

The Growth of Renal Cysts According to the Exophytic Index of the RENAL Nephrometry Scoring System

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higher than mild and moderate exophytic renal cyst.

Key words: Kidney; Renal cyst; Size; Growth; Exophytic; Progression

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ABSTRACT

AIM: To investigate the growth patterns of renal cysts according to location, exophytic degree and Bosniak classification.

METHODS: From December 2000 to September 2012, a total of 252 patients (340 renal cysts) were included in this study. All patients had undergone computed tomography (CT) scans of the kidney level at least twice, and six months apart for any reason. Renal cyst data were assessed according to cyst side (right or left), location (upper, mid or lower), characteristics (Bosniak classification), and exophytic degree (1, 2, and 3) which were stratified using the RENAL nephrometry score. The growth rate of renal cyst was analyzed according to each parameter using linear correlation analysis.

RESULTS: The mean size of renal cyst increased from 3.81 cm to 3.85 cm during a mean follow-up of 20.1 months, not significantly ($p = 0.121$). Among 340 renal cyst units, 180 renal cysts had an exophytic degree index of 1 (52.9%), 90 had an index 2 (26.5%), and 70 had an index of 3 (20.6%). After a mean of 20.1 months of follow-up, only exophytic degree 3 renal cysts increased in size significantly from 4.54 to 5.76 cm ($p = 0.018$). The annual growth rate in exophytic degree 3 renal cysts was 2.4 mm ($r^2 = 0.263$), which was higher than that for renal cysts at other site locations.

CONCLUSION: The growth rate of renal cysts varied according to exophytic location. The growth rate of exophytic renal cysts was

INTRODUCTION

Renal cysts are acquired lesions that most commonly affect the elderly population^[1]. Autopsy studies have reported a 50% incidence of renal cysts after the age of 50 years^[2]. The prevalence of renal cysts is approximately 10%, ranging from 4% in the third decade to 19% in the sixth decade^[3]. There is an increase in the size and number of cysts over time in cyst-bearing individuals. Previous long-term follow-up data have shown that, simple renal cysts continue to increase in size with age > 10 years, and sometimes increase rapidly, particularly in younger patients^[4]. However, this study also showed decreased growth rate of cysts with increased age. Renal cysts originate from weakened of the tubular basement membrane of the distal convoluted or collecting duct cells^[2]. As results, a diverticulum is formed, which can subsequently develop into a simple renal cyst^[5,6]. The reported risk factors for renal cysts include old age, male gender, renal dysfunction, and hypertension^[7]. However, given the retrospective nature of these studies, the associations could be coincidental. The only persistent confounder among all reported associations was increasing age^[4,7,8]. Therefore, we analyzed the discrepancy of an increasing rate of simple renal cysts according to initial size, location, and exophytic index stratified using the RENAL nephrometry scoring system in this study.

MATERIALS AND METHODS

Study population

This study was conducted after receiving approval from our

Institutional Review Board. Our prospectively maintained institutional kidney center database was queried to identify all patients from December 2000 to September 2012 who had undergone computed tomography (CT) scans of the kidney (the abdominal pelvis, liver, kidney, or bladder) at least twice, and six months apart for any reason. Among these patients, we selected those who had renal cysts. Using the Bosniak renal cyst classification system, we excluded all category 3 and 4 renal cysts, multi-loculated cysts are included into category 2.

Evaluation

Preoperative CT images were reviewed in the axial and coronal planes, and we defined renal cyst size as the longest diameter at any image section. Renal cyst data were assessed according to cyst side (right or left), location (upper, mid or lower pole), characteristics (Bosniak classification 1, 2, or 2f), and exophytic degree which was stratified using the RENAL nephrometry score, as described by Kutikov and Uzzo⁹¹. According to their definitions, renal tumors that are ≥ 50% exophytic are assigned 1 point, tumors that are < 50% exophytic are assigned 2 points, while those that are entirely endophytic (encircled 360° by uninvolved renal parenchyma) are assigned 3 points. We applied these categories to all renal cysts in this analysis. Clinical data on age, gender, height, body weight, body mass index, hypertension, and diabetes mellitus were recorded during physical examination or obtained from hospital records. Serum Cr levels were measured, and GFR levels were calculated using the abbreviated MDRD (modification of diet in renal disease) equation¹⁰¹. The equations used was MDRD-GFR in mL/min/1.73 m² = 186.3 × Cr-1.154 × age-0.203 (× 0.742 if female).

Statistical analysis

The results are reported as the mean ± standard deviation(SD). The 3 sets of results were compared among 3 observers to assess measurement reliability. Renal cyst size was measured at initial presentation and after at least 6 months of follow-up. The change in the renal cyst was analyzed according to renal cyst location, exophytic degree score, and Bosniak classification by using the paired t-test. The increasing growth rate in each month was evaluated for each exophytic degree using a linear regression model, and equations, including the slope of the line, were calculated for each exophytic degree score. The SPSS software package, version 15.0 (Statistical Package for Social Sciences™, Chicago, IL, USA), was used for all statistical analyses. A 2-tailed *p*-value < 0.05 was considered significant for all analyses.

RESULTS

A total of 252 patients and 340 renal cysts were included in this analysis. The mean age was 61.63 years, and the mean renal cyst size at initial presentation was 3.81 ± 2.56 cm (Table 1). During the mean follow-up duration of 20.1 months (median, 18.7 months), the renal cyst size increased to 3.85 ± 2.62 cm. Among 252 patients, 156 (61.9%) were male, and 142 (56.3%) had a history of hypertension. Among 340 renal cysts, 180 had an exophytic index of 1 (52.9%), 90 had an index of 2 (26.5%), and 70 had an index of 3 (20.6%). Most renal cysts were Bosniak classification 1 (152/340, 44.7%) and 2 (172/340, 50.6%), and the remaining 16 renal cysts were class II_f. Five renal cysts were surgically excised either because they had progressed to class III cyst (*n* = 2) or because a renal tumor (*n* = 3) had been incidentally detected at another site of the ipsilateral kidney. Renal function between initial presentation and follow-up

presentation was similar (mean GFR 71.98 vs 72.78 mL/min/1.73 m²). We investigated the various risk factors that have been identified in the literature that increase renal cyst growth (Table 2). According to renal cyst location, the mean size of the renal cyst was 4.57 cm in the upper pole, 3.22 cm in the mid pole, and 3.56 cm in lower pole at initial presentation. After a mean 20.1 months of follow-up, the size of the renal cyst in the upper pole only increased to 5.04 cm (not a significant increase). According to the exophytic degree, the mean sizes of exophytic degree 1, 2 and 3 renal cysts were 4.54, 3.03, and 1.94 cm, respectively. After a mean of 20.8 months of follow-up, only exophytic renal cysts (degree index 1) significantly increased to 5.76 cm (*p* = 0.018). According to the Bosniak classification, there was no difference in renal cyst size at initial presentation. Renal cysts with Bosniak 2_f characteristics showed an increase from 2.78 to 3.69 cm (not a significant increase); however, other cysts with Bosniak classification 1 and 2 showed similar sizes at follow-up presentation (median follow-up, 20.4 months).

Figure 1 shows each cyst-increasing pattern according to exophytic degree. The equation relating renal cyst size to time was renal cyst

Table 1 Characteristics of included patients.

Details	Value
Total population	252
Total renal cyst unit	340
Mean age at presentation ± SD	61.63 ± 10.83
Median age (range)	63.0 (30-85)
Mean follow up (months)	20.11 ± 21.19
Median follow up (range)	18.7 (6.8-89.0)
Sex (%)	
Male	156 (61.9)
Female	96 (38.1)
Mean body mass index ± SD (kg/m ²)	23.64 ± 2.39
Diabetic mellitus (%)	40 (15.9)
Hypertension (%)	142 (56.3)
Renal cyst position	
Lt/Rt	162 (47.6)/178 (52.4)
Upper/mid/lower pole	132 (38.8)/130 (38.2)/78 (22.9)
Exophytic degree 1/2/3	180 (52.9)/90 (26.5)/70 (20.6)
Bosniak classification	
1/2/2 _f	152 (44.7)/172 (50.6)/16 (4.7)
Mean number of cyst in a person	2.69 ± 2.48
Renal profile at initial presentation	
Mean size of renal cyst ± SD (cm)	3.81 ± 2.56
Mean serum creatinine ± SD (mg/dL)	1.18 ± 0.99
Mean MDRD GFR ± SD (mL/min/1.73m ²)	71.98 ± 19.32
Renal profile at last follow up	
Mean size of renal cyst ± SD (cm)	3.85 ± 2.62
Mean serum creatinine ± SD (mg/dL)	1.12 ± 0.83
Mean MDRD GFR ± SD (mL/min/1.73m ²)	72.78 ± 19.88

SD: standard deviation; MDRD GFR: modification of diet in renal disease glomerular filtration rate.

Table 2 Size variation of renal cyst during follow up measured by computed tomography.

Variable	Initial presentation	Follow up presentation	<i>p</i> -value
According to position (cm) ± SD			
Upper pole	4.57 ± 2.82	5.04 ± 2.90	0.631
Mid pole	3.22 ± 2.16	3.32 ± 2.17	0.999
Lower pole	3.56 ± 2.51	3.55 ± 2.51	0.922
According to Exophytic degree (cm) ± SD			
Exophytic degree 1	4.54 ± 2.64	5.76 ± 2.82	0.018
Exophytic degree 2	3.03 ± 1.78	3.54 ± 1.82	0.267
Exophytic degree 3	1.94 ± 0.28	2.59 ± 1.56	0.400
According to Bosniak classification (cm) ± SD			
1	3.42 ± 2.86	3.53 ± 3.02	0.947
2	4.20 ± 2.32	4.51 ± 2.22	0.440
2 _f	2.78 ± 1.09	3.69 ± 1.12	0.069

SD: standard deviation

size (cm) = 0.2 + 0.02 months for exophytic renal cyst. The annual growth rate of exophytic degree 1 renal cysts was 2.4 mm. The r^2 value (power of explanation of the correlation between two variables) of the slope was 0.263 for exophytic degree 1 renal cysts. The equation for exophytic degree 2 renal cyst size (cm) = 0.06 + 0.0071 months ($r^2 = 0.043$). The equation for exophytic degree 3 renal cysts was renal cyst size (cm) = 0.01 + 0.0041 months ($r^2 = 0.032$). The annual growth rates of exophytic degree 2 and 3 renal cysts were 0.85 mm and 0.49 mm, respectively.

DISCUSSION

We found that the simple renal cyst size growth rate varied according to the exophytic degree and location (50% or more exophytic) significantly increased compared to other renal cysts at a mean 20.1 months of follow-up. We also investigated the renal cyst growth rate according to renal cyst upper-mid-lower pole location, according to the Bosniak classification. We found no significant difference in growth rate based on location, between initial presentation and at the last follow-up.

Marumo *et al*^[11] found that the annual growth rate of the mean maximum diameter was 4.2% during a 3-year follow-up period among 55 patients with simple renal cysts and asymptomatic microscopic hematuria. In our results, the annual growth rate in all 340 simple renal cysts was 1.1% during a mean of 20.1 months of follow-up. The low growth rate in our series might be because of many larger cysts were included at the initial presentation (3.81 cm in our study) than that reported previously. Terada *et al*^[3] showed a natural history of simple renal cysts in their first report describing 45 patients. Their results revealed that the majority of cysts increased in size and number. The average increase in size and the rate of enlargement was 2.82 mm. They also investigated predictors of significant renal cyst growth rate, including sex, age at diagnosis, initial cyst size, laterality, and cyst shape. They only identified age and multi-loculated renal cysts as predictors of renal cyst growth. Their results were promising in the assessment of predictors of renal cyst growth; however, all renal cysts were measured by ultrasonography. Therefore, there is potential inter-observational and intra-observational bias during measurement. Our study using CT imaging of the kidney region might provide a more standard imaging protocol to measure renal cyst outcomes. More recent data by Terada *et al*^[4] demonstrated that only cyst shape was found to be an independent predictor of aggressive cyst growth, with linear regression analysis. This study determined that only initial cyst size was an independent predictor for aggressiveness. However, gender, age, and creatinine levels were not correlated with increased cyst size. Although there was no relationship between age and annual growth rates, the age at diagnosis was lower in patients with increased cyst size.

The simple cyst is frequently an asymptomatic incidental finding during abdominal imaging. Occasionally, they become symptomatic and might present with abdominal discomfort, flank pain, a palpable mass, or hematuria^[8]. These clinical symptoms can be a result of complications (hemorrhage, infection, and rupture), or a complaint because of an enlarging cyst, and clinical symptoms might raise the possibility of an associated malignancy^[12-14]. However, the relationship between renal cyst and renal malignancy has not been confirmed. When pathology was correlated with the Bosniak classification, the risk of malignancy occurring in a simple cystic lesion was only 1.7%^[15]. In a prospective study of 61 patients with simple renal cysts followed for up to 14 years, only two developed

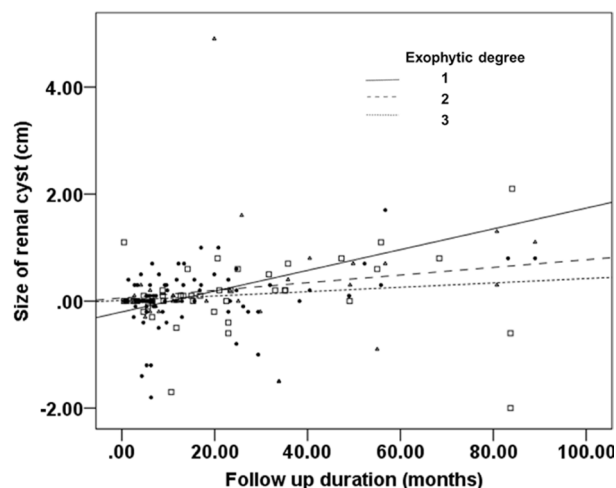


Figure 1 The growth rate of renal cyst according to exophytic degree. The r^2 value of the slope was 0.263 for exophytic degree 1 ($\geq 50\%$ exophytic), 0.043 for exophytic degree 2 ($< 50\%$ exophytic) and 0.032 for exophytic degree 3 (encircled 360° by uninvolved renal parenchyma).

renal neoplasms originating from the renal cyst^[4]. These studies indicated that neither the actual size nor size changes were specific to the development of a renal neoplasm. The rate of increase in cyst size in patients with renal cancer was similar to that in other patients of the same age^[2]. In our review of simple renal cysts, only 5 cysts were excluded as 2 were Bosniak class III renal cysts (1.1%) and 3 were excised because renal tumor was incidentally detected at another site (1.7%). Conversely, an established association exists between renal cysts and hypertension, particularly in men; individuals over the age of 60 years; and those with multiple, large, or peripheral cysts^[16]. Local ischemia caused by cyst expansion leads to the activation of the renin-angiotensin system. As a result, hypertension affects 50-75% of adults with autosomal dominant polycystic kidney disease and up to 80% of those with end-stage renal failure^[17,18]. In our analysis, the number of patients who had hypertension was very high, at 56.3%. Although we could not confirm that these hypertensive diseases were originated from renal cystic cause, it might assume the positive correlation between hypertension and renal cyst.

Our study was, to our knowledge, the first report that investigated renal cysts according to exophytic location using a well-known kidney location measurement system. Exophytic renal cysts had a higher growth rate than endophytic renal cysts. This finding might be explained by the fact that renal cysts originate from a weakening of the tubular layer of the collecting duct and form diverticula. Therefore, exophytic renal cysts may grow more easily than endophytic renal cysts because of more space available^[5,6]. However, our study has several limitations. Initially, there was sample number disparity according to exophytic degree. Half of all renal cysts were located in the exophytic position. We could not adjust this limitation due to the retrospective nature of our data. Future studies should adjust the sample size in each exophytic group. The second limitation was the relatively short mean follow-up period. Despite this, some renal cysts had up to 7 years of follow-up. Another limitation was the small sample size, which may result in false-positive bias. However, our study using CT modality was the first study to analyze the simple renal cyst to determine predictors according to exophytic degree.

In conclusions, this study is the first report of renal cyst growth disparity according to exophytic location of the renal cyst. Among the renal cysts, of which 50% or more were exophytic degree 1 located, the estimated annual growth rate was 2.4 mm, which was higher than

that of exophytic degree 2 and 3 renal cysts. Therefore, clinicians should be vigilant of patients who have exophytic renal cysts, given the potential for increased growth. Further large-scale prospective studies are needed to clarify these correlations.

CONFLICT OF INTERESTS

The authors have no potential conflicts of interest relevant to this article to report.

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