

# Differential Diagnosis of Complex Renal Cysts Based on Lesion Size along with the Bosniak Renal Cyst Classification

Hyun Ho Han,<sup>1</sup> Kyung Hwa Choi,<sup>1</sup> Young Taik Oh,<sup>2</sup> Seung Choul Yang,<sup>1</sup> and Woong Kyu Han<sup>1</sup>

<sup>1</sup>Department of Urology, Urological Science Institute, Yonsei University College of Medicine, Seoul;

<sup>2</sup>Department of Diagnostic Radiology, Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Korea.

Received: August 24, 2011

Revised: October 16, 2011

Accepted: October 18, 2011

Corresponding author: Dr. Woong Kyu Han,

Department of Urology,

Urological Science Institute,

Yonsei University College of Medicine,

50 Yonsei-ro, Seodaemun-gu,

Seoul 120-752, Korea.

Tel: 82-2-2228-2323, Fax: 82-2-312-2538

E-mail: hanwk@yuhs.ac

The authors have no financial conflicts of interest.

**Purpose:** To identify size criteria for complex cystic renal masses that can distinguish renal cell carcinoma from benign cysts supplementing the Bosniak classification. **Materials and Methods:** We reviewed the records of 97 patients who underwent surgery for complex cystic renal masses from January 2001 to April 2010. The pathological results were compared with the lesion sizes measured by preoperative computed tomography and other radiological features (contrast enhancement, irregularities of cyst walls and septa, and calcification) were also obtained for categorization according to the Bosniak renal cyst classification. **Results:** Malignancy was significantly associated with cyst size (>2 cm), male gender, and younger patient age (<50 years). According to the Bosniak classification, there was no category I cyst, and all 8 category II cysts were benign. However, 3 of 18 (17%) category IIF cysts, 21 of 39 (54%) category III cysts, and 29 of 32 (90%) category IV cysts were malignant. All category IIF cysts were benign in patients older than 50 years of age. **Conclusion:** Many complex cystic renal masses smaller than 2 cm were benign. We suggest that lesion size should be taken into account when formulating treatment plans for complex cystic renal masses.

**Key Words:** Kidney, cysts, kidney diseases, cystic, carcinoma, renal cell, computed tomography, X-ray

## INTRODUCTION

The incidence of renal tumors has gradually increased, which can partly be explained by increased detection. As imaging modalities such as ultrasonography and computed tomography (CT) have become widely available, they are used in numerous fields and often detect renal cell carcinoma (RCC) incidentally.

These incidentally found cancers tend to be smaller than those found with symptoms, and they have more favorable prognosis. As the tumor node metastasis staging system (AJCC, 2002) indicates, an RCC locally confined in the kidney has varying prognosis according to its size. In general, smaller size of a tumor suggests benignity and a better outcome if it turns out to be cancerous.

Renal cell carcinoma can also appear as a cystic renal mass on CT, which should be differentiated from benign cysts. For the differential diagnosis of cystic renal

### © Copyright:

Yonsei University College of Medicine 2012

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

mass, the gold standard is the Bosniak renal cyst classification system.<sup>1</sup> There is a description for high-attenuating cystic lesions that are 3 cm or greater, but no other criterion for lesion size exists in the classification.<sup>2</sup> To determine whether combining cyst size with the Bosniak classification could improve diagnostic accuracy, we reviewed cases of complex renal cysts at our institution that were treated surgically.

## MATERIALS AND METHODS

A total of 152 renal cyst patients were surgically treated at our institution from January 2001 to April 2010. We excluded 48 patients with coexisting renal pathologies other than complex renal cysts. We also excluded patients with CT scans that could not be reviewed (n=5) and those who received surgery more than 4 weeks after the day of the CT scan (n=2). Ultimately, 97 patients were evaluated in this study.

The images were obtained preoperatively using multislice 64 detector row helical CT scanner (Lightspeed, GE Medical System, Milwaukee, WI, USA). CT images were obtained in the precontrast phase, corticomedullary phase (30-45 seconds after contrast injection), nephrographic phase (85-120 seconds after contrast injection), and excretory. All image interpretation was done by a urologist and a radiologist who had 10 years of experience with renal cyst imaging and were familiar with the Bosniak classification system. Lesion size was determined in the axial plane (larg-

est diameter). The number of septa (0, 1-4, 5-9, or >9), wall thickness (not thickened, hairline thin, minimally thickened, or grossly thickened and irregularly shaped), and calcification (present or absent) were determined. Contrast enhancement was described as not enhanced, minimally enhanced, measurable enhancement present, or enhancement of soft tissue components present. Then, all lesions were categorized according to the Bosniak classification.

Surgical specimens were classified as benign or malignant according to the pathology report. For cases of RCC, histological subtypes and Fuhrman nuclear grade were recorded.

Statistical analysis was carried out with SPSS software (SPSS Inc., Chicago, IL, USA). The chi-square test, Student's t-test, and ANOVA test were used to compare qualitative and quantitative variables. Values of  $p < 0.05$  were considered statistically significant.

The study was approved by the institutional review board of research associates at our institution, with a waiver of informed consent.

## RESULTS

Among the 97 complex cystic renal mass patients, 61 were male. The mean age at presentation was  $48.7 \pm 13.6$  years (range, 1-76 years). Clinical features of the patients are described in Table 1. Forty-eight (49%) cases were right-sided. Nineteen (20%) patients were symptomatic (gross hematuria,

**Table 1. Clinical Features**

	Benign	Malignant	<i>p</i> value
Gender			
Male	23	39	0.020*
Female	21	14	
Age, yrs (mean±SD)	49.7±12.7	47.9±14.3	0.520 <sup>†</sup>
≥50 yrs (%)	26	22	0.044*
<50 yrs (%)	18	31	
BMI, kg/m <sup>2</sup> (mean±SD)	23.2±2.7	23.4±3.0	0.818 <sup>†</sup>
Symptom			
Gross hematuria	6	6	
Flank pain	3	3	
Palpable mass	0	1	
Asymptomatic	35	43	
Medical history			
ESRD	8	13	
Renal allograft	5	2	
vHLD	0	3	

BMI, body mass index; ESRD, end-stage renal disease; vHLD, von Hippel-Lindau disease.

\*Chi-square test.

<sup>†</sup>Student's t-test.

n=12; flank pain, n=6; palpable mass, n=1), 21 had end-stage renal disease, 7 had undergone renal allograft, and 3 had von Hippel-Lindau disease. Treatments of choice were radical nephrectomy (n=63) and nephron-sparing surgery (n=34).

Forty-four (45%) patients had benign cysts (including cystic angiomyolipoma, n=1; cystic lymphangioma, n=1; and hemorrhagic oncocytoma, n=1), while 53 (55%) had RCCs (clear cell, n=44; papillary, n=7; chromophobe n=1; unclassified n=1). Preoperative images of 44 benign cysts were classified as 9 category II cysts, 15 category IIF cysts, 18 category III cysts, and 3 category IV cysts. In contrast, 53 RCCs were preoperatively classified as 3 category IIF cysts, 21 category III cysts, and 29 category IV cysts. Fuhrman nuclear grade was assessed in 47 cases of RCC (grade 1, n=19; grade 2, n=16; grade 3, n=12, grade 4, n=0). All RCC lesions were confined in the kidney or in the surgical specimen of partial nephrectomy, and there was no lymph nodal metastasis. Thus, all cancers were pT1aN0M0 (n=31) or pT1bN0M0 (n=22).

As shown in Table 1, RCCs were found more frequently in men than in women ( $p=0.020$ ). Mean age did not differ significantly between the patients with benign cysts and those with RCC ( $p=0.520$ ). However, younger patients (<50 years) had more RCCs than the patients older than 50 years of age. [31/49 (63.3%) vs. 22/48 (45.8%),  $p=0.044$ ].

#### Lesion size and Bosniak category

There were no Bosniak category I lesions. Also, there was no RCC in Bosniak category II (0/9). RCC appeared in 3 of 18 cases (16.7%) in category IIF, 21 of 39 cases (53.8%) in

category III, and 29 of 32 cases (90.1%) in category IV.

The mean size of benign cysts did not differ significantly from that of RCC ( $3.8\pm 2.5$  cm vs.  $4.3\pm 2.4$  cm,  $p=0.373$ ). However, the mean size of each Bosniak category differed significantly in an increasing manner ( $p=0.007$ ) (Table 2).

Smaller lesions (size <2 cm) were more likely to be benign than larger lesions [9/12 (75.0%) vs. 32/82 (39.0%),  $p=0.002$ ] (Table 2). All three category IIF cysts that were found to be malignant were greater than 2 cm. There were 4 cysts that were smaller than 2 cm in categories III and IV, and 3 (75.0%) of them were RCCs. Two cysts were Fuhrman nuclear grade I and one was grade II.

#### Patient age and Bosniak category

Particularly in the category IIF, all 11 patients who were older than 50 years of age had benign cysts, while 3 of 7 (43%) younger patients had RCC (Table 3). The incidences were not different in the other categories, however. Also, the mean age of each Bosniak category was not different.

## DISCUSSION

The Bosniak renal cyst classification has been used widely to determine the complexity of a renal cyst.<sup>3-8</sup> During its development, a new category (category IIF) has been introduced for cases that were difficult to classify as category II or III.<sup>2,9,10</sup> Israel, et al.<sup>11</sup> evaluated a series of 42 category IIF cysts that were observed for at least 2 years, and only 2 of

**Table 2.** Renal Cyst Size and Number of Malignancy

Category	Size, cm (mean±SD)	No. of malignancy/No. of case (%)		p value
		<2 cm	≥2 cm	
II	2.0±1.3	0/5 (0)	0/3 (0)	0.007*
IIF	3.1±1.9	0/6 (0)	3/12 (0)	
III	4.6±2.1	1/2 (50)	20/37 (54)	
IV	4.5±2.8	2/2 (100)	27/30 (90)	
Total	4.1±2.4	3/15 (20)	50/82 (61)	0.002 <sup>†</sup>

\*ANOVA test.

<sup>†</sup>Fisher's exact test.

**Table 3.** Patient Age and Bosniak Category

Category	Age (mean±SD)	No. of malignancy/No. of case (%)		p value
		<50 yrs	≥50 yrs	
II	54.1±7.8	0/2 (0)	0/6 (0)	0.017*
IIF	51.1±12.4	3/7 (43)	0/11 (0)	
III	45.1±14.7	13/23 (57)	8/16 (50)	
IV	50.5±13.4	18/16 (89)	13/14 (93)	

\*Fisher's exact test.

<sup>†</sup>Chi-square test.

**Table 4.** Cyst Wall Thickness and Gender

	Not thickened	Hairline thin	Slightly thickened	Grossly thickened and irregular
Male	3	4	10	45
Female	4	6	10	15

them turned out to be malignant with low potential. In the study by O'Malley, et al.,<sup>8</sup> 81 category IIF lesions were followed, and progression in radiological complexity was observed only in 12 cases, and only 5 of them were reported to be malignant. Thus, the frequency of malignancy in category IIF proved to be low (5% to 6%), thereby reducing the number of unnecessary nephrectomy surgeries. In our study, 18 patients with Bosniak category IIF cysts underwent surgery, and 3 had RCC (17%). Nine of them underwent surgery before the category IIF was used in practice. Two patients had end-stage renal disease, and we decided to remove the non-functioning kidney instead of performing serial contrast CT scan. One of them had RCC. Five patients underwent surgery after imaging study follow-up, and two of them had RCC. The mean follow-up duration was 10.2 months (range-6 to 20.5 months). Four of the category IIF cysts showed increased size and thickened septations. Interestingly, the remaining one category IIF cyst decreased in size (4.5 cm to 1.8 cm in 6 months), and it turned out to be a Fuhrman grade I RCC.

This follow-up strategy has some weak points. The possibility of malignancy being missed may cause patient anxiety. As imaging studies have become more widely used, asymptomatic renal cysts are more likely to be detected, which leads to increased cost and time for serial follow-up imaging tests if the strategy is applied. In our study, three of the patients who underwent surgery after being diagnosed as category IIF cysts were all younger than 50 years of age. More detailed indications for nephron-sparing surgery may be required, especially for those of younger population.

In 2000, Curry, et al.<sup>7</sup> evaluated 166 cases of cystic renal masses and reported that 2-18% of the masses were smaller than 2 cm and 29-33% of the masses were smaller than 3 cm. In our study, cystic renal masses that were smaller than 2 cm had significantly less chance of being malignant than the larger lesions. It is well known that the size of a solid renal tumor is related to the probability of renal cell carcinoma and poorer prognosis.<sup>12,13</sup> It is also known that the size of a simple renal cyst is not related to cancer, and the chance of a simple renal cyst being a cancer is very low. What we were interested first was the probable relationship

between the size of a cystic renal tumor - not solid - and the possibility of cancer. Indeed, we found possible linear relationship between mass size and cancer, but it was insignificant. The only linear relationship we found was the mean size of those tumors and Bosniak categories, which are shown in Table 2. Then, we tried several cut-off values of a mass size that can separate benign from malignant tumors (1 cm, 1.5 cm, 2 cm, 4 cm, 7 cm...), and found significance only with the boundary point of 2 cm.

Gender and age of patients are important predictors of the pathological features of solid renal masses. Gillett, et al.<sup>14</sup> reported that the distribution of histological subtypes in patients younger than 40 years of age differed from those in patients older than 60 years of age. Also, Zisman, et al.<sup>15</sup> reported that patient gender and age were independent predictors of pathological outcomes. Another retrospective study from Korea suggested that female gender, cystic renal lesions, and smaller tumor size are independent predictors of benign features of renal lesions.<sup>16</sup> In the present study, female gender and smaller lesion size (<2 cm) were associated with benignity, but multivariate analysis was not performed.

To categorize a lesion more objectively, we separately described each mass by its number of internal septation, irregular wall thickness, presence of calcification, and enhancement characteristics. When those mass characteristics were compared to patient gender or age group, a significant relationship between wall thickness and gender was found (Table 4). There were more grossly thickened irregular cyst walls in male patients than in female patients ( $p=0.034$ ). We also analyzed the relationship of lesion size and patient gender or age group, and found that the mean lesion size was not significantly different between gender or age groups.

Overall, mass size itself cannot predict malignancy in a cystic renal mass, but lesions smaller than 2 cm seem to be safely followed by performing serial imaging study even if the lesion showed suspicious wall thickening or enhancement. This is because enhancement of the adjacent normal renal parenchyma may result in an overestimation of enhancement in small cystic lesions (particularly less than 2 cm in diameter), which is known as the "pseudoenhancement" phenomenon.<sup>17</sup>

There was one pediatric patient in our study. Wallis, et al.<sup>18</sup> suggested that the Bosniak classification can be used in the pediatric population with slight modifications. The 1-year old patient in our study had a 8.5-cm sized multiseptated cyst. We suspected that it was a category III multicystic nephroma. Therefore, we performed partial nephrectomy and confirmed that it was a nephroma.

A limitation of our study was the potential for selection bias due to the retrospective design and the fact that we evaluated only patients who underwent surgery. Pathological proof was available for all 44 benign cysts and 53 RCCs. However, Fuhrman nuclear grade was assessed in only 47 of these cases. Because the sample size was relatively small, additional studies with larger numbers of patients, including those who underwent follow-up examinations, would be useful.

## REFERENCES

- Bosniak MA. The current radiological approach to renal cysts. *Radiology* 1986;158:1-10.
- Israel GM, Bosniak MA. An update of the Bosniak renal cyst classification system. *Urology* 2005;66:484-8.
- Aronson S, Frazier HA, Baluch JD, Hartman DS, Christenson PJ. Cystic renal masses: usefulness of the Bosniak classification. *Urol Radiol* 1991;13:83-90.
- Wilson TE, Doelle EA, Cohan RH, Wojno K, Korobkin M. Cystic renal masses: a reevaluation of the usefulness of the Bosniak classification system. *Acad Radiol* 1996;3:564-70.
- Siegel CL, McFarland EG, Brink JA, Fisher AJ, Humphrey P, Heiken JP. CT of cystic renal masses: analysis of diagnostic performance and interobserver variation. *AJR Am J Roentgenol* 1997;169:813-8.
- Cloix P, Martin X, Pangaud C, Maréchal JM, Bouvier R, Barat D, et al. Surgical management of complex renal cysts: a series of 32 cases. *J Urol* 1996;156:28-30.
- Curry NS, Cochran ST, Bissada NK. Cystic renal masses: accurate Bosniak classification requires adequate renal CT. *AJR Am J Roentgenol* 2000;175:339-42.
- O'Malley RL, Godoy G, Hecht EM, Stifelman MD, Taneja SS. Bosniak category IIF designation and surgery for complex renal cysts. *J Urol* 2009;182:1091-5.
- Bosniak MA. Problems in the radiologic diagnosis of renal parenchymal tumors. *Urol Clin North Am* 1993;20:217-30.
- Bosniak MA. Diagnosis and management of patients with complicated cystic lesions of the kidney. *AJR Am J Roentgenol* 1997;169:819-21.
- Israel GM, Bosniak MA. Follow-up CT of moderately complex cystic lesions of the kidney (Bosniak category IIF). *AJR Am J Roentgenol* 2003;181:627-33.
- Schachter LR, Cookson MS, Chang SS, Smith JA Jr, Dietrich MS, Jayaram G, et al. Second prize: frequency of benign renal cortical tumors and histologic subtypes based on size in a contemporary series: what to tell our patients. *J Endourol* 2007;21:819-23.
- Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol* 2003;170(6 Pt 1):2217-20.
- Gillett MD, Cheville JC, Karnes RJ, Lohse CM, Kwon ED, Leibovich BC, et al. Comparison of presentation and outcome for patients 18 to 40 and 60 to 70 years old with solid renal masses. *J Urol* 2005;173:1893-6.
- Zisman A, Patard JJ, Raz O, Klatté T, Haifler M, Mendlovic S, et al. Sex, age, and surgeon decision on nephron-sparing surgery are independent predictors of renal masses with benign histologic findings--a multicenter survey. *Urology* 2010;76:541-6.
- Park SY, Jeon SS, Lee SY, Jeong BC, Seo SI, Lee HM, et al. Incidence and predictive factors of benign renal lesions in Korean patients with preoperative imaging diagnoses of renal cell carcinoma. *J Korean Med Sci* 2011;26:360-4.
- Prasad SR, Dalrymple NC, Surabhi VR. Cross-sectional imaging evaluation of renal masses. *Radiol Clin North Am* 2008;46:95-111.
- Wallis MC, Lorenzo AJ, Farhat WA, Bägli DJ, Khoury AE, Pippi Salle JL. Risk assessment of incidentally detected complex renal cysts in children: potential role for a modification of the Bosniak classification. *J Urol* 2008;180:317-21.