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의학석사 학위논문

**Predictors of perioperative outcomes during  
robot-assisted partial nephrectomy**

로봇 보조 부분신절제술의 수술 전후 결과를  
예측하는 예후 인자에 대한 연구

2014년 2월

서울대학교 대학원  
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# 로봇 보조 부분신절제술의 수술 전후 결과를 예측하는 예후 인자에 대한 연구

## Predictors of perioperative outcomes during robot-assisted partial nephrectomy

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## **Abstract (English)**

### **Purpose:**

Robot-assisted partial nephrectomy (RPN) has emerged as an alternative treatment for the management of small renal masses. This study was designed to investigate parameters that predict perioperative outcomes during RPN.

### **Materials and methods:**

We retrospectively reviewed the medical records of 113 patients who underwent RPN between September 2008 and May 2012, at the Seoul National University Bundang Hospital. Clinical parameters, including warm ischemia time (WIT), estimated blood loss (EBL), R.E.N.A.L and PADUA score, were evaluated to predict perioperative outcomes.

### **Results:**

Of the 113 patients, 81 were men and 32 women. Mean age was 53.5 years, and mean body mass index was 22.3 kg/m<sup>2</sup>. Age, gender, and mass laterality had no effect on perioperative complications, WIT, or EBL. Univariate analysis revealed that the distance between the tumor and the collecting system ≤4 mm or renal mass size >4cm were associated with adverse profiles of WIT and EBL. However, multivariate analysis showed no association between the predictive parameters and tumor complexity as assessed by nephrometry scores. Tumor size of >4 cm increased the risk of blood loss >300 mL(OR: 3.5, 95% CI 1.3-9.7, P = 0.016). A distance between the tumor and the collecting system of ≤4 mm was associated with increased risk of WIT exceeding 20 min (OR: 2.8, 95% CI 1.3-6.3, P = 0.012).

### **Conclusions:**

Tumor size and proximity of the mass to the collecting system showed significant association with EBL and WIT, respectively, during RPN. R.E.N.A.L and PADUA nephrometry scoring system itself did not predict perioperative outcomes.

**Keywords:** Carcinoma, Renal cell; Nephrectomy; Robotics; Warm Ischemia; Blood Loss, Surgical

**Student Number:** 2012-22706

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## **Introduction**

The worldwide incidence of renal cell carcinoma (RCC) is increasing. Early stage RCC cases have become more common because of the widespread screening with imaging modalities. Nephron sparing surgery (NSS) is the current treatment of choice for early small renal tumors. Partial nephrectomy can be used for achieving oncological outcomes equivalent to that with radical nephrectomy and is associated with reduced overall mortality [1-3]. However, partial nephrectomy is a difficult and relatively challenging procedure compared to radical nephrectomy [4], and evaluating predictive factors prior to the surgery is therefore important.

The R.E.N.A.L nephrometry score is an anatomical scoring system for assessing the complexity of renal tumor [5]. The acronym refers to Radius, Endophytic/exophytic aspect, Nearness of sinus, Anterior/posterior aspect, Location relative to the polar lines [5]. Similarly, PADUA nephrometry system uses some dimensional and anatomical parameters in scoring. It considers tumor location in various aspects, relationships with sinus and collecting system, as well as tumor size and endophytic/exophytic feature [6]. The nephrometry score is a recognized predictor of perioperative complications during open partial nephrectomy [7]. This scoring system is useful for deciding whether renal tumor cases should be treated with surgery or conservative management. Numerous issues such as age, comorbidities, life expectancy, and classification of renal mass complexity are significant determinants of treatment for renal masses. The probability of perioperative complications is also an important factor when surgery is being considered.

Robot-assisted nephron sparing surgery is performed in an increasing number of cases. The procedure has the advantages of low morbidity rates and few perioperative complications [8-10]. The non-compromised oncological efficacy obtained using this procedure is comparable to that obtained with conventional open partial nephrectomy [11]. Blood loss during surgery, ischemia time during nephron sparing procedure, and other perioperative complications are important factors for patient's morbidity and decision making of treatment modality. Nephrometry scoring systems evaluating anatomical complexity of renal tumors are used for validating perioperative outcomes of partial

nephrectomy. However, there are few studies applying the scoring systems to robot-assisted partial nephrectomy (RPN).

The purpose of present study is to validate the predictive value of various parameters, including R.E.N.A.L and PADUA nephrometry scoring systems, for perioperative outcomes during RPN.

## **Materials and methods**

### **Patients' characteristics**

We collected and analyzed data from 113 patients with renal tumor who underwent RPN between September 2008 and May 2012 at the Seoul National University Bundang Hospital. Cases in which RPN was changed to radical nephrectomy were excluded. The institutional review board of Seoul National University Bundang Hospital approved this retrospective study. (IRB No. B-1304/198-108)

### **Clinical parameters**

Each patient underwent preoperative CT evaluation, and all R.E.N.A.L nephrometry scores were obtained from these images. “R” or radius of the renal tumor represented the lesion size. “E” described the appearance of the mass from the renal surface. “N” was determined as nearness of the tumor margin to the renal sinus or collecting system. “A” described the location of the mass, anterior vs. posterior. “L” represented the location with respect to polarity [9]. Similarly, PADUA nephrometry scoring was also measured from those data resources. Each score was calculated by two senior urologists, and concordance between the observers was met without conflict throughout the whole cases.

Perioperative clinical parameters, including warm ischemia time (WIT), estimated blood loss (EBL), and perioperative and postoperative complications were analyzed. We determined the complication divergence point as 20 min for WIT and 300 mL for EBL. It is known that WIT longer than 20 min leads to the decrease of renal function [12]. Minimal invasive partial nephrectomy tends to have less bleeding, approximately below 300 mL [9,13,14,20,22]. Therefore we decided it as a criteria point of considerable bleeding.

### **Statistical analysis**

Data were expressed as mean  $\pm$  standard deviation. Categorical variables were analyzed using chi-square test. Univariate and multivariate logistic regression models were also employed for statistical analyses. A  $P$  value of below 0.05 was considered statistically significant. PASW<sup>®</sup> Statistics 17.0 (SPSS Inc., Chicago, IL, USA) software was used for statistical analysis.

## Results

Patient demographics are shown in Table 1. The study population included 81 men and 32 women, with a mean age of  $53.5 \pm 11.0$  years. Mean body mass index was calculated as  $25.3 \pm 10.7 \text{ kg/m}^2$ . Preoperative mean serum creatinine levels were  $0.94 \pm 0.19 \text{ mg/dL}$ , and estimated glomerular filtration rate (GFR) (Modification of Diet in Renal Disease [MDRD] 7) was  $81.5 \pm 18.0 \text{ mL/min/1.7 m}^2$ . Mean renal mass size was  $3.1 \pm 2.4 \text{ cm}$ , and 62 (55.4%) lesions were found in the left kidney. Calculated R.E.N.A.L nephrometry score was  $7.0 \pm 1.6$ . As indicators of perioperative complications, mean values of WIT and EBL were  $22.1 \pm 8.0 \text{ min}$  and  $179.3 \pm 144.3 \text{ mL}$ , respectively. Table 1 displays pathologic outcomes. A total of 96 cases (85%) were proven to be RCC. There was no case with positive surgical margin.

Univariate and multivariate logistic regression analyses of perioperative complications, WIT and EBL were performed to evaluate their predictive value. Univariate analysis (Table 2) showed no difference in perioperative complications between patients younger and older than 60 years. Gender of patients and laterality of renal tumors also had no effect on complications, or on WIT and EBL. Patients were divided into 2 groups by R.E.N.A.L and PADUA nephrometry score (<7 vs.  $\geq 7$  and <9 vs.  $\geq 9$ , respectively). A total of 70 patients received R.E.N.A.L nephrometry score of 7 or greater (62%). WIT greater than 20 min was associated with nephrometry score  $\geq 7$ , but perioperative complications and EBL  $> 300 \text{ mL}$  had no statistically significant relationship with nephrometry score. Total of 48 patients were graded as 9 or greater in PADUA nephrometry score (42%), and no association was revealed in statistical analysis, either.

We isolated each element of R.E.N.A.L nephrometry score for intensified analysis. There was an increased tendency of WIT  $> 20 \text{ min}$  ( $P = 0.016$ ) and EBL  $> 300 \text{ mL}$  ( $P = 0.018$ ) when the renal mass was larger than 4 cm. Exophytic property of mass (comparison between entirely endophytic masses and others) had no effect on any of the complication parameters. Nearness of the tumor to the collecting system or sinus had an association with a bad profile of WIT and EBL. The frequency of WIT  $> 20 \text{ min}$  and EBL  $> 300 \text{ mL}$  was greater when the distance between the tumor and collecting

duct was <4 mm. Other elements of R.E.N.A.L nephrometry score such as the face of the tumor and polar location had no correlation with complication parameters.

Results of multivariate analyses are shown in Tables 3. Size of renal tumor and nearness of the mass to the collecting system or sinus were significant predictors of RPN complications. The risk of bleeding resulting in a blood loss of >300 mL increased 3.5 times (95% CI 1.3-9.7) when the tumor was larger than 4 cm. The frequency of long WIT was greater (OR: 2.8, 95% CI 1.3-6.3) when the distance between the tumor margin and collecting system or sinus was less than 4 mm.

Perioperative complications occurred in 16 patients, including 6 perirenal organ injuries, 2 open conversions, 3 wound complications, 3 gross hematuria cases, etc (Table 1). Organ injury cases were consisted of 2 renal vein lacerations, 2 spleen injuries, 1 liver and colon injuries. Two open conversions were determined due to difficulty in approaching to the isolated renal tumor, and absolutely small peritoneal cavity for robot control, respectively. Postoperatively, there were 3 hematuria and transfusion cases, 1 wound problem, 1 ileus and 1 minor problem case those ranked as Clavien I or II grade. Other 2 Wound problem cases needed repairing, and 1 abdominal fluid collection required percutaneous drainage were major postoperative complications as classified grade III of Clavien system.

Univariate and multivariate analyses revealed that no parameter showed significant correlation with perioperative complications.

## **Discussion**

Currently, NSS for early stage renal tumor is a standard therapeutic modality. Laparoscopic partial nephrectomy is considered comparable to conventional open surgery with respect to cancer control and perioperative complications [13-16]. RPN is emerging as alternative to purely laparoscopic surgery with comparable oncological outcomes and the extent of invasiveness [8-11]. However, RPN is a challenging procedure for which many factors such as WIT, EBL, and perioperative complications should be considered [9]. WIT correlates with residual renal function after the operation [17]; therefore, the expected duration of NSS should be estimated preoperatively, as the benefits of nephron sparing may not outweigh the increased risk of bleeding [4]. Excessive blood loss and perioperative complications should be avoided depending on the types of comorbidities in the patients. For this, the identification of the significant predictive factors that affect WIT, EBL, and perioperative complications is very important. The present study reveals that the size of the renal mass has significant associations with WIT, EBL, and perioperative complications. Proximity or nearness of the tumor to the collecting duct may also be a significant predictor of longer WIT and high volume of EBL. However, multivariate analysis demonstrated that tumor size is associated with high EBL, while nearness only predicts long WIT. Nephrometry score was not found to be a definitive indicator of EBL, WIT, or perioperative complications. Previous studies have shown an association of nephrometry scores with longer ischemia time and higher volumes of blood loss in cases of open and laparoscopic partial nephrectomy [18,19].

Several factors may account for those results. The resected surface area of larger tumors would be correspondingly larger. As the sliced surface area contains many bleeding points such as venules or arterioles and occasionally larger vessels, the amount of blood loss would be anticipated to increase with size of the resected tumor.

The probability of damaging the collecting system or sinuses during resection increases when the tumor is located deeper. More repair procedures are needed for a mass located close to the collecting duct, compared with the one located at a greater distance. The repair procedure of the tumor bed and parenchymal renorrhaphy plays an important role in determining WIT. Ischemia time is predicted to

increase as the distance between the collecting system and the mass decreases. Nonetheless, tumors located at the hilum cannot be treated using RPN with precision[20,21], and also the overall outcomes of the procedure for renal mass with nephrometry score of  $\geq 7$  was acceptable [22].

Previous study showed the correlation between the nephrometry score and WIT, EBL during RPN [21]. Interestingly, the present study could not find the relationship. Instead, there were other relations of the components of R.E.N.A.L score with WIT or EBL. The differences in result might be based on the disparity of data composition. The profile of nephrometry score of the previous study was distributed relatively unequally. For 67 patients, they were placed as 62 versus 5, and 12 versus 55, in ‘R’ and ‘N’ component, respectively. Those weighted distribution of ‘R’ and ‘N’ component may overwhelmed the whole nephrometry score, consequently affecting the result.

This study has inherent limitations. The number of cases included is relatively small, and the study is retrospective in nature, based on the review of medical records. There may also be a selection bias, since more complex tumors would be recommended for open partial nephrectomy or radical nephrectomy. Further investigation should be done with larger volume of cases, including other important parameters such as postoperative renal functional change and long-term oncological data.

## **Conclusion**

The present study investigated the parameters including nephrometry system to predict perioperative complications, WIT, and EBL in RPN. Overall tumor complexity as assessed by R.E.N.A.L and PADUA nephrometry scoring was not a definitive risk factor for perioperative outcomes. Tumor size and nearness of the mass to the collecting system or sinus were significant indicators of EBL and WIT, respectively. Further large-scale research would be necessary to clarify the results of this study.

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Table 1. Patient demographics and perioperative clinical parameters

Variables	Patients (n = 113)
Age (years)	53.5 ± 11.0
BMI (kg/m <sup>2</sup> )	25.3 ± 3.3
Gender	
Male	81
Female	32
Preoperative creatinine (mg/dl)	0.9 ± 0.2
Preoperative estimated GFR (kg/cm <sup>2</sup> )	81.5 ± 21.9
Size of renal mass (cm)	3.1 ± 2.4
Site (%)	
Left	62 (55.4)
Right	50 (44.6)
R.E.N.A.L score	7.0 ± 1.6
PADUA score	8.5 ± 1.6
Operation time (min)	172.6 ± 100.3
Warm ischemia time (min)	22.1 ± 8.0
Estimated blood loss (ml)	179.3 ± 144.3
Pathologic data	
Renal cell carcinoma (%)	96 (85.0)
Clear cell	84
Papillary	7
Chromophobe	5
Collecting duct	0
Unclassified	0
Angiomyolipoma (%)	6 (5.3)
Oncocytoma (%)	6 (5.3)
Others (%)	5 (4.4)
Pathological tumor stage	
T1a	80
T1b	16
Fuhrman nuclear grade (I/II/III/IV)	0/50/43/3
Positive surgical margin	0
Intraoperative complication (no.)	Postoperative complication (no./Clavien grade)

Organ injury cases (6) Open conversion cases (2)	Minor complication	Wound problem (1/I) Ileus (1/I) Minor problem needed monitoring (1/I) Gross hematuria with transfusion (3/II)
	Major complication	Wound problem with repairing procedure (2/IIIa) Abdominal fluid collection with drain insertion (1/IIIa)

\* BMI = body mass index, estimated GFR = calculated GFR using the Modification of Diet in Renal Disease study (MDRD) equation

\* The complication cases have some redundancy in patients.

Table 2. Univariate logistic regression analysis to predict perioperative complications, WIT > 20 min and EBL > 300 ml

Variables	Perioperative complications		WIT > 20 min		EBL > 300ml	
	Cases (%)	P value	Cases (%)	P value	Cases (%)	P value
Age (years)		0.912		0.820		0.792
< 60	12/86 (13.9)		53/86 (61.6)		20/86 (23.3)	
≥ 60	4/27 (14.8)		18/27 (66.7)		5/27 (18.5)	
Sex		0.116		0.130		0.329
Male	9/81 (11.1)		47/81 (58.0)		16/81 (19.8)	
Female	7/32 (21.9)		24/32 (75.0)		9/32 (28.1)	
Site (%)		0.248		0.435		0.070
Left	11/62 (17.7)		41/62 (66.1)		18/62 (29.0)	
Right	5/50 (10.0)		29/50 (58.0)		7/50 (14.0)	
Renal mass size (%)		0.163		0.016		0.018
≤ 4 cm	11/92 (11.9)		53/92 (57.6)		16/92 (17.4)	
> 4 cm	5/21 (23.8)		18/21 (85.7)		9/21 (42.9)	
Exophytic property (%)		0.761		0.452		1.000
Exophytic	14/96 (14.6)		60/96 (62.5)		21/96 (21.9)	
Entirely endophytic	2/17 (11.8)		11/17 (64.7)		4/17 (23.5)	
Nearness of the tumor to the collecting system or sinus		0.846		0.013		0.031
> 4 mm	9/61 (14.8)		32/61 (52.5)		11/61 (18.0)	
≤ 4 mm	7/52 (13.5)		39/52 (75.0)		14/52 (26.9)	
Polar location		0.591		0.693		0.249
Upper & Lower pole	8/51 (15.7)		31/51 (60.8)		10/51 (19.6)	
Cross polar line	4/27 (14.8)		16/27 (59.3)		4/27 (14.8)	
Entirely between polar line	4/35 (11.4)		24/35 (68.6)		11/35 (31.4)	
Face		0.791		0.907		0.260
Anterior	8/60 (13.3)		38/60 (63.3)		16/60 (26.7)	
Posterior	8/53 (15.1)		33/53 (62.3)		9/53 (17.0)	
R.E.N.A.L score		0.292		0.016		0.110
< 7	8/43 (18.6)		21/43 (48.8)		6/43 (14.0)	

$\geq 7$	8/70 (11.4)	50/70 (71.4)	19/70 (27.1)	
PADUA score		0.515	0.133	0.123
< 9	8/65 (12.3)	37/65 (56.9)	11/65 (16.9)	
$\geq 9$	8/48 (16.7)	34/48 (70.8)	14/48 (29.1)	

WIT= Warm ischemia time, EBL= Estimated blood loss

Table 3. Multivariate logistic regression analysis to predict parameters of perioperative complications, WIT > 20 min and EBL > 300 ml

Variables	Perioperative complications	WIT > 20 min	EBL > 300ml
	P value	P value	P value
Age (years)	0.928	0.143	0.879
Sex	0.098	0.077	0.289
Laterality	0.244	0.482	0.056
Renal mass size (≤ 4 cm vs > 4 cm)	0.166	0.056	OR: 3.516 95% CI 1.269-9.739 P = 0.016
Exophytic property	0.747	0.839	0.475
Nearness of the tumor to the collecting system or sinus (> 4 mm vs ≤ 4 mm)	0.817	OR: 2.806 95% CI 1.253-6.286 P = 0.012	0.604
Polar location	0.876	0.457	0.099
Face (anterior vs posterior)	0.817	0.570	0.115
R.E.N.A.L score (< 7 vs ≥ 7)	0.302	0.485	0.239
PADUA score (< 9 vs ≥ 9)	0.533	0.943	0.382

WIT= Warm ischemia time, EBL= Estimated blood loss

## 초 록

### 서론:

로봇 보조 부분신절제술은 작은 신종괴에 대한 치료법으로, 기존 개복 수술 및 복강경 수술에 대한 최소침습적 대안으로 대두되고 있다. 본 연구에서는 로봇 보조 부분신절제술과 관련한 결과를 예측할 수 있는 인자를, nephrometry score를 포함하여 조사하고자 하였다.

### 방법:

2008년 9월부터 2012년 5월까지, 분당서울대학교병원에서 로봇 보조 부분신절제술을 시행한 113명의 환자에 대한 의무기록을 후향적으로 분석하였다. 수술 관련 결과를 평가하기 위하여 온허혈시간 및 실혈량, 수술 관련 합병증, 병리 결과 등을 조사하였고, 예측 인자로서 R.E.N.A.L 및 PADUA nephrometry score를 비롯한 여러 인자들을 분석하였다.

### 결과:

113명의 환자는 81명의 남성과 32명의 여성으로 구성되었고, 평균 나이는 53.5세였으며, 평균 체질량지수는  $22.3\text{kg}/\text{m}^2$ 였다. 연령, 성별, 종괴의 좌/우 편측성은 온허혈시간, 실혈량, 수술관련 합병증과 관련이 없었다. 단변량분석에서, R.E.N.A.L score는 온허혈시간과 연관이 있었고, 신종괴의 크기가 4cm를 넘거나 종괴와 집합관의 거리가 4mm 이하인 경우에는 온허혈시간과 실혈량에 부정적인 결과가 보고되었다. 다변량분석에서, 신종괴의 크기가 4cm를 초과하면 실혈량이 300mL를 넘는 경향이 발견되었으며(OR: 3.5, 95% CI 1.3-9.7, P = 0.016), 종괴와 집합관의 거리가 4mm 이하인 경우 온허혈시간이 20분을 초과하는 것과 상관관계가 있었다(OR: 2.8, 95% CI 1.3-6.3, P = 0.012). 반면, nephrometry score로는 예측 할 수 있는 인자가 없었다.

### 결론:

신종괴의 크기 및 집합관과 가까운 정도는 각각 실혈량과 온허혈시간에 연관성을 보였다. 반면, R.E.N.A.L 및 PADUA nephrometry scoring system은 수술 관련한 합병증이나 실혈량, 온허혈시간을 예측할 수 없었다.

**주요어:** 신장암, 로봇 보조 부분신절제술, 온허혈시간, 수술 중 실혈량

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