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Running Head: **Retroperitoneal partial nephrectomy**

**Retroperitoneal Nephrometry Scoring System (RETRO) for Minimal-Invasive Partial  
Nephrectomy**

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SY Y, LX Z and SW had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: SY Y, LX Z, PW, SW.

Acquisition of data: LX Z, XX S, XX, FZ, XLY, YD.

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Drafting of the manuscript: SYY, LXZ, DX.

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Administrative, technical, or material support: YD, DX, SW.

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#### **Conflict of Interest**

The authors declared that there is no conflict of interest.

#### **Ethics statement**

The study was obtained local ethic committee approval.

#### **Data sharing statement**

We can share our data with the journal for representing analysis and interpretation of the data.

However, we do not want the readers to view or download our data.

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## **Abstract**

**Purpose:** To propose a standardized scoring system of renal tumors suitable for partial nephrectomy based on mini-invasiveness and retroperitoneal approach.

**Materials and Methods:** One-hundred and five patients in retroperitoneal group were prospectively enrolled from January 2017 to December 2018. Perioperative characteristics of all patients were collected: age, gender, BMI, preoperative blood test and imaging results, operation time (the time period starts from the skin incision to the final skin closure), estimated blood lost, clamping time, complications within 30 days, American Society of Anesthesiologists (ASA) score, pathology. An algorithm was extracted, and it was used to predict the risk of complications.

**Results:** Symptoms, ASA score and RETRO score were significantly correlated to postoperative complications, excluding tumor size, ischemia time and operation time. Adjusted RETRO points were an independent factor to predict complication rate ( $p=0.006$ ). Limitation was that it did not analyze the relationship between the RETRO score and the long-term outcomes.

**Conclusions:** The RETRO score simplifies the risk evaluation of partial nephrectomy for patients with renal tumor, especially benefits those surgeries performed under robot-assisted laparoscope via retroperitoneal approach. The new RETRO score system that we developed is a selection criterion to perform surgery via different approach, and an accurate system to evaluate the complexity during partial nephrectomy.

**Key Words:** Partial nephrectomy; Retroperitoneal nephrometry; surgical approach; score system; mini-invasive



Accepted

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## Background

Partial nephrectomy (PN) is becoming the standard treatment for patients with low-stage renal tumor <sup>(1)</sup>. The 2019 updated Guidelines on renal cell carcinoma illustrated that localized T1 tumors are best managed by partial nephrectomy rather than radical nephrectomy, irrespective of the surgical approach (LE: 1b). Tan et al. analyzed more than 3000 patients with low-stage renal cell carcinoma under radical nephrectomy or partial nephrectomy, they found that the long-term overall survival was similar between radical and partial nephrectomy <sup>(2)</sup>. While the risk of development of metabolic or cardiovascular disorders is increased after radical nephrectomy <sup>(3)</sup>. Patients with T2a also received PN, estimated blood lost and perioperative complications were higher, the all-cause mortality and oncologic outcomes were similar compared to radical nephrectomy (RN)<sup>(4,5)</sup>.

With the development of robot-assisted surgical technique, more and more patients received robot-assisted laparoscopic partial nephrectomy. Off-clamp technique was used in totally endophytic renal tumors under robotic platform<sup>(6)</sup>. There are different approaches for partial nephrectomy, transperitoneal way is undertaken by most urologists over the world. Retroperitoneal approach also has its unique advantages, especially for those tumors located posterior side of the hilar, the kidney does not need to be mobilized around <sup>(7)</sup>. It saves time and makes the manipulation much more easily.

The nephrometry scoring system-R.E.N.A.L was reported in 2009 <sup>(8)</sup>. It gave a qualitative and standardized evaluation system for various tumors. Lots of other nephrometry scoring systems also emerged, PADUA classification, C-Index method, and NePhRO system et al. <sup>(9-11)</sup>. However, none of these scoring systems are correlated with different surgical approaches.

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Especially for surgeons who are used to perform PN via retroperitoneal way, there is no evaluation criteria to be used.

The objectives of this study are (1) to propose a standardized scoring system of renal tumors suitable for partial nephrectomy based on mini-invasiveness and retroperitoneal approach; (2) to evaluate the effectiveness and predict overall complications after PN according to this classification system.

## **Methods**

### **Patients and tumors**

We prospectively included 122 patients who underwent Robot-Assisted Laparoscopic Partial Nephrectomy (RALPN) between January 2017 and December 2018. Inclusion criteria: (1) clinical stage 1 (cT1) renal tumors; (2) solitary kidney tumor; (3) age < 80 years; (4) enhanced CT was performed in our medical center. Patients with abnormal coagulation function or acute inflammation (temperature > 38.0°C) were excluded. Among these patients, 105 cases received the operation through retroperitoneal approach, 17 cases were via transperitoneal way. All these surgeries were performed by one surgeon (Dr. Wang), minimizing the methodological bias. All included patients received non-invasive renal angiography through computed tomography (CTA) examination. Three urologists independently read CT images and evaluated these parameters of each tumor: (1) diameter of the tumor (**R**adius); (2) **E**ndophytic; (3) relationships with anterior lip (**T**ransperitoneal/retroperitoneal); (4) relationships with renal vessel trunk (vessel **R**ete), vessel trunk includes the first and secondary renal artery/vein, or the diameter of the artery is larger than 3 mm; (5) relationships with renal polar (**O**rigin). We call it **RETRO** nephrometry classification system (Table 1).

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When tumors locate in the front lip of the hilum, the manipulation will become difficult via retroperitoneal approach. The transperitoneal way is recommended. The definition of the “front lip” is that the space contains in the front side of the hilum, the inner boundary line is the inner edge of the kidney, the outer boundary is the line links the orifice of the hilum, the upper boundary is the line links the high point of the orifice and the up corner of the hilum, the inferior boundary is the line links the lower point to the orifice and the lower corner of the hilum (see Figure 1a). This space is a “forbidden zone” when the retroperitoneal approach is used. Tumors in this area are difficult to be handled, and it’s hard for surgeon to do the resection and suture. Any tumor which “invades” this “forbidden zone” will be recommended to be removed from transperitoneal group (see Figure 1d). Otherwise, retroperitoneal way is suggested when tumors locate in other area of the kidney. The first parameter is an impression for the surgeon to judge which surgical approach is best for the patient.

The maximal diameter of the tumor is also a critical factor affecting the surgical manipulation. One point is given to tumors that are 2cm or smaller, 2 points are given to tumors between 2-4 cm, 3 points are given to tumors between 4-6 cm, and each 2 cm larger gets another 1 point. No ceiling of the score is set. The classification is different from the TNM staging system, because the retroperitoneal cavity is not as large as the peritoneal space, and the diameter plays a more sensitive role (see Figure 1b).

Another parameter is the percent of the protrusion of tumors. Exophytic masses are easily to be resected than endophytic one. Totally endophytic tumor is assigned 3 points. Tumors that are 50% or more endophytic are assigned 2 points. Tumors that are less than 50% endophytic are assigned 1 point (see Figure 1c).

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The relationship between the tumor and main vessels also affects the surgical manipulation. Main vessels include the primary or secondary artery/vein, or those with diameter larger than 3mm. The distance that is 0.6cm or larger is assigned 1 point. The distance which is less than 0.6cm is assigned 2 points. If the tumor closely touches or compresses main vessels, or vessels go through the tumor, 3 points are assigned (see Figure 1e).

It is assigned 1 point if tumors originate from the middle 1/3 portion of the outer boundary edge. Tumors that originate from the superior or the inferior 1/3 of the outer edge are assigned 2 points. Based on 2 points, tumors which are on the ventral side of kidney are assigned as 3 points (see Figure 1f).

Patients received retroperitoneal RALPN in full flank (decubitus) position. Vessel clamping was routinely used. All tumors were removed with an adequate margin to make sure the integrity of pseudo capsule. Clinical features of all patients were collected: age, gender, BMI, preoperative blood test and imaging results, operation time (the time period starts from the skin incision to the final skin suture), estimated blood lost, clamping time, complications within 30 days, American Society of Anesthesiologists (ASA) score, pathology. Postoperative complications were evaluated by the Clavien-Dindo classification system <sup>(12,13)</sup>.

### **Statistical analysis**

The student *t* test was used for continuous variables, and they were given as the mean plus standard deviation (The homogeneity of variance of each test has been assessed). The Mann-Whitney U test was used for non-Normally distributed continuous variables, and they were given as the median and interquartile range (IQR). The Pearson or Likelihood Ratio  $\chi^2$  test was used for categorized variables. Both Logistic regression and ROC curve were used (The



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multicollinearity of independent variables has been assessed). Backward: Conditional method was used in regression analysis. Y was a dependent variable, X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>--- were independent variables,  $Y = b_0 + b_1X_1 + b_2X_2 + \dots + b_kX_k$ , probability  $P = \frac{e^Y}{1+e^Y}$ . A two-sided  $p < 0.05$  was considered statistically significant. All data were analyzed with the Statistical Package for Social Sciences software, v.20.0 (SPSS Inc., Chicago, IL, USA).

## Results

In retroperitoneal group, 63 patients (60.0%) were male and 42 patients (40.0%) were female. The median age was 54y (IQR: 46-63), and the median BMI was 24.3 (IQR: 22.2-26.3). In transperitoneal group, 12 patients (70.6%) were male and 5 patients (29.4%) were female. The median age was 56y (IQR: 53-63), and the median BMI was 22.6 (IQR: 20.8-25.0) (Table 2). Among the perioperative characteristics, most were comparable between two groups. While BMI, operation time and overall complication rate were significantly different. Operation time was a little longer, and overall complication rate was also higher in transperitoneal group. BMI was higher in retroperitoneal group, that might because we preferred to use retroperitoneal approach for patients with relatively high BMI. The operation time was longer in transperitoneal group, that because the time of preparing patients' position, placement of trocars and the skin closure were longer. The post-operative complication rate (Grade I) was high in transperitoneal group, there were 14 cases (82.4%) after operation. The ischemia time was similar. It was 18 (IQR:15-22.5) minutes in retroperitoneal group, and 17 (IQR:12-27.5) minutes in transperitoneal group ( $p=0.891$ ).

In univariate analysis (Table 3), symptoms, ASA score and RETRO score were related to postoperative complications in retroperitoneal group. The median RETRO score was 7 (IQR:

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5-9). And the score of RETRO classification could significantly affected the postoperative complication rate ( $p<0.05$ ). The other factors did not impact on complication, even the radius did not affect the overall complication rate. While in the transperitoneal group, the radius was the only factor which had a significant impact on complication rate.

In logistic regression analysis, the overall complication rate in retroperitoneal group was associated with symptoms, ASA score and RETRO score. The algorithm was extracted from the logistic analysis,  $Y=-2.413+20.909X_1+0.729X_2+0.972X_3$ ,  $X_1$  indicated symptoms,  $X_2$  indicated ASA score, and  $X_3$  indicated RETRO score. Complication probability  $P=\frac{e^Y}{1+e^Y}$ . RETRO score was classified into three categories, 4-6 was indicated 1 point, 7-10 was indicated 2 points, and  $\geq 11$  was indicated 3 points. If a patient had symptom ( $X_1=1$ ), ASA score was 3 ( $X_2=3$ ), RETRO score was larger than 11 ( $X_3=3$ ), then  $Y=-2.413+20.909 \times 1+0.729 \times 3+0.972 \times 3=23.599$ ,  $P=\frac{e^Y}{1+e^Y} \approx 1$ . This patient was most probably had a complication. Another finding from the regression analysis was that patients with RETRO scored 2 were 1.85-fold higher risk of complication compared to those patients with RETRO scored 1. The complication risk of patients with RETRO scored 3 points were dramatically higher compared to those with RETRO scored 1 point.

During the 1-year follow-up, two cases in transperitoneal group relapsed. The pathology is clear cell renal carcinoma (ccRCC, Fuhrman grade III) and papillary renal cell carcinoma (pRCC). The recurrence rate in transperitoneal group was significantly higher than that in retroperitoneal group ( $p=0.008$ ). The 2-year progression-free survival rate in retroperitoneal group was 99%, while it was 88.2% in transperitoneal group.

## **Discussion**

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This study originally proposed a new nephrometry scoring system for PN via retroperitoneal approach. It was named “RETRO” scoring system. Furthermore, a formula was extracted from the logistic analysis, which could predict the probability of the post-operative complication rate. The main factors affecting the complication rate were symptoms, ASA score and RETRO score. The fat round the kidney, especially the adhesive perinephric fat would bring difficulties during the surgery <sup>(14)</sup>. The adhesive perinephric fat did have a significant influence during the laparoscopic single-site donor nephrectomy <sup>(15)</sup>. All patients included in this study received operations under robot-assisted laparoscope. RALPN had lower morbidity and incidence of CKD upstaging <sup>(16-18)</sup>. A novel trifecta for RALPN was conceived<sup>(19)</sup>. Off-clamp technique was recommended since it decreased the probability of severe chronic kidney disease in the long-term<sup>(20)</sup>.

The “RETRO” classification system includes five major parameters. The “T” indicates the approach for operation. Tumors those invades “forbidden zone” do not mean that they cannot be removed through retroperitoneal way. It indicates the manipulation via retroperitoneal cavity will become very complicated. It needs more operation time and retroperitoneal experience. The other four parameters are quantitative factors. According to our experience, the nearness to major vessel is more critical than that to the collecting system. And under the 3D scope, the collecting system is more easily to be noticed and repaired. On the contrary, the vessel trunks near the mass should be more taken care of. It was reported that the hemorrhage was among 4%-5% after partial nephrectomy, and they needed invasive treatment instead of blood transfusion <sup>(21,22)</sup>. Thus, in our series, all cases received robot-assisted laparoscopic nephrectomy and were performed by the same surgeon. It avoided the heterogeneity caused by

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the surgical tools and different manipulation skills. The fourth parameter is the polar location of the mass. Under retroperitoneal way, it will be easier if the mass nears the renal equator. The two polar tumors are more difficult to be exposed and make the suture more complicated.

## Conclusions

Different renal tumor conditions need individualized treatment strategy. The “RETRO” scoring system provides an approach selection and evaluation criterion for surgeons, especially for those used to perform PN via retroperitoneal approach under mini-invasive platform, and predicts a postoperative complication rate estimation. RETRO nephrometry system is a beneficial addition to REANL and PADUA scoring systems.

Table 1. The specific score associated with each retroperitoneal anatomical feature included in RETRO classification.

Table 2. Perioperative characteristics of included patients.

Table 3. Factors related to complications: univariate analysis.

Figure 1. (a) The blue square space is the “front lip”; (b) tumor size classification; (c) endophytic degree of tumors; (d) if tumor invades the “front lip”, transperitoneal approach is recommended; (e) The relationship with major vessels; (f) polar location of the tumor.

Figure 2. RETRO score,  $2+2+1+1=6$ ; RENAL score,  $1+2+1+a+3=7a$ .

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Table 1 The specific score associated with each retroperitoneal anatomical feature included in RETRO classification.

Retroperitoneal anatomical features	Score*
<b>Radius (R)</b>	
≤2cm	1
2-4cm	2
4-6cm	3
6-8cm	4
...	...
<b>Endophytic (E)</b>	
≤50%	1
50-100%	2
100%	3
<b>Trans-anterior lip (T)</b>	
Not involved	Retroperitoneal approach
Involved	Transperitoneal approach
<b>Relationship with renal vessel trunk (R)</b>	
≥0.6cm	1
0-0.6cm	2
0	3
<b>Originate from (O)</b>	

Middle 1/3 part	1
Upper or lower 1/3 part	2
Ventral side plus upper or lower 1/3 part	3

\* Easy: 4-6 points; Moderate: 7-10 points; Difficult:  $\geq 11$  points.

Table 2 Perioperative characteristics of included patients

	Retroperitoneal (n=105)	Transperitoneal (n=17)	p value
Sex			0.405
Male	63 (60%)	12 (70.6%)	
Female	42 (40%)	5 (29.4%)	
Age			0.427
Median	54	56	
IQR	46-63	53-63	
BMI			0.039
Median	24.3	22.6	
IQR	22.2-26.3	20.8-25.0	
Charlson score			0.691
$\leq 1$	82	14	
$>1$	23	3	



Symptoms			0.358
Yes	5	0	
No	100	17	
ASA score			0.929
1	56	9	
2	34	5	
3	15	3	
Location			0.684
Left	50	9	
Right	55	8	
Size			0.146
Median	3.3	3.6	
IQR	2.3-4.1	2.8-4.9	
Endophytic			0.958
≤50%	58	9	
>50%	37	6	
=100%	10	2	
Operation time			0.010
Median	90	111	
IQR	75-109	97.5-136	
Ischemia time			0.891

Median	18	17	
IQR	15-22.5	12-27.5	
Clavien-Dindo classification	60 (57.1%)	14 (82.4%)	0.048
Grade I	55	14	
Grade II	5	0	
Pathology			
ccRCC (Fuhrman grade)			
I	12	1	
II	53	8	
III	9	1	
IV	1	1	
Papillary RCC	6	1	
Chromophobe carcinoma	3	1	
Oncocytoma	5	0	
Angiomyolipoma	11	2	
others	5	2	

Table 3 Factors related to complications: univariate analysis

Surgical approaches	Retroperitoneal (n=105)			Transperitoneal (n=17)		
	Present	Absent	P value	Present	Absent	P value
Sex			0.421			0.218
Male	34 (32.4%)	29 (27.6%)		9 (53.0%)	3 (17.6%)	
Female	26 (24.8%)	16 (15.2%)		5 (29.4%)	0 (0%)	
Age (yr)			0.285			0.761
≤60	42	27		8	2	
>60	18	18		6	1	
BMI			0.687			0.659
≤25	35	28		11	2	
>25	25	17		3	1	
Charlson score			0.376			0.432
≤1	45	37		12	2	
>1	15	8		2	1	
Symptoms			0.047			-
Yes	5	0		0	0	
No	55	45		14	3	
ASA score			0.049			0.673
1	26	30		8	1	

2	21	13	4	1
3	12	3	2	1
Location			0.310	0.761
Left	26	24	8	1
Right	34	21	6	2
Radius (cm)			0.074	0.043
≤4	40	37	9	0
>4	20	8	5	3
Endophytic			0.921	0.755
≤50%	33	25	7	2
>50%	20	16	5	1
=100%	5	5	2	0
Vessel Rete (cm)			0.643	0.659
≥0.6	36	29	3	1
<0.6	24	16	11	2
Origin			0.08	0.633
Not polar	18	21	1	0
Polar or ventral	42	24	13	3
hilum side				
Operation time (min)			0.080	0.377

≤90	27	28	3	0		
>90	33	17	11	3		
Ischemia time (min)			0.071	0.29		
≤25	53	44	10	3		
>25	7	1	4	0		
RETRO score			0.031	0.523		
4-6	21	22	2	0		
7-10	34	23	11	3		
≥11	5	0	1	0		
Recurrence	1	104	0.008*	2	15	/

\*comparison between retro and transperitoneal group.