



Predictive Factors of Perioperative Significant Complications Following Partial Nephrectomy for Renal Cell Cancer

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Abstract

Objective: Estimating surgical complications is crucial to assess the benefit-harm balance of partial nephrectomy (PN), a complex surgical option compared to radical nephrectomy. This study aimed to assess the factors affecting the occurrence of modified Clavien-Dindo grade 2 or higher complications after PN.

Materials and Methods: Data of patients who underwent PN due to renal cancer from January 2015 to June 2018 were prospectively collected. Database was analysed retrospectively by dividing into two groups with Clavien-Dindo grade 0-1 complications (group 1) and with grade 2 or higher complications (group 2). The resection technique was classified by the surgeon as enucleation, enucleo-resection or resection according to the Surface-Intermediate-Base (SIB) margin scores of 0, 1 and 2, respectively. Factors affecting the occurrence of grade 2 or higher complications were evaluated by univariate and multivariate regression analysis.

Results: A total of 161 patients were included in the study. The overall rate of perioperative complications was 18.6%. Twenty-four patients (14.9%) had grade 2 or higher complications and 11 patients (6.8%) had serious complications (grade 3 or higher). SIB-score was 0 in 103 (63.9%) patients, 1 in 36 (22.4%) patients and 2 in 22 (13.7%) patients. Multivariate binary logistic regression analysis revealed that the C-index [odds ratio (OR): 0.224, 95% confidence interval (CI): 0.092-0.493, p=0.001], laparoscopic surgical technique (OR: 12.668, 95% CI: 2.825-59.326, p=0.001), and SIB-score 1-2 (OR: 2.852, 95% CI: 1.416-9.826, p=0.002) are independent factors in predicting complications of Clavien-Dindo grade 2 or higher.

Conclusion: C-index, laparoscopic approach and resection techniques (SIB-score 1-2) are independent factors in predicting perioperative complications of Clavien-Dindo grade 2 or higher following PN.

Keywords: Complication, partial nephrectomy, predictors, renal cell cancer, resection technique

Introduction

The incidence of renal cell cancer (RCC) is the 6th most common type of cancer in men and the 10th most common type of cancer in women. Its rate among all cancers is 5% in men and 3% in women (1). Radical nephrectomy was the only treatment option for these tumours in the past; however, the frequency of partial nephrectomy (PN) has been increasing gradually, as studies reported in recent years demonstrated better renal function and similar oncological results (2). A study even reported that PN had better survival outcomes (3).

However, complications are not uncommon in these challenging cases. Complication rates after PN have been reported up to 30% (4,5), and major life-threatening complications have been reported with a rate of 3%-6% (6). Numerous renal scoring systems have been identified to predict complications. However, results of these scoring systems also vary. Thus, revealing the benefit-harm balance of PN is thoroughly necessary. Evaluating complications plays an important role in reducing perioperative deficiencies and improving patient care. Complications that require additional medical or surgical treatment or require intensive care can have devastating effects on the patient.

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Therefore, this study aimed to determine the factors affecting significant complications.

Materials and Methods

Data of patients who underwent PN for RCC from January 2015 to June 2018 were prospectively collected. Demographic data, radiological features, perioperative characteristics, histopathological and follow-up outcomes of patients were recorded. Computed tomography and/or magnetic resonance imaging were used for preoperative kidney and tumour imaging, and thoracic X-ray or computed tomography data were recorded. The size of the tumour, its location in the kidney, clinical stage, surgical technique and characteristics were recorded using the patient follow-up cards. Tumour size was calculated as the longest diameter of the tumour. Renal scoring systems such as tumour centrality index (C-index), Radius exophytic-endophytic nearness anterior-posterior location (RENAL) nephrometry score and preoperative aspects and dimensions used for anatomic (PADUA) classification were calculated by the same urologists in a team of two. Surgeries were undertaken by a team of 4 experienced urologists with at least 10 years of urooncological experience. Histopathological evaluations were performed by a pathologist with 18 years of experience.

The resection technique was divided into 3 categories by the surgeon according to the Surface-Intermediate-Base (SIB) margin scores. The SIB margin score of these categories, defined as enucleation, enucleo-resection or resection, was recorded as 0, 1 or 2, respectively. Perioperative complications were assessed according to the modified Clavien-Dindo classification (7). Grade 2 or higher complications were defined as significant complications. Factors affecting the occurrence of significant complications were evaluated by univariate and multivariate regression analysis. Impact of SIB-score on significant complications of PN was also assessed. This database was reviewed retrospectively by dividing into two groups with Clavien-Dindo grade 0-1 complications (group 1) and with grade 2 or higher complications (group 2). Masses with benign pathology (n=12), non-RCC malignant masses (n=9), and patients with missing data or who have not been evaluated for complications (n=24) were excluded from the current study. This study was approved by the institutional research ethics committee of our tertiary health care provider hospital (Institutional review board decision number IRB-97/11, dated 05.10.2020).

Statistical Analysis

One-sample Kolmogorov-Smirnov test was used to control the distribution of data for numerical variables. These quantitative variables were compared with Student's t-test when parametric test criteria were found. In the absence of these criteria, Mann-Whitney U test was used. Pearson chi-square test and Fisher's exact test were used to determine whether a difference between percentages of categorical variables is present. Binary logistic regression analysis was used to obtain independent risk factors affecting major complications after PN. The probability of first type error was $\alpha=0.05$ for all tests. Statistical analysis of the study was performed using the International Business Machines

Statistical Package for the Social Sciences 22.0 package programme.

Results

Out of 206 patients who underwent PN in our clinic, data of 161 patients were analysed in the study (Figure 1). The overall rate of perioperative complications was 18.6%. A total of 24 patients (14.9%) had grade 2 or higher complications and 11 patients (6.8%) had serious complications (grade 3 or higher) (Table 1). The mean age was 59.2 ± 12.4 years in group 1 and 57.1 ± 13.1 years in group 2. Interestingly, female gender is dominant in

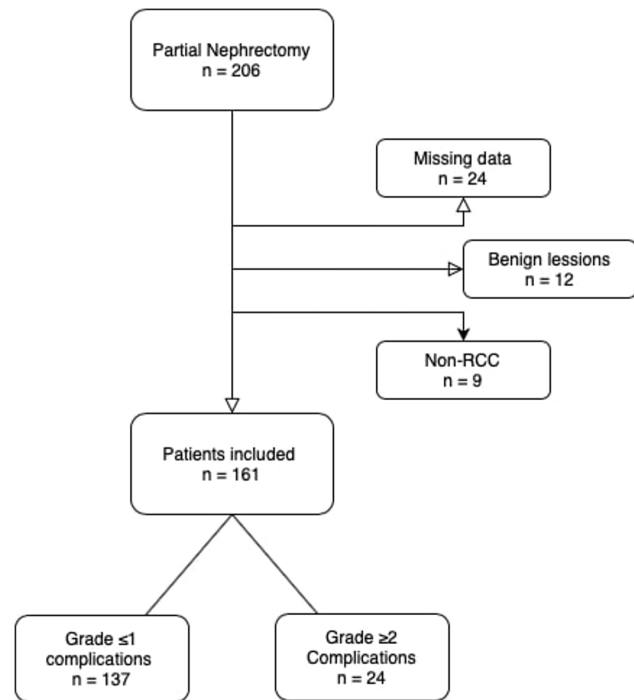


Figure 1. Flow chart of patients who met study inclusion and exclusion criteria
RCC: Renal cell cancer

Table 1. Clavien-Dindo classification of surgical complications

Grade	Number of patients, n (%)	Definition
Grade 1	6 (3.7)	Any deviation from the normal postoperative course without the need for pharmacological treatment other than antiemetics, antipyretics, analgesics, diuretics, electrolytes or physiotherapy. Wound infections opened at the bedside.
Grade 2	13 (8.1)	Requiring pharmacological treatment with drugs other than which were allowed for grade 1 complications. Blood transfusions and total parenteral nutrition.
Grade 3	6 (3.7)	Requiring surgical, endoscopic or radiological intervention.
Grade 4	4 (2.5)	Life-threatening complication requiring intensive care unit management.
Grade 5	1 (0.6)	Death of the patient.

group 2, but not statistically significant ($p=0.097$). Among the renal nephrometry systems, only the C-index was statistically different. The C-index was higher in group 1 compared to group 2 (2.7 ± 1.1 vs 1.8 ± 0.8 , respectively, $p=0.006$) (Table 2). A laparoscopic procedure was performed in 33.3% of patients in group 1 and 62.5% of patients in group 2 ($p=0.016$). SIB-score was 0 in 103 (63.9%) patients, 1 in 36 (22.4%) patients and 2 in 22 (13.7%) patients. Tumour excision was performed in 45 patients (32.8%) in group 1 and in 13 patients (54.2%) in group 2 by resection or enucleo-resection method ($p=0.045$). Histopathological outcomes were similar in both groups. Intraoperative blood transfusion was administered to 5 patients (3.1%), whereas 7 patients (4.3%) received a postoperative blood transfusion. Intraoperative blood transfusion was performed in 2 patients (1.5%) in group 1, which was not required during the postoperative period, whereas blood transfusion was given to 10 patients (41.7%) in group 2 during the perioperative period. The volume of intraoperative bleeding was higher in group 2 than in group 1 ($p=0.002$). Similarly, haemoglobin drop was more pronounced in group 2 ($p=0.048$). In addition, hospitalisation in group 2 was longer as expected ($p<0.001$) (Table 3). Multivariate binary logistic regression analysis revealed that the C-index [odds ratio (OR): 0.224, 95% confidence interval (CI): 0.092-0.493, $p=0.001$], laparoscopic surgical technique (OR: 12.668, 95% CI: 2.825-59.326, $p=0.001$) and SIB-score of 1-2 (OR: 2.852, 95% CI: 1.416-9.826, $p=0.002$) are independent factors in predicting complications of Clavien-Dindo grade 2 or higher (Table 4).

Table 2. Demographic characteristics of patients and radiological assessments of renal masses

	Group 1 (n=137)	Group 2 (n=24)	p-value
Age, years	59.2±12.4	57.1±13.1	0.372
Gender (male/female)	82/55	10/14	0.097
Body mass index, kg/m ²	27.1±4.4	28.9±6.3	0.104
Charlson Comorbidity index	3.4±2.1	2.8±2.2	0.275
ECOG performance score			
0	50 (36.5)	8 (33.3)	0.876
1	53 (38.7)	11 (45.8)	
2	30 (21.9)	4 (16.7)	
3	4 (2.9)	1 (4.2)	
Tumour size, mm	36.2±15.2	41.6±16.8	0.208
PADUA score	8.5±1.9	9.2±1.6	0.194
RENAL nephrometry score	7.0±1.8	7.8±2.2	0.096
C-index	2.7±1.1	1.8±0.8	0.006
ECOG: Eastern cooperative oncology group, PADUA: Preoperative aspects and dimensions used for anatomic classification, RENAL: Radius exophytic-endophytic nearness anterior-posterior location nephrometry score, C-index: Centrality index			

Discussion

Estimating surgical complications is crucial to assess the benefit-harm balance of PN, a complex surgical option compared

to radical nephrectomy. In the current study, the overall perioperative surgical complication rate was 18.6%, and the major complication (grade 3 or higher) rate was 6.8%. Perioperative complication rates of PN have been reported in the literature up to 30% (4,5). Mari et al. (8) reported the total and major complication rates as 10.2% and 2.5%, respectively. In the perioperative outcomes of the Italian RECORD 1 study

Table 3. Perioperative characteristics, resection techniques and histopathological outcomes of patients

	Group 1 (n=137)	Group 2 (n=24)	p-value
Surgical technique, n (%)			0.016
Open	87 (66.7)	9 (37.5)	
Laparoscopic	50 (33.3)	15 (62.5)	
Surgical approach, n (%)			0.720
TP/RP	21/116	3/21	
Presence of ischaemia, n (%)	93 (67.9)	15 (62.5)	0.102
Ischaemia time, min (± SD)	23.0±5.6	25.8±7.6	0.193
SIB-score, n (%)			0.039
0 (Enucleation)	92 (67.2)	11 (45.8)	
1 (Enucleo-resection)	30 (21.9)	6 (25)	
2 (Resection)	15 (10.9)	7 (29.2)	
SIB-score subgroup, n (%)			0.045
Enucleation	92 (67.2)	11 (45.8)	
Resection	45 (32.8)	13 (54.2)	
Operative time, min	112.6±32.4	126.9±31.1	0.069
Bleeding volume, mL	319.2±139.2	541.3±401.2	0.002
Haematocrit drop, %	7.4±3.3	9.7±6.3	0.097
Haemoglobin drop, g/dL	2.4±1.0	3.3±2.1	0.048
Serum creatinine elevation, mg/dL	0.2±0.2	0.3±0.4	0.246
eGFR decrease, mL/min/1.73 m²	4.3±16.7	9.1±20.2	0.268
Hospitalisation, day	3.8±1.4	6.9±4.5	<0.001
pT stage, n (%)			0.178
pT1	132 (96.4)	21 (87.5)	
pT2	3 (2.2)	2 (8.3)	
pT3	2 (1.4)	1 (4.2)	
Subtype of RCC, n (%)			0.884
Clear cell	110 (80.3)	20 (83.3)	
Papillary	16 (11.7)	2 (8.3)	
Chromophobe	8 (5.8)	1 (4.2)	
Other	3 (2.2)	1 (4.2)	
Nuclear grade, n (%)			0.070
Low grade (I-II)	104 (75.9)	13 (54.2)	
High grade (III-IV)	21 (15.3)	8 (33.3)	
Not available	12 (8.8)	3 (12.5)	
TP: Transperitoneal, RP: Retroperitoneal, SIB: Surface-intermediate-base margin scores, eGFR: Estimated glomerular filtration rate, pT: Pathological T-stage, RCC: Renal cell cancer, SD: Standard deviation			

Table 4. Univariate and multivariate binary logistic regression analysis of factors affecting complications after partial nephrectomy

	Univariate model					Multivariate model				
	OR (95% CI)				p	OR (95% CI)				p
Age, years	0.987	0.958	-	1.028	0.364	-	-	-	-	-
Female gender	2.137	0.984	-	6.911	0.066	-	-	-	-	-
Body mass index, kg/m ²	1.132	0.914	-	1.451	0.098	-	-	-	-	-
Charlson Comorbidity index	0.903	0.719	-	1.168	0.274	-	-	-	-	-
ASA score										
1-2	1.014	0.988	-	1.042	0.340	-	-	-	-	-
3-4	1.420	0.780	-	2.18	0.180					
Tumour size, mm	1.014	0.996	-	1.034	0.221	-	-	-	-	-
PADUA score	1.256	0.728	-	1.812	0.283	-	-	-	-	-
RENAL nephrometry score	1.318	0.886	-	1.827	0.102	-	-	-	-	-
C-index	0.368	0.182	-	0.724	0.011	0.224	0.092	-	0.493	0.001
Surgery technique, Laparoscopy	3.210	1.097	-	9.112	0.022	12.668	2.825	-	59.326	0.001
Retroperitoneal approach	1.820	0.382	-	8.410	0.428	-	-	-	-	-
SIB-score (1-2), Enucleo-resection Resection	1.984	1.030	-	5.260	0.034	2.852	1.416	-	9.826	0.002
Operative time	1.492	0.923	-	2.258	0.092	-	-	-	-	-

*The p-value of the model was <0.001 and the R-square was 0.283.
 ASA: American Society of Anaesthesiologists, PADUA: Preoperative aspects and dimensions used for anatomic classification, RENAL: Radius exophytic/endophytic nearness anterior/posterior location nephrometry score, C-index: Centrality index, SIB: Surface-intermediate-base margin scores, CI: Confidence interval, OR: Odds ratio

designed between 2008 and 2012, these rates were reported as 13.1% and 3.5%, respectively (5). Similar to our current study, the overall complication rate was 17.8%, whereas the grade ≥ 3 a complication rate was reported as 5% in the study, including 1,044 patients who underwent PN in 2001-2012 as participated by 10 centres (9). Complication rates were very high in a study participated by approximately 2,000 patients that underwent PN with older and high comorbidity scores, the total complication rate was reported as 37%. The data of this study were obtained from SEER database registry (4).

The relationship between resection techniques and complications has also been examined in many studies (10,11,12,13). Standard or traditional technique resects a width approximately 5-10 mm of paratumour tissue for ensuring a negative surgical margin (14,15). Minervini et al. (10) reported that grade >2 complications more frequently occurred after enucleo-resection than after enucleation (10.7% vs 4.2%, $p=0.01$) and resection (10.7% vs 3.3%, $p=0.04$) technique. Similar to our study, Takagi et al. (11) found that enucleation was associated with lower complication rate. Unlikely, the resection technique was reported to not affect the complication (12). Dong et al. (13) stated that the overall complication rates of enucleo-resection and standard technique in laparoscopic PN cases were similar (11.2% vs 16.3%, respectively, $p=0.3$), and that enucleo-resection technique caused less bleeding.

Moreover, the renal score was reported to be associated with the incidence of complications (16). The complication rate increases as the tumour approaches the centre of the kidney. In our study, tumour centrality determined by C-index was one of the independent risk factors predicting grade >2 complications.

In another study, tumour size was reported to be a predictive factor for complication (17,18,19,20). Schiavina et al. (18) noticed that the diameter of clinical tumour was significantly correlated to grade 3-4 complications. The common feature of all these renal scoring systems is the aim to predict the difficulty of surgery and complications that may occur. PADUA and RENAL nephrometry scores were higher in group with grade >2 complications in our current study; however, only the C-index was found to be statistically significant.

In a study participated by 1,308 patients comparing open, laparoscopic and robotic PN, intraoperative complications were found to be statistically significantly higher in laparoscopic technique ($p=0.001$). In the same study, two groups were not different from each other for grade 3 and higher complications (21). However, only intraoperative complications were evaluated instead of perioperative complications as in our study. In the present study, grade >2 complications were found to be higher in patients who underwent laparoscopic PN. The operation time was not statistically significantly different between two groups; however, it may have played a role in the increase of major complications in laparoscopic cases. The transperitoneal and retroperitoneal approach have been used for PN according to tumour characteristics and/or surgeon's preferences. In addition, the transperitoneal approach offers a greater working area and well-known landmarks but requires bowel mobilisation to demonstrate the kidney. The retroperitoneal approach has positive aspects such as not requiring bowel mobilisation; however, with shorter operative time and direct access to the kidney, disorientation can be seen without enough surgical experience. Moreover, it offers a more convenient access,

especially in posteriorly located tumours (22). The retroperitoneal approach is mostly preferred due to the experience in our clinic. Both approach methods have positive and negative aspects; however, we think that complications will be reduced by using the method with extensive surgical experience.

The traditional resection in PN has been reported to cause more postoperative bleeding and complications than enucleo-resection. In the same study, the rate of total complications was found to be similar (13). However, most studies reported that enucleation technique causes less complication than enucleo-resection or resection (10,11,12,23). The technique of dissecting the renal mass from the renal parenchyma is used in the avascular plane extending along the fibrous pseudo-capsule in enucleation. Therefore, enucleation appears to be more minimally invasive compared to resection techniques as it will cause less disruption in the vascular structure. Similarly, the resection technique in our study was performed more frequently in the group with significant complications. The bleeding volume and haemoglobin drop were also higher in this group, as expected. A statistical difference was observed; however, due to a small number of patients who applied blood transfusion, a definitive conclusion could not be correctly reached. In addition, major complications result in longer hospitalisations to complete treatment. In our study, hospitalisation was longer in group 2.

A multivariable analysis was established to predict the risk of occurrence of perioperative significant complications following PN. Age, gender, body mass index, comorbidity score, tumour size, tumour location, surgical approach and techniques were analysed in this model, which was constructed to predict significant life-threatening complications including blood transfusion. C-index, laparoscopic technique and SIB-score 1-2 were significant predictive factors of perioperative significant complications. We found that as the centrality of the tumour increased, the complication rates increased (OR: 0.224, $p=0.001$). According to the study results, laparoscopic PN increased the risk of complications by 12,668 times compared to open PN. Additionally, we revealed that the use of enucleo-resection or resection techniques in tumour excision increased the risk of significant complications by 2.852 times ($p=0.002$).

Study Limitations

Several limitations of this study warrant mention in addition to the retrospective design and a population of tertiary care patients. The relatively small number of patients with major complications after PN may have affected the results. Additionally, excision techniques selection was dependent upon surgeons. Finally, SIB-score determination inherently shows a certain degree of inter-observer subjectivity. Nonetheless, despite these limitations, renal scoring and SIB-score were determined by the same two urologists. In addition, one of the strengths of our study is that all cases belong to a single centre.

Conclusion

Major complications that occur after PN may have significant effects on the patient and may be life-threatening. Therefore, it is very important that these complications are detected and treated early. Tumour centrality index, laparoscopic approach

and resection techniques (SIB-score 1-2) are independent factors in predicting perioperative complications of Clavien-Dindo grade 2 or higher after PN.

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Ethics

Ethics Committee Approval: This study was approved by the institutional research ethics committee of our tertiary health care provider hospital (Institutional review board decision number IRB-97/11, dated 05.10.2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.Ç.Ç., N.K., E.H., Design: M.Ç.Ç., N.K., A.K., S.S., E.H., F.Y., Data Collection or Processing: M.Ç.Ç., A.K., G.Ö., E.H., Analysis or Interpretation: M.Ç.Ç., N.K., G.Ö., S.S., F.Y., Literature Search: M.Ç.Ç., N.K., A.K., G.Ö., S.S., Writing: M.Ç.Ç., N.K., S.S., F.Y.

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