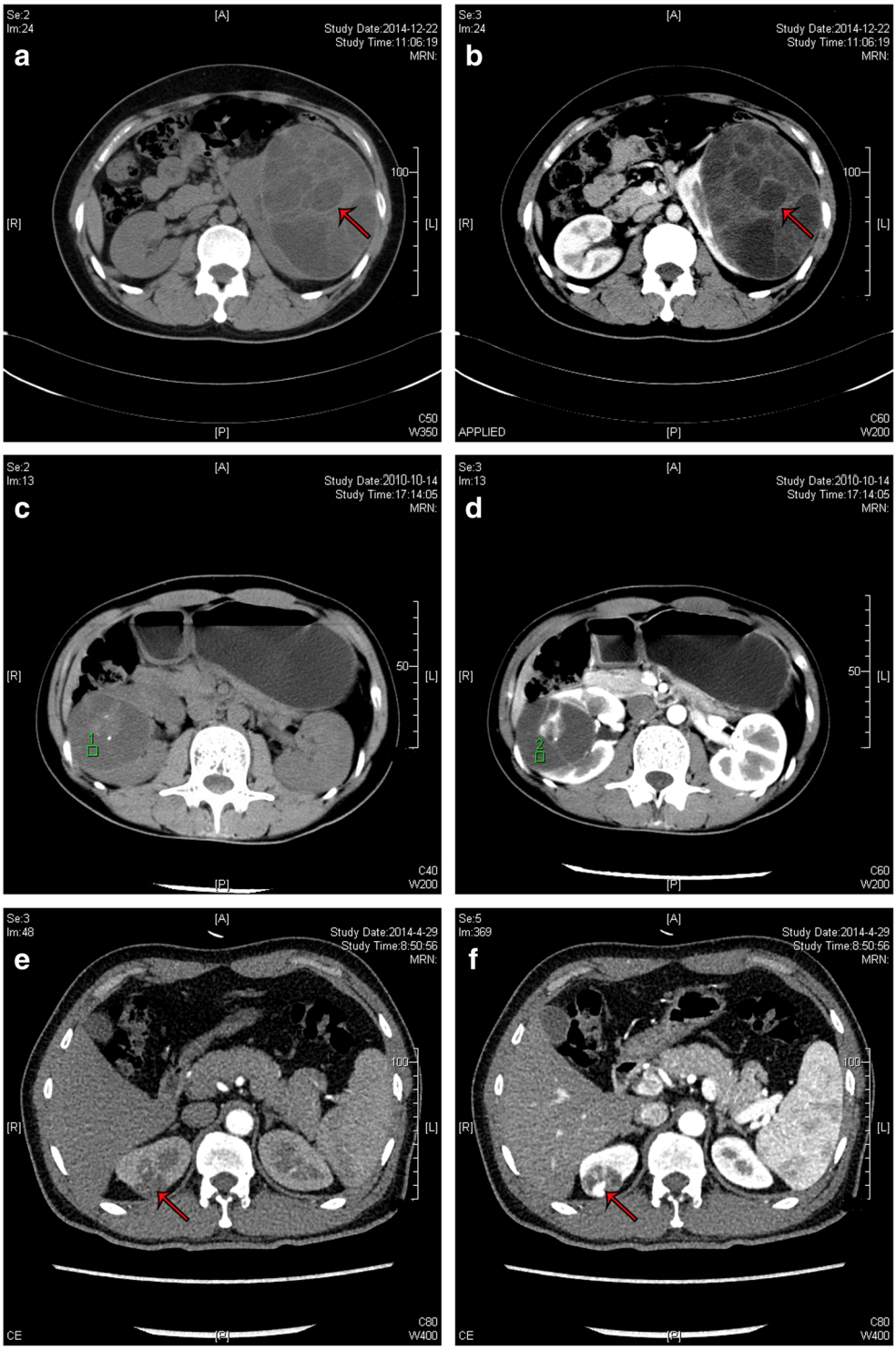

Fig. 2 **a** and **b** Septum point = 2. Both septa were visible in the pre-contrast phases (PCP) and the corticomedullary phases (CMP). This mass was proven to be a papillary renal cell carcinoma (female, 35 years). **c** and **d** Cyst content point = 2. The mean CT value of Box 1 is 26; the mean CT value of Box 2 is 29. This mass was proven to be a papillary renal cell carcinoma (female, 32 years). **e** and **f** Nodule point = 3. As indicated by the arrows, the CT values of the nodule in the pre-contrast phase and the corticomedullary phase were 39.8 and 343, respectively. This mass was proven to be a cystic clear cell renal cell carcinoma (male, 48 years)

was used to compare the malignancy prediction ability of the RCI and Bosniak classification. In this part, the RCI was also applied to 152 cystic renal masses resected in our institution between January 2015 and January 2016 (n = 89) as well as between August 2016 and March 2017 (n = 63). Two experienced radiologists (D.C.C. and Z.J.J.) were asked to preoperatively interpret the CT images of these masses, and they scored each of them. Masses were roughly determined as benign masses or malignant masses based on the threshold of the RCI. These preoperative determinations did not influence

clinical decision-making. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated to assess the efficiency of these models.

All tests were two-sided, with $p < 0.05$ considered to indicate statistical significance. All analyses were performed by SPSS software version 22.0 (IBM SPSS), Stata version 14.0, or MedCalc version 15, and the nomogram and decision curve were developed by R-3.3.1 [26].

Results

Four hundred forty-one patients (266 males and 175 females) with 474 masses were enrolled in our study. No lesions were biopsied prior to resection. Of these lesions, 94 masses were malignant, including 77 cystic clear cell renal cell carcinomas (ccRCCs), 12 papillary carcinomas, 2 chromophobe carcinomas, 1 spindle cell carcinoma, and 2 unclassified renal cell carcinomas, while 380 masses were benign, including 231 simple cysts, 141 benign complex cysts, 2 cystic nephromas, 3 nerve sheath tumours, 1 inflammatory focus, and 2 tuberculous granulomas. The patient demographics and mass characteristics are shown in Table 2. The cyst wall points, septum points, nodule points, cyst content points, and RCI were significantly higher in the malignant group (all $p < 0.001$).

Binary logistic regression and development of the weighted formula

In the univariate binary logistic regression analysis, the cyst wall points, septum points, nodule points, cyst content points, RCI (OR = 1.241, 95% CI = 1.194–1.299, $p < 0.001$), and gender (male vs. female OR = 2.420, 95% CI = 1.450–4.039, $p = 0.001$) were significantly associated with malignant pathological features (Table 3). However, "septum point = 2" was not significantly associated with the malignant pathological features; thus, "septum point = 2" was combined with "septum point = 1".

Table 2 Patient demographics and mass characteristics

	All patients (masses = 474; patients = 441)	Benign (masses = 380; Patients = 353)	Malignant (masses = 94; patients = 88)	*p* value
Gender				
Male (*n*)	266	199	67	0.001[a]
Female (*n*)	175	154	21	
Left (*n*)	236	184	52	0.250 [a]
Age (X ± SD)	57.10 ± 12.76	56.76 ± 12.59	58.47 ± 13.43	0.260[b]
Size (X ± SD)	5.46 ± 2.90	5.41 ± 2.82	5.68 ± 3.22	0.421 [b]
Wall points (*n*)				< 0.001 [a]
1	343	334	9	
2	41	32	9	
3	90	14	76	
Septum points (*n*)				< 0.001 [a]
1	294	257	37	
2	92	86	6	
3	88	37	51	
Nodule points (*n*)				< 0.001 [a]
1	374	355	19	
2	29	19	10	
3	71	6	65	
Content points (*n*)				< 0.001 [a]
1	392	365	27	
2	7	1	6	
3	75	14	61	
RCI (mean, range)	10.43 (4–55.74)	5.64 (4–36.74)	29.76 (4–55.74)	< 0.001[c]

RCI Renal cyst index

[a] Pearson chi-square test

[b] Student's *t* test

[c] Mann-Whitney U test

The cyst wall, septum, nodule, and cyst content points still showed significant associations with malignant pathological features in the multivariate logistic analysis (Table 3). To vividly reflect the different weights of these four indexes in predicting a malignant mass, a nomogram was developed based on the results from the multivariable logistic regression model (Fig. 3a and b). The C index of the multivariable logistic regression model was 0.972.

Based on the findings above, a formula was developed to calculate the RCI: RCI = A (A = 1 if the wall point = 1; A = 5.711 if the wall point = 2; A = 12.665 if the wall point = 3) + B (B = 1 if the septum point = 1 or 2; B = 3.325 if the septum point = 3) + C (C = 1 if the nodule point = 1; C = 4.588 if the nodule point = 2; C = 17.032 if the nodule point = 3) + D (D = 1 if the content point = 1; D = 22.822 if the content point = 2; D = 2.723 if the content point = 3) (Table 1). An ROC analysis was also performed for the RCI to predict the malignancy risk of the cystic renal masses. The AUC of the RCI was 0.972 (95% CI = 0.954-0.989, $p < 0.001$, Fig. 3c). The two thresholds of the RCI were determined as six and ten based on the results of the ROC. For example, masses with RCI < 6 can be regarded as simple cysts and do not require treatment, while masses with RCI ≥ 10 have a large risk of malignancy, and resection is suggested for these masses. The malignancy risk of masses with an RCI value > 6 but < 10 were determined by the nomogram, and the management of these masses will be by clinicians based on the malignancy risk and their experience.

Comparing the RCI with the Bosniak classification

We also compared the malignancy prediction ability of the RCI and the Bosniak classification in different groups of RCMs. The AUC of the RCI was slightly higher than that of the Bosniak classification in all 474 masses but did not reach significance (0.972 vs. 0.960, $p = 0.110$); however, the malignancy prediction ability of the RCI was significantly superior than that of the Bosniak classification in Bosniak IIF and III masses (AUC: 0.912 vs. 0.753, $p = 0.001$, Fig. 3d). The decision curve analysis also showed that the net benefit of the RCI in predicting malignant masses was superior to that of the Bosniak classification, with a probability threshold of 0.05–0.8 (Fig. 4).

Prospective validation of RCI

In the extended cohort for the validation of the two models, there were 19 malignant masses and 133 benign masses. The data showed that the univariate model based on the threshold of the RCI was effective in predicting a malignant mass. In the univariate model based on a threshold of RCI = 10 (masses with RCI ≥ 10 were diagnosed as malignant masses, while masses with RCI < 10 were diagnosed as benign masses), the sensitivity, specificity, positive predictive value, and negative predictive value were 94.74%, 96.24%, 78.26%, and 99.22%, respectively (Supplemental Table 2).

Table 3 Univariate and multivariable analysis of factors with an impact on malignant risk

		Univariate analysis			Multivariate analysis		
		OR	95% CI	*p* value	OR	95% CI	*p* value
Size		1.032	0.956–1.114	0.421			
Wall point	1	Ref.			Ref.		
	2	10.437	3.868–28.162	< 0.001	5.711	1.734–18.808	0.004
	3	201.460	84.095–482.627	< 0.001	12.665	3.750–42.770	< 0.001
Septum points	1	Ref.			Ref.		
	2	0.485	0.198–1.18	0.113	Ref.		
	3	9.574	5.547–16.525	< 0.001	3.325	1.272–8.692	0.014
Nodule points	1	Ref.			Ref.		
	2	9.834	4.022–24.044	< 0.001	4.588	1.429–14.729	< 0.001
	3	202.412	77.878–526.091	< 0.001	17.032	5.017–57.820	0.010
Content points	1	Ref.			Ref.		
	2	81.111	9.422–698.273	< 0.001	22.822	1.041–495.995	0.047
	3	58.902	29.246–118.628	< 0.001	2.723	1.296–10.696	0.015
RCI (every one point increase)		1.247	1.197–1.299	< 0.001			
Gender (male vs. female)		2.420	1.450–4.039	0.001			
Age (every 1 year increase)		1.010	0.992–1.028	0.287			

OR Odds ratio, *RCI* Renal cyst index

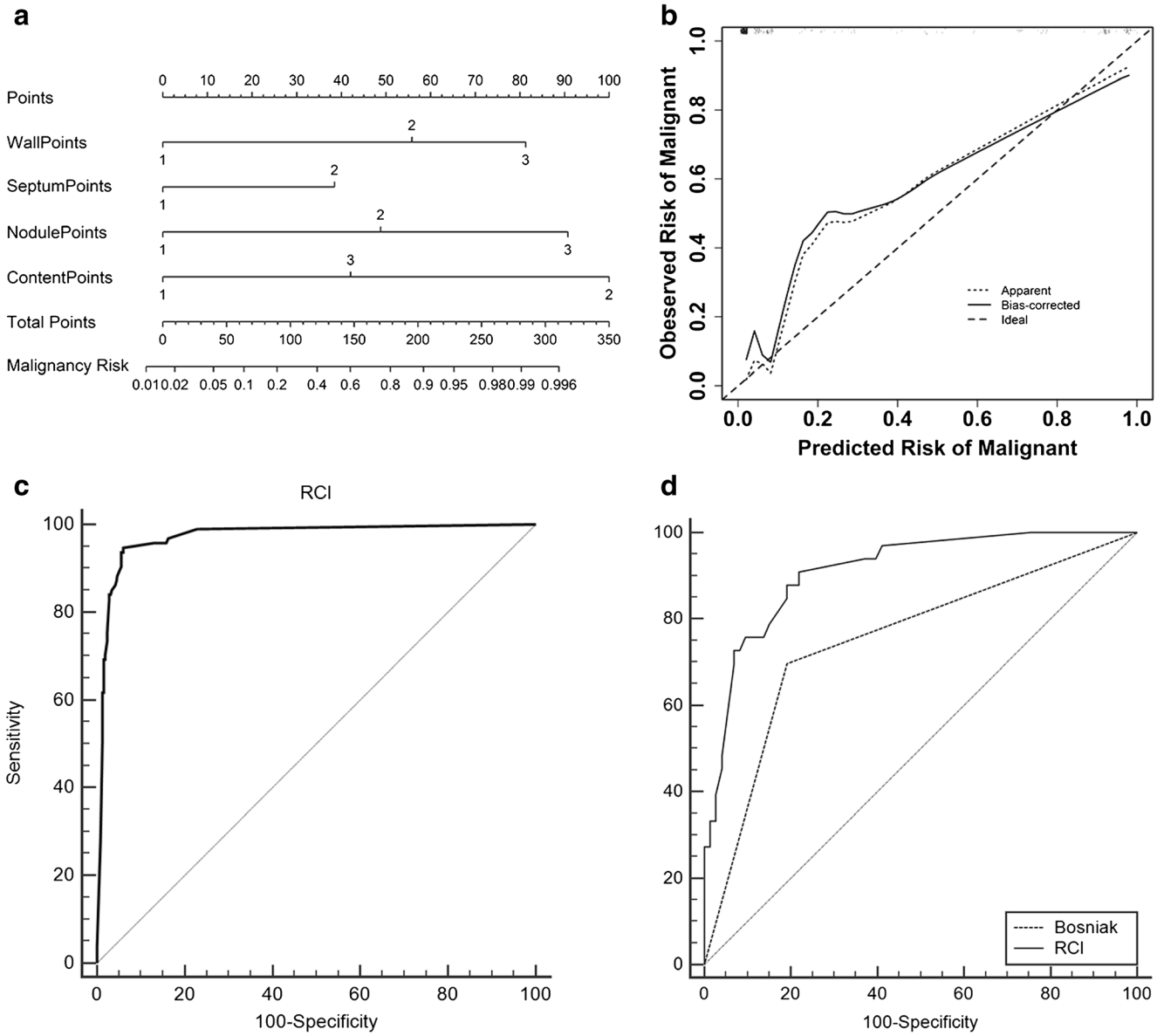

Fig. 3 **a** A nomogram to predict the malignancy risk of cystic renal masses. **b** Calibration plot for the logistic regression model. **c** ROC for the renal cyst index to predict the malignancy risk of cystic renal masses. **d** ROC of the RCI and the Bosniak classification for Bosniak IIF and III masses (AUC: 0.912 vs. 0.753, $p = 0.001$)

Discussion

In this study, we proposed and prospectively validated a novel weighted quantitative classification system, namely, the RCI, for the diagnosis of CRMs. We validated the outstanding ability of this model in predicting the pathological features of CRMs.

Many factors were believed to be related to malignancy, such as the cyst wall, septa, nodule, and cyst contents, as well as a history of RCC, a coexisting Bosniak IV lesion, male gender, hypertension, and body mass index [27, 28]. Based on previous studies [29–31] and for the convenience of application, cyst wall, septum, nodule, and cyst content points were finally selected to compose the RCI. As expected, these four parameters and the RCI were all significantly associated with malignancy.

To our knowledge, the RCI is the first quantitative scoring system containing four different weighting parameters aimed at preoperatively predicting the features of CRMs. The RCI showed an outstanding ability in predicting a malignant CRM (Table 3). Masses with RCI < 6 were regarded as benign masses; masses with RCI ≥ 10 were regarded as malignant masses; masses with RCI > 6 but < 10 were assessed by the nomogram to determine the malignancy risk. Additionally, since the RCI was a quantitative scoring system, urologists continuously monitored the risk of malignancy during active surveillance. If the malignancy risk of a CRM significantly

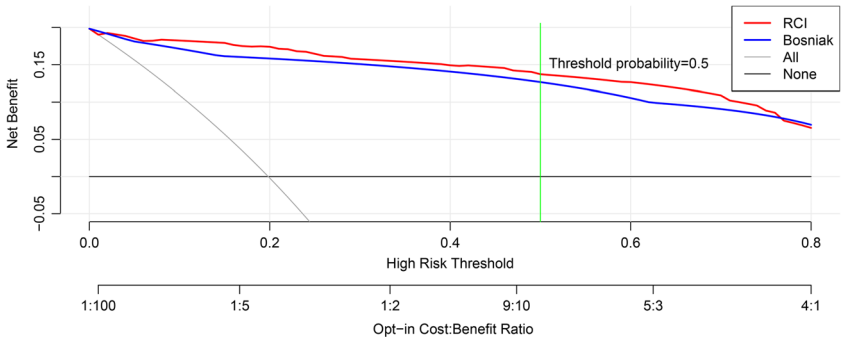

Fig. 4 The decision curve of the RCI and Bosniak classification. Solid black line: assumes no mass is malignant. Solid grey line: assumes all masses are malignant. Blue line: RCI. Red line: Bosniak classification. Green line: the threshold of 0.5

increased during the active surveillance, this mass was treated as a malignant mass.

It was universally acknowledged that the difficulty in accurately diagnosing Bosniak IIF and III masses was a limitation of the Bosniak classification. Although the prediction ability of the RCI was not significantly higher than that of the Bosniak classification in all 474 masses (AUC: 0.972 vs. 0.960, $p = 0.110$), the malignancy prediction ability of the RCI was significantly superior to the Bosniak classification in Bosniak IIF and III masses (AUC: 0.912 vs. 0.753, $p = 0.001$, Fig. 3d). For example, the mass shown in Fig. 5a and b was a Bosniak IIF mass because it lacked measurable enhancement. However, its RCI was 12.299, which indicates a high risk of malignancy. This mass was finally proven to be a papillary carcinoma. The mass shown in Fig. 5c and d was a Bosniak III mass because of the thickened septum with a

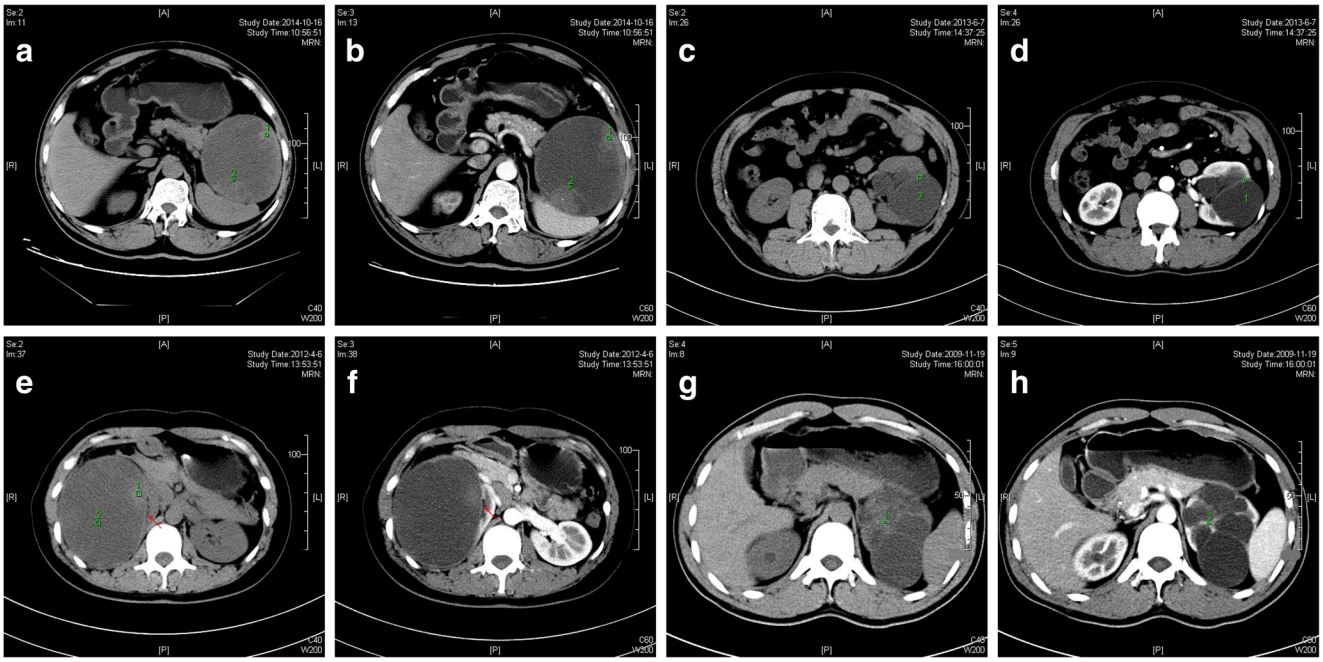

Fig. 5 **a** and **b** A Bosniak IIF mass. **a** The pre-contrast phase. **b** The corticomedullary phase. The septa and wall of this mass were thickened, but there was no measurable enhancement. The CT value of Box 1 in (**a**) is 33.7; the CT value of Box 2 in (**a**) is 29.4; the CT value of Box 1 in (**b**) is 48.2; the CT value of Box 2 in (**b**) is 41.2. The wall point of this mass is 2, the septum point is 2, the nodule point is 2, and the content point is 1; thus, the RCI of this mass is 12.299, which indicates a higher risk of malignancy. This mass was proven to be a papillary renal cell carcinoma. **c** and **d** A Bosniak III mass. **c** The pre-contrast phase. **d** The corticomedullary phase. The septa of this mass are thickened, which measurable enhancement. The CT value of Box 2 in (**c**) is 15.6; the CT value of Box 1 in (**d**) is 39.6. The wall point of this mass is 1, the septum point is 3, the nodule point is 1, and the content point is 1; thus, the RCI of this mass is 6.325, which indicates a lower risk of malignancy. This mass was proven to be a benign complex renal cyst. **e** and **f** A Bosniak IIF mass. **e** The pre-contrast phase. **f** The corticomedullary phase. The CT value of Box 1 in (**e**) is 17.1; the CT value of Box 2 in (**e**) is 40.9. The wall of this mass was thickened, but there was no measurable enhancement (indicated by arrow). The wall point of this mass is 2, the septum point is 1, the nodule point is 1, and the content point is 3; thus, the RCI is 10.434, which indicates a higher risk of malignancy. This mass was proven to be a cystic clear cell renal cell carcinoma with haemorrhage. **g** and **h** A Bosniak III mass. **g** The pre-contrast phase. **h** The corticomedullary phase. The CT value of Box 1 in (**g**) is 37; the CT value of Box 1 in (**h**) is 88.7. The septa of this mass are thickened, with measurable enhancement. The wall point of this mass is 1, the septum point is 3, the nodule point is 1, and the content point is 1; thus, the RCI of this mass is 6.325, which indicates a lower risk of malignancy. This mass was proven to be a benign complex renal cyst

measurable enhancement. However, its RCI was 6.325, which indicates a low risk of malignancy. This mass was proven to be a benign complicated cyst. There were some reasons that may explain this finding. (1) Some parameters that the Bosniak classification includes, such as calcifications [13], the number of septa, and the size of cyst, may not predict the malignancy accurately, which dilutes its ability to predict the pathological features of CRM. In contrast, the RCI only included the four most important parameters, and all these parameters were significantly associated with malignancy. (2) The Bosniak classification is reader-dependent and lacks a strict definition of some criteria; thus, a CRM may be under- or overestimated by different doctors, whereas we defined the criteria more strictly in the RCI, and thus masses would be assessed more accurately with the RCI. (3) The Bosniak classification is not a quantitative scoring system, which prevents it from discriminating the small differences in CRMs. For example, a mass with an enhanced cyst wall and a mass with both a cyst wall and enhanced septa were both regarded as Bosniak III masses; however, in our study, both the enhancement of the septa and the cyst wall were independent indicators of malignancy; thus, a mass with both a cyst wall and enhanced septa would have a higher malignancy risk than a mass with only a cyst wall or enhanced septa. Therefore, the RCI is more accurate in the prediction of malignancy than the Bosniak classification in Bosniak IIF and III masses and can replace the Bosniak classification in some ways.

We recognise that the RCI is not a perfect scoring system, as some complicated cysts, cystic nephroma, tuberculous granuloma, inflammatory focus, and other special types of benign tumours with a high RCI (RCI $\geq$ 10) were misjudged as malignant masses, while some papillary RCCs with a low RCI (RCI < 10) were misjudged as benign masses (Supplemental Table 3). In addition to CT images, urologists should also pay attention to patient gender, age, and history [18]. For instance, a mass with RCI = 10 in an elderly male should bear a higher malignancy risk than that in a young female with a history of tuberculosis.

We admit that there were some limitations to our study. First, the study was a single centre and retrospective study, and only patients who underwent surgery were enrolled. Second, the CT image interpretations were affected by different equipment, technologies, and many scans that were done as part of a routine post-contrast abdominal CT; only CMP images were used for analysis, which may cause an underestimation in the change of CT values in papillary carcinoma [3]. Third, some septa may be subjectively enhanced if the PCP and CMP images were compared side by side; thus, the septal points may be overestimated (Supplemental Fig. 1). This phenomenon was regarded as "perceived" enhancement by Bosniak. Fourth, the renal cyst pseudo-enhancement may lead to an overestimation of the RCI, especially when the nodule was overestimated (because the weighted coefficient of the nodule is the highest one). However, the dual-energy multidetector CT with optimal-energy virtual monochromatic images can overcome renal cyst pseudo-enhancement. Thus, we believe that the proposed model will bring substantial improvements to the RCI system [32]. Fifth, the content point = 2 has a higher OR than the content point = 3, which seems to be slightly contradictory to our clinical experience. We speculate that this finding may be due to the relatively small number of patients a content point = 2; this should be the focus of further studies.

Despite these limitations, our findings suggest that the RCI is a useful quantitative scoring system to preoperatively predict the malignancy risk of CRMs and that it is superior to the Bosniak classification for Bosniak IIF and III masses. The interobserver reproducibility between two radiologists in assessing the RCI was excellent (all $\kappa > 0.7$, Supplemental Table 4). Further studies are needed to validate and improve this scoring system in larger samples and in other institutions.

To summarise, the RCI is a useful quantitative scoring system to preoperatively predict the malignancy risk of CRMs, and it outperforms the Bosniak classification, especially for Bosniak IIF and III masses. In the future, the validation and improvement of our findings in a larger sample and in other institutions are warranted.

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was not required for this study because this study is a retrospective study and patients have full autonomy in decision-making.

Ethical approval Institutional Review Board approval was not required because this study is a retrospective study and patients have full autonomy in decision-making.

Methodology
- retrospective
- diagnostic or prognostic study
- performed at one institution

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