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## IMPLICATION OF CYSTIC FLUID CYTOLOGY OF RENAL CELL CARCINOMA ON SURGICAL PRACTICE

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#### Abstract

Background: Cystic renal tumours are a type of lesion that has both solid and liquid components. These lesions, which include multilocular cystic nephroma (MCN), renal cell carcinoma (RCC), and papillary adenocarcinoma, can be benign or malignant (PAC). The MCN is a rare neoplasm composed of numerous loculated cystic masses separated by septa. The tumour is benign, although there are some rare reports of malignant cases. The RCC and PAC can both have cystic patterns. The term "responsibility" refers to the act of determining whether or not a person is responsible for his or her own actions. PAC is a rare type of renal tumour that manifests as a large mass with a unilocular large cystic space. Materials and Methods: All cystic renal tumours diagnosed by abdominal computed tomography (CT) scan were evaluated. Demographic information, cystic tumour size, clinical stage, and Bosniak ethnicity were gathered, as well as postoperative histologic and cytological results. All patients were evaluated with a clinical examination, laboratory tests such as a complete blood cell count, liver function tests, and electrolyte profiles, as well as a chest and abdominal CT scan on a regular basis with a follow-up period of 6-32 months. Result: From January 2021 to December 2021, 274 RCC patients were surgically resected at our facility. 37 of them were radiologically diagnosed with cystic renal tumours. Two cases had insufficient fluid sampling, while the other two cases were found to be benign simple cyst or oncocytoma at final histology. There were 22 men and 13 women among the final 35 patients who were enrolled. Table 1 shows the demographics and tumour characteristics of patients with positive and negative cystic fluid cytology. Positive cytology was identified in 17 (48.6%) patients. In positive cytology group, cystic mass size ranged from 1.1 to 14 cm with a median of 3 cm in positive cytology group. Bosniak category III cystic lesions were shown in 5 patients (26.5%) while 12 patients (73.5%) were shown category IV. Conclusion: Patients' age (> 55 years) and higher Bosniak grade (IV) were found to be significant risk factors for positive cytology in cystic RCC in the current study. The answer is yes. Further cell studies and culture under similar conditions and pressure are recommended to better understand the ability of cystic fluid cells to implant and grow.

### **INTRODUCTION**

Cystic renal tumours are a type of lesion that has both solid and liquid components. These lesions, which include multilocular cystic nephroma (MCN), renal cell carcinoma (RCC), and papillary adenocarcinoma, can be benign or malignant (PAC). The MCN is a rare neoplasm composed of numerous loculated cystic masses separated by septa.<sup>[1]</sup> The tumour is benign, although there are some rare reports of malignant cases. The RCC and PAC can both have cystic patterns. The term "responsibility" refers to the act of determining whether or not a person is responsible for his or her own actions. PAC is a rare type of renal tumour that manifests as a large mass with a unilocular large cystic space.<sup>[2]</sup>

However, if clinical practise is based on previous reports, urologists may be less cautious during cystic RCC surgery.<sup>[3]</sup> As a result, the risk of cystic rupture and the least amount of tumour cell seeding may be underestimated. Furthermore, previous reports were based on preoperative FNA studies, which had limitations such as insufficient sampling and high false negative rates. Previous studies did not fully assess the presence and incidence of malignant cells in cystic fluid.<sup>[4]</sup>

As a result, we conducted a prospective study to determine the prevalence of positive and negative cystic fluid cytology in histologically confirmed cystic RCC and its risk factors.<sup>[5]</sup> Our purpose is to precisely access the actual presence of malignant cells in the cystic fluid of RCC by performing direct cystic fluid aspiration from the retrieved specimen in the surgical field, emphasizing its oncological implication on the current clinical practise.

## **MATERIALS AND METHODS**

All cystic renal tumours diagnosed by abdominal computed tomography (CT) scan were evaluated. Demographic information, cystic tumour size, clinical stage, and Bosniak ethnicity were gathered, as well as postoperative histologic and cytological results. All patients were evaluated with a clinical examination, laboratory tests such as a complete blood cell count, liver function tests, and electrolyte profiles, as well as a chest and abdominal CT scan on a regular basis with a follow-up period of 6-32 months.

#### **Inclusion Criteria**

The patients included were those with Bosniak category III and IV on preoperative CT scan.

#### **Exclusion Criteria**

Cystic degeneration tumours were excluded as exclusion criteria. Cases with insufficient cystic fluid sampling volume (less than 5 ml) or benign histology discovered at final pathology were excluded. Polycystic kidney disease cases were also excluded.

A single high-volume surgeon performed all of the surgeries. Surgical methods included laparoscopic partial nephrectomy (LPN), laparoscopic radical nephrectomy (LRN), and robot-assisted partial nephrectomy (RAPN).

Following specimen retrieval, cystic fluid was aspirated directly from the cysts in the surgical field using a 14 Gauge needle. The largest sample volume possible was obtained. The sample was sent to the pathology laboratory, where it was centrifuged for 5

minutes and the supernatant liquid was discarded. After mixing the cell pellet and the washing solution, a 10-minute second centrifugation was performed. After centrifugation, a slide preparation was made by combining the cell pellet and 20 ml of washing solution. Prepared slides were stained with Papanicolaou smear. Pathologists who were specialized in urologic specimen analysis performed the cytological study under high power field light microscope.

Cytological diagnosis was classified into 3 categories of definite malignant cells, atypical cells and negative for malignant cells. Positive cytology was defined as the presence of definitive malignant cells or suspicious atypical cells.

Statistical evaluation: IBM SPSS Statistics ver. 24.0 was used to analyse the data (IBM Co., Armonk, New York, USA). Demographic and perioperative data of each group were compared using paired t-test. Pearson's chi-square test was used to compare two independent cytology groups. To determine the influential factors of positive cystic fluid cytology, univariate and multivariate linear regression analysis were used. The p value of 0.05 was considered statistically significant.

### RESULTS

From January 2021 to December 2021, 274 RCC patients were surgically resected at our facility. 37 of them were radiologically diagnosed with cystic renal tumours. Two cases had insufficient fluid sampling, while the other two cases were found to be benign simple cyst or oncocytoma at final histology.

There were 22 men and 13 women among the final 35 patients who were enrolled. Table 1 shows the demographics and tumour characteristics of patients with positive and negative cystic fluid cytology. Positive cytology was identified in 17 (48.6%) patients. In positive cytology group, cystic mass size ranged from 1.1 to 14 cm with a median of 3 cm in positive cytology group. Bosniak category III cystic lesions were shown in 5 patients (26.5%) while 12 patients (73.5%) were shown category IV.

Table 1: Patients' demographics and tumor characteristics of cystic renal cell carcinoma cytology (total number = 35)					
Variables	Positive Cytology (N=17)	Negative Cytology (N=18)	P value		
Age in years	55.1 ± 2.7	48.2±2.17	0.037		
BMI (kg/m2)	25±5.2	26.2±2.1	0.425		
Gender					
Male	11 (64.7%)	10 (58.3%)			
Female	6 (35.3%)	8 (42%)			
Tumor size (cm)	3.5±0.21	3.80±0.2	0.588		
Median tumour size (cm)	3.0	3.3			
Operation type					
RAPN	13(76.5%)	15 (83.3%)			
LPN	3 (17.7%)	2(13%)			
LRN	1 (5.8%)	1 (5.8%)			
Bosniak classification			0.002		
III	4 (26.5%)	10 (55.6%)			
IV	12 (73.5%)	8 (44.4%)			
Clinical stage			0.53		
cT1a	10 (58.8%)	12 (66.6%)			

cT1b	5 (32.4%)	5 (27.7%)	
cT2a	2(7.6%)	1 (5.7%)	
Histology subtype			0.084
Clear cell	12 (70.8%)	13 (72.2%)	
Papillary	2 (11.7%)	3 (16.6%)	
Collecting duct	2 (8%)	1(2.9%)	
Chromophobe	1(2.9%)	1 (2.9%)	
MiT family Xp11.2 translocation	1(2.9%)	0	
Histology grades			0.14
Grade 1	5(32.4%)	5 (27.7%)	
Grade 2	7 (41.1%)	9(50%)	
Grade 3	4 (26.5%)	4(26.5%)	

Table 2: Univariate analysis of risk factors ass	sociated with positive and	negative cystic fluid cytology groups	

	R2	β	t	95% CI	P Value
Age (>55 years)	0.116	0.340	3.0	0.112-0.561	0.004*
Gender (male)	0.02	- 0.104	- 0.846	- 0.351-0.143	0.403
Tumor size (>4 cm)	0.002	- 0.04	- 0.33	-0.059-0.042	0.742
Bosniak grade	0.157	0.397	3.563	0.15-0.533	0.001*

Table 3: Multivariate analysis of risk factors associated with positive and n	negative cystic fluid cytology groups
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	OR	β	t	95% CI	P Value
Age (> 55 years)	1.23	0.249	2.157	0.018-0.48	0.035*
Gender (male)	0.642	- 0.003	- 0.026	- 0.235-0.229	0.98
Tumor size (>4 cm)	0.46	0.033	0.284	- 0.041-0.055	0.777
Bosniak grade	3.64	0.336	2.828	0.085-0.494	0.006*

## DISCUSSION

Limb et al. performed a laparoscopic evaluation of 57 indeterminate renal cysts, including cystic wall biopsy and fluid sampling. Eleven patients were diagnosed with RCC, with only one (9%) demonstrating positive cystic fluid cytology. During the follow-up period, there was no peritoneal or port site recurrence. Laparoscopic or robotic nephron sparing surgery for complex renal cysts is safe, feasible, and not inferior to open surgery for solid renal masses.<sup>[6]</sup>

Li et al. reported 10 positive percutaneous FNAC (48%) after surgery in 21 documented RCC. Among those 11 positive cytology cases, there were 4 cases of suspected malignant and 7 cases of clearly malignant cells. One patient had a false positive histology-proven benign cyst result.<sup>[7]</sup>

In our study, cystic fluid cytology was positive in nearly half (48.6%) of 35 cystic RCC patients with various histologic subtypes, with clear cell type being the most common. To the best of our knowledge, this is the highest incidence of positive cystic RCC cytology compared with the previous published literatures.<sup>[8]</sup> The term "responsibility" refers to the act of determining whether or not a person is responsible for the actions of another person. Furthermore, using a light microscope, we discovered the presence of cancer cells in cystic fluid, which calls for meticulous dissection during cystic RCC surgery to avoid tumour cell seeding caused by cystic rupture. We performed direct cystic fluid aspiration from the delivered specimen in the surgical field to overcome the challenges and limitations of inadequate sampling in CT or ultrasonography guided FNAC. Furthermore, risk factors for positive cystic fluid cytology were

assessed using retrieved specimens that did not have cystic rupture.<sup>[9]</sup>

Fourteen of the 17 positive cytology cases had definite malignant cells, while the other six had highly suspicious atypical cells. We included atypical cells in the same group as positive malignant cells because they were assumed to have tumorous characteristics similar to malignant cells, based on the cell components' dysmorphic nucleus and high nucleus to cytoplasmic ratio. However, due to the lack of cystic fibrosis, actual evaluation of these cells' behaviour was limited.<sup>[10]</sup>

## **CONCLUSION**

Patients' age (> 55 years) and higher Bosniak grade (IV) were found to be significant risk factors for positive cytology in cystic RCC in the current study. The answer is yes. Further cell studies and culture under similar conditions and pressure are recommended to better understand the ability of cystic fluid cells to implant and grow.

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