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ORIGINAL RESEARCH

Impact of Active Surveillance on Nephrometric Scores of Bosniak III and IV Renal Cysts

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Purpose: Active surveillance (AS) has been widely explored for small renal masses, but its role in complex renal cysts (CRCs) categorized as Bosniak (Bk) III and IV remains unclear. This study aims to evaluate changes in nephrometry scores (s-RENAL and s-PADUA) during AS and their potential impact on surgical complexity.

Methods: A retrospective, multicentric, observational study was conducted, analyzing 101 CRCs from 95 patients across three institutions. Nephrometry scores were evaluated at baseline and after a minimum follow-up of two years using computed tomography (CT) and magnetic resonance imaging (MRI). Statistical analysis included chi-square and marginal homogeneity tests, with data managed using REDCap.

Results: Among the 101 CRCs, 39 were Bk IV and 62 Bk III, with a mean follow-up of 4.2 years. The initial mean lesion size was 2.77 cm (0.50–11.8 cm), increasing to 3.0 cm (0.40–13.10 cm) at follow-up. Complexity scores increased in 4% of cases according to s-RENAL and 5% according to s-PADUA. Tumor growth was observed in 45 cases (44.5%), while 37 (36.6%) remained stable, and 19 (18.8%) decreased in size. Bk IV cysts tended to increase in size more than Bk III and had a smaller chance of decreasing. Median growth and shrinkage velocities were 0.19 cm/year and 0.21 cm/year, respectively.

Conclusion: Active surveillance is a viable and safe strategy for managing select Bk III and IV CRCs. A small but significant proportion of CRCs under AS exhibit increased nephrometry complexity, which may impact surgical planning. These findings suggest that nephrometry score evolution should be considered when selecting patients for AS versus early surgical intervention.

Keywords: renal cysts, Bosniak III and IV, nephrometry scores, active surveillance, R.E.N.A.L., P.A.D.U.A.

Introduction

The widespread use of imaging exams has increased the detection of asymptomatic renal masses, both cystic and solid. Currently, more than 50% of renal lesions are diagnosed incidentally.[1] Although the true incidence of cystic lesions in adults remains uncertain, it is estimated that 50% of the population over 50 years old presents with simple or minimally complicated renal lesions.[2] Notably, 4–10% of incidental renal masses are represented by complex cystic lesions, often associated with neoplasia.[3]

Bosniak (Bk) classification was developed in 1986, based on CT imaging, and was the first to use radiological findings to guide the treatment of renal cystic lesions.[4] It remains the most accepted method for differentiating renal cysts with neoplastic potential (Bk III and IV) from those with lower risk (Bk I and II). Approximately 50–60% of Bk III and more than 90% of Bk IV cysts present malignant lesions in surgical specimens.[5]

For this reason, surgical resection is the treatment of choice for both categories. After resection and confirmation of malignancy, most of the tumors are small (pT1 in 79–83%) and have low nuclear differentiation grade (Fuhrman grade)

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in over 90%. The risk of recurrence is also low (1–1.4%), suggesting a non-aggressive behavior with excellent prognosis and a cancer-specific survival rate of 100%.[6]

Despite the benefits of cancer control with surgery, this approach is associated with the highest complication rates among the treatment options available for complex renal cysts (CRCs).[7] Active surveillance (AS) is also possible, mainly for elderly patients, frail individuals, those with comorbidities, short life expectancy, or patients with impaired renal function.[8] Despite high malignancy rates, the outcomes of AS for Bk III and IV are compatible with indolent lesion behavior. Metastasis and disease-specific mortality are very low (0 to 1%) in most studies with a minimum follow-up of 2 years.[6] On the other hand, AS can also delay surgery in some patients, for whom nephron-sparing surgery could be performed at the diagnosis. In these patients, the procedure may become more complex after follow-up, leading to greater renal function loss or even complete loss of the renal unit.[7]

Nephrometry systems (NS) were developed to better measure, demonstrate, and compare the surgical complexity of solid renal lesions. The anatomical characteristics are measured and scored according to radiological findings. The most used NS are the R.E.N.A.L. score (s-RENAL) and the P.A.D.U.A. score (s-PADUA); the higher the score, the more complex the surgery and the risk of complications.[9,10]

Considering the good oncological prognosis of AS for CRCs, where unnecessary surgeries and all associated complications can be avoided, it is important to evaluate changes in NS of lesions during the follow-up period.[11] These changes are crucial in the treatment of these patients, as the anatomical relation of the lesion with other renal structures (such as the collector system and renal vessels) can determine worsening in surgical prognosis.

This study aims to assess the difference between PADUA and RENAL scores at the diagnosis of CRCs and the end of a 2-year follow-up period in patients on AS, as well as compare the radiological characteristics of the cysts and their changes in size during the same period. Such knowledge would help in therapeutic decision-making at the time of diagnosis of these cysts.

Materials and Methods

Study Design and Patient Selection

We performed an observational, multicenter, retrospective cohort study. Data were collected from three institutions: Hospital de Amor de Barretos - Fundação Pio XII, Hospital das Clínicas da Faculdade de Medicina de Ribeirao Preto - USP, and the The University of Texas, MD Anderson Cancer Center, Houston, TX, USA.

Ethical approval was obtained from the Hospital de Amor de Barretos - Fundação Pio XII institutional review board (IRB), CAAE: 64081516.0.2001.5437, which waived the requirement for patient consent to review medical records. This waiver was granted on the grounds that the study involved minimal risk to participants and used de-identified retrospective data collected as part of routine clinical care. All patient data were handled with strict confidentiality, in compliance with ethical standards and data protection regulations, ensuring that no identifiable information was disclosed at any stage of the analysis.

Patients aged 18 years or older with Bk III and IV renal cysts, identified through contrast-enhanced CT/MRI, followed for at least two years and had not undergone any form of treatment for the renal unit where the CRC was detected, were included. Cases in which imaging was inadequate for assessment, specifically those without intravenous contrast, and where follow-up images were incomplete or unavailable, were excluded.

The 2019 revision of the Bosniak classification further improved diagnostic precision by integrating MRI criteria, acknowledging its growing role in the evaluation of complex renal cysts and contributing to better risk stratification for active surveillance.[4]

Sample

Anonymized data from all patients diagnosed with CRCs through CT/MRI between 2003 and 2016 were retrieved from the medical informatics systems of the radiology databases of each institution. Initially, the cases were classified according to the Bk system. Medical records and CT/MRI images of all Bk III and IV patients who met the inclusion and exclusion criteria, regardless of gender, were analyzed. After data collection and image review, 95 patients with 101

Bk III and IV lesions fulfilled the study criteria. Demographic and radiological data for the entire cohort were collected and stored on the REDCap platform. Six lesions, initially under active surveillance (AS), underwent surgical intervention after at least two years of clinical follow-up.

Radiological Classification

Cyst classification was based on CT or MRI data and images, following the Bk criteria.[4] The starting point for analysis was the date of the first exam (CT/MRI) describing the lesion. The endpoint was the date of the last exam before surgery for operated cases. For non-operated cases, the endpoint was the date of the most recent available high-quality image.

Anatomical Evaluation of Lesions

All images were evaluated by a group of four radiologists specializing in oncological studies. These reports and images were jointly analyzed with a uro-oncologist with over 10 years of experience in the field. Lesions were classified based on radiological and anatomical renal criteria using morphometric measurements from the s-RENAL[9] and s-PADUA[10] systems. The variables included were lesion diameter, relationship to the renal surface and parenchyma, location, relationship to the renal sinus, proximity to the renal sinus, percentage of solid intracystic component, and polar line positioning.

Statistical Analysis

Radiological variables and their changes over time were compared. Data were described using mean, median, and standard deviation for quantitative variables, and frequency and percentage tables for qualitative variables. Changes in lesion diameter and thickness over time (primary outcome) were assessed at 12-month intervals using imaging exams. Descriptive analyses and associations between independent variables were compared using Fisher's Exact Test and/or Chi-square test. The significance of changes over time was analyzed using the Marginal Homogeneity Test.

The annual growth or reduction rate of CRCs was assessed by comparing the initial and final radii using the Wilcoxon signed-rank test. The relationship between nephrometric scores (s-RENAL and s-PADUA) at baseline and at the end of follow-up was calculated using the Marginal Homogeneity Test. The relationship between two radiological variables was assessed using Fisher's Exact Test. A 5% significance level was adopted for all statistical tests.

Results

A total of 95 patients with 101 lesions were included. Two patients presented with bilateral CRCs, while two others, diagnosed with VHL syndrome, exhibited multiple lesions within a single renal unit: one had three Bk IV lesions in the left kidney, and the other had two Bk III lesions in the right kidney. Most patients were male (52.2%) and of white ethnicity (78.7%). The mean age was 63.8 years, and the mean BMI was 25.8 Kg/m². The mean follow-up period was 4.27 years. Demographic data are presented in Tables 1 and 2.

Table 1 Quantitative Demographic Data

Variable	Mean	Standard Deviation	Median	Minimum	Maximum
Age (years)	63.8	13.6	68.2	29.3	91.5
Weight (Kg)	69.6	17.3	68	40	117
Height (m)	1.64	0.10	1.6	1.4	1.8
BMI (kg/m²)	25.8	5.3	25.5	15.2	45.7
Follow-up duration (years)	4.2	2.1	3.6	2.0	12.3

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Table 2 Frequency and Percentage Distribution of Demographic Variables

Variable	Sub-Variable	N (%)
Gender		
	Female	29 (47.5)
	Male	32 (52.5)
Ethnicity		
	White	48 (78.7)
	Black	1 (1.6)
	Mixed	10 (16.4)
	Undefined	1 (1.6)
	Unknown	1 (1.6)
Smoking status		
	Non-smoker	39 (63.9)
	Former smoker	8 (13.1)
	Smoker	13 (21.3)
	Unknown	1 (1.6)
Alcohol consumption		
	Non-drinker	49 (80.3)
	Former-drinker	3 (4.9)
	Alcoholic	7 (11.5)
	Unknown	2 (3.3)
Hypertension		
	No	33 (54.1)
	Yes	25 (41.0)
	Unknown	3 (4.9)
Diabetes		
	No	51 (85.0)
	Yes	7 (11.7)
	Unknown	2 (3.3)

Imaging Characteristics and Univariate Analysis

The mean initial lesion diameter was 2.77 cm (range: 0.50–11.8 cm), and the mean final diameter was 3.0 cm (range: 0.40–13.10 cm) – Table 3. Regarding the Bk classification, most lesions (61.4%) were categorized as Bk III and 38.6% as Bk IV.

Regarding lesion size variation over time, 19 lesions decreased in diameter, 45 increased, and 37 remained stable Most lesions, whether classified as Bk III or IV, had an initial diameter of ≤ 4 cm. The mean annual growth rate was

Table 3 Radiological Values for Quantitative Variables

Variable	Mean	Standard Deviation	Median	Minimum	Maximum
Initial Diameter (cm)	2.77	1.8	2.2	0.5	11.8
Final Diameter (cm)	3.0	1.9	2.4	0.4	13.1
Number of CT/MRI Scans per year	4.0	2.0	3.0	1.0	10.0

Table 4 Bosniak Classification (Bk III and IV) and Significant Variables in the Univariate Model

Variable	Bk III (%)	Bk IV (%)	Total (%)	p-value
Gender				0.017
Female	23 (59.0)	6 (27.3)	29 (47.5)	
Male	16 (41.0)	16 (72.7)	32 (52.5)	
Total	39 (100)	22 (100)	61 (100)	
% Solid Component				0.02
0 to 25%	61 (99.3)	10 (25.6)	71 (69.7)	
25 to 50%	1 (0.6)	19 (48.7)	20 (20.2)	
50 to 75%	0 (0.0)	5 (12.8)	5 (5.1)	
75 to 100%	0 (0.0)	5 (12.8)	5 (5.1)	
Lesion Size Variation				0.013
Decreased	16 (25.8)	3 (7.6)	19 (18.8)	
Increased	23 (37.0)	22 (56.4)	45 (44.5)	
Stable	23 (37.0)	14 (35.8)	37 (36.6)	
Total	62 (100)	39 (100)	101 (100)	

0.19 cm/year, while the mean shrinkage rate was 0.21 cm/year. Among Bk IV lesions, 56.4% increase in diameter, whereas 7.6% decreased. In contrast, 37.0% of Bk III lesions increased, whereas 25.8% showed a size reduction.

Overall, Bk IV lesions demonstrated a greater tendency for growth, while Bk III lesions were more likely to decrease in size in comparison to Bk IV cysts. These differences were statistically significant ($p = 0.013$, chi-square test), as shown in Table 4. Logistic regression analysis indicated that Bk IV lesions were five times more likely to increase in size compared to Bk III lesions (OR = 5.1, 95% CI: 1.3–19.9, $p = 0.019$).

Bk IV lesions were significantly more prevalent in males (72.7%), whereas Bk III lesions were more frequent in females (59%) ($p = 0.017$). Regarding the percentage of the solid component, most Bk III lesions (99.3%) fell within the first quartile (0–25%), while 48.7% of Bk IV lesions were in the second quartile (25–50%) ($p = 0.02$).

Over time, nine lesions exhibited an increase in the solid component percentage, six of which were Bk IV and three were Bk III. Conversely, 14 lesions showed a decrease in the solid component, with four being Bk IV and 10 Bk III lesions (Table 4). Regarding changes in Bk classification, 11 out of 101 lesions (10.8%) were downgraded, while three lesions (2.9%) were upgraded.

Paired Analysis (s-RENAL and s-PADUA)

Tables 5 and 6 present the complexity categories distributions at the beginning and end of follow-up. In the s-RENAL nephrometric system, five lesions (four Bk III and one Bk IV) changed complexity categories. The variation rates were 1% (1/101) for those that decreased in complexity and 3.9% (4/101) for those that increased. In the s-PADUA

Table 5 Complexity Categories of s-RENAL at the Beginning and End of Follow-up

Complexity	Initial Frequency (%)	Final Frequency (%)
Low	39 (38.6)	38 (37.6)
Medium	53 (52.5)	52 (51.2)
High	9 (8.9)	11 (10.9)
Total	101 (100)	101 (100)

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Table 6 Complexity Categories of s-PADUA at the Beginning and End of Follow-up

Complexity	Initial Frequency (%)	Final Frequency (%)
Low	72 (71.3)	68 (67.3)
Medium	22 (21.8)	26 (25.7)
High	7 (6.9)	7 (6.9)
Total	101 (100)	101 (100)

nephrometric system, seven lesions (four Bk III and three Bk IV) changed complexity categories, with variation rates of 2% (2/101) for those that decreased in complexity and 4.9% (5/101) for those that increased.

Among the 101 lesions, six underwent surgical intervention after a follow-up period of two years. The primary indications for surgery were an increase in the percentage of the solid component (three cases), an increase in lesion diameter with greater contrast enhancement (two cases), and other clinical factors (one case). Of these cases, four had complete medical records available, and all underwent partial nephrectomy. Histopathological analysis confirmed clear cell renal cell carcinoma in all cases. Three patients had Fuhrman grade II tumors, while one had a Fuhrman grade I tumor.

No cases of metastatic disease were observed during active surveillance. The only case of metastasis occurred in a patient who underwent surgery. This was a 60-year-old patient who was initially diagnosed with a 1 cm Bk IIF renal cyst, which progressed with an increase in the solid component and diameter to 1.6 cm, leading to its reclassification as Bk IV. The patient remained under active surveillance for 4.6 years. Two years and two months after undergoing right partial nephrectomy, metastases were identified.

Discussion

This study analyzed the epidemiological and radiological characteristics of CRCs, particularly Bk III and IV lesions, and their behavior under AS. Our findings revealed a mean patient age of 63.8 years, with a slight male predominance (52.5%). While obesity, smoking, and hypertension have been linked to malignancy in renal cystic lesions, our univariate analysis did not establish a significant association between these factors and CRC malignancy. Additionally, Bk IV cysts were more frequent in males, whereas Bk III cysts were more prevalent in females, an observation not commonly reported in previous literature. Notably, 63.3% of lesions changed in diameter during follow-up, with an annual growth rate of 0.19 cm for enlarging lesions and 0.21 cm for shrinking ones.

Our results align with existing literature regarding the natural history of solid renal masses and CRCs. Prior studies have reported that small renal masses exhibit slow growth rates, ranging from 0.17 cm to 0.40 cm per year, with metastasis occurring in less than 2% of cases.[12] Similar behavior has been observed in CRCs, with Bk IIF cysts growing at 0.11 cm/year and Bk III cysts at 0.19–0.25 cm/year.[13] Recent studies continue to support the safety of active surveillance for selected renal cystic lesions, particularly for those classified under lower-risk Bk categories.[14] The present study confirmed these trends, reinforcing the indolent nature of most CRCs under AS. Importantly, no patient developed metastases or succumbed to their disease during a mean follow-up of 4.2 years, further supporting AS as a viable management strategy for select CRCs.

Our findings also contribute to the ongoing debate regarding imaging-based CRC classification and reassessment. Bk classification remains the gold standard for stratifying cystic renal lesions, but its subjectivity and reliance on computed tomography (CT) findings have been widely discussed.[15] Recent reviews have highlighted the evolution of the Bk classification, proposing refinements to improve interobserver agreement and diagnostic accuracy.[16] Magnetic resonance imaging (MRI) has demonstrated superior resolution and sensitivity in detecting septa, intracystic solid components, and enhancement, leading to lesion reclassification in up to 23% of cases.[17]

Recent comparative studies analyzing the 2019 and 2005 Bk classification versions highlight the increased diagnostic accuracy and inter-rater reliability with MRI over CT for complex renal cysts.[18] In our cohort, 91% of cases were initially

evaluated by CT and 36% by MRI, with approximately 25% having both imaging modalities. Given the observed discrepancies, our data support the use of MRI for further evaluation when CT findings are inconclusive.

Interobserver variability remains a key concern in CRC assessment. Prior studies have demonstrated strong agreement in measuring objective parameters, such as lesion diameter and proximity to the renal sinus, but lower concordance for subjective factors, such as septal thickening and nodularity.[19] In our study, interobserver disagreement was more pronounced for Bk III cysts, particularly regarding the percentage of intracystic solid components, whereas Bk IV cysts had greater diagnostic consensus. These findings reinforce the need for standardized assessment criteria and advanced imaging techniques to minimize classification discrepancies.

A notable aspect of our study was the evaluation of nephrometric complexity over time using the R.E.N.A.L. and PADUA scoring systems. The R.E.N.A.L. system showed that 5 lesions (4 Bk III and 1 Bk IV) changed complexity categories, with a 1% rate of downgrade and a 3.9% rate of upgrade. Similarly, in the PADUA system, 7 lesions (4 Bk III and 3 Bk IV) shifted complexity categories, with a 2% downgrade rate and a 4.9% upgrade rate. These findings indicate that while most CRCs remain stable, a subset of lesions increases in complexity over time, potentially impacting surgical decision-making. Previous studies have suggested that higher nephrometry scores are associated with increased surgical morbidity, supporting the importance of long-term monitoring for these patients.[20,21]

One of the most relevant clinical implications of our study is the confirmation of AS as a safe approach for managing Bk III lesions. Prior research has shown that approximately 50% of Bk III cysts do not harbor malignancy, and unnecessary surgeries remain a concern.[22] Our results corroborate these findings, as 25.8% of Bk III lesions regressed in size during follow-up, further supporting their indolent nature. Moreover, our study showed a low rate (5%) of surgical intervention, and among these cases, the risk of increased surgical complexity over time was 4% and 5% based on R.E.N.A.L. and PADUA nephrometry scores, respectively. While low, this risk should be factored into clinical decision-making when considering AS.

Conversely, Bk IV cysts exhibited a fivefold higher malignancy risk compared to Bk III cysts, consistent with previous findings.[23] Given their higher likelihood of harboring aggressive neoplasms, intervention should be considered when feasible, considering patient age, comorbidities, renal function, and life expectancy.[24] Notably, in this study, even among patients with Bk IV cysts, some lesions regressed in size or solid component percentage. While spontaneous regression of CRCs has been described, particularly in oncologic patients receiving tyrosine kinase inhibitors, the impact of systemic therapies on CRC evolution remains uncertain.[25]

This study has several limitations that should be acknowledged. First, its retrospective nature introduces potential biases. Second, although in accordance with the last Bosniak classification version,[4] imaging techniques (CT/MRI) varied across the three participating institutions, and patients presented with scans obtained at different time points, leading to potential inconsistencies in acquisition protocols. Third, interobserver variability, particularly in estimating the percentage of intracystic solid components, may have influenced lesion classification. Additionally, although tumor volume measurement would provide a more accurate assessment of lesion progression, changes in complexity would make the surgical procedure more difficult. Postoperative follow-up of patients who underwent surgery is limited to histological diagnosis and functional progression, and surgical complications are beyond the scope of the current study.

Despite these limitations, this study adds to the growing body of evidence supporting AS as a safe and effective strategy for managing CRCs, particularly Bk III lesions. Future studies with longer follow-up periods and standardized imaging protocols are needed to further refine risk stratification and optimize management guidelines. Standardization of imaging interpretation and the potential role of artificial intelligence in lesion classification may help reduce variability and improve diagnostic accuracy. Ultimately, personalized approaches considering lesion characteristics, patient comorbidities, and evolving imaging modalities will be crucial for optimizing outcomes in patients with CRCs.

Conclusion

AS has proven to be a viable and safe strategy for managing select CRCs classified as Bk III and IV. Over a mean follow-up of 4.2 years, most lesions remained stable or exhibited slow growth, with a low risk of metastasis. However, 4–5% of cases showed increased nephrometric complexity, which may impact surgical planning and long-term renal function.

While AS remains an appropriate approach for many Bk III cysts, Bk IV lesions require closer monitoring due to their higher malignant potential. The use of advanced imaging techniques, such as MRI and CT, combined with standardized nephrometry scoring, can enhance risk stratification and improve clinical decision-making.

Despite the retrospective nature of this study and variability in imaging assessments, our findings support AS as a management option for CRCs, if lesion complexity is reassessed regularly. Future research with longer follow-up periods and artificial intelligence driven imaging analysis may further refine patient selection criteria, optimizing treatment strategies for complex renal cysts.

Data Sharing Statement

The authors confirm that the data supporting this study's findings are available within the article.

Ethics Approval

Approval was obtained from the Hospital de Amor de Barretos - Fundação Pio XII institutional review board, CAAE: 64081516.0.2001.5437. Performed following the institutional ethical guidelines and standards in the 1964 Declaration of Helsinki and its later amendments.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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