Asian Journal of Surgery (2019) 42, 326–331

Available online at www.sciencedirect.com

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journal homepage: www.e-asianjournalsurgery.com

ORIGINAL ARTICLE

The role of RENAL, PADUA and C-index scoring systems in predicting the results of partial nephrectomy without ischemia

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Received 30 January 2018; received in revised form 23 May 2018; accepted 15 June 2018
Available online 6 August 2018

KEYWORDS
Partial nephrectomy;
Off-clamp;
RENAL;
PADUA;
C-index

Summary *Objective:* To evaluate the feasibility and renoprotective effect of off-clamp partial nephrectomy (PN) by renal scoring systems.
Methods: After approval of the local ethics committee, the radiological and clinical data of patients with renal masses who underwent PN between January 2012 and January 2017 were evaluated in two university hospitals. Total 132 patients who underwent open surgery and off-clamp technique were included. All patients underwent contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) preoperatively. Preoperative demographic data, estimated glomerular filtration rate (e-GFR) and hematocrit changes, operation time, tumor volume and hospitalization time from patients were evaluated separately and statistically for each of the three scoring systems.
Results: Our study consisted of 132 patients with a mean age of 53.9 ± 13.9 with 69 male and 63 female. Statistically significant difference between the risk groups in RENAL and PADUA scoring were found according to tumor T stage and tumor volüme **($p < 0.005$).** Statistically significant difference was only found between risk groups of RENAL scoring system in e-GFR reduction **($p<0.05$).** There was no statistically significant difference between the groups in the complications of all three classification systems ($p > 0.005$).
Conclusions: In our study, all three scoring sytem successfully predicted the surgical complexity ve surgical outcomes and our results indicate that off-clamp PN has similar success and complications rates when compared to the literature. The off-clamp PN must be kept in mind to maintain postoperative renal functions eligible patients.

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https://doi.org/10.1016/j.asjsur.2018.06.006

1. Introduction

Due to the technological improvements in imaging methods, the rates of operation have increased significantly with the easier diagnosis of renal masses, and partial nephrectomy (PN) has become the standard treatment for surgery of appropriate renal masses.[1,2] Classification of renal masses according to their anatomical characteristics is also very important for planning of operation, preservation of renal function, avoidance of surgical complications, and an ideal system should guide the clinician in anticipating both operative complexity and perioperative results.[3] The basis of these scoring systems utilizes the data of the PN series performed by different surgical methods. When the urological literature is examined in general, it is seen that RENAL, PADUA and C-index scoring systems are frequently used.[4–6]

In addition to the oncologic outcomes after PN, the functions of the remaining renal tissue are vital for the patient's rest of life. Although more nephron units may be preserved with PN, renal hilar clamping injury may expose remaining nephrons to ischemia-reperfusion injury, thus reducing the renoprotective purpose of the procedure.[7] For this purpose, off-clamp PN has been introduced into the literature in recent years in addition to conventional warm or cold ischemic approaches. Also, the off-clamp technique has been reported to have superiority in preserving renal function compared to hilar clamping techniques.[8,9]

In this study, we aimed to determine the preoperative surgical complexity and to evaluate the feasibility and renoprotective effect of this technique by preoperative renal scoring of patients who were treated with renal tumor using off-clamp technique.

2. Methods

2.1. Patients

After approval of the local ethics committee, the radiological and clinical data of patients with renal masses who underwent PN between January 2012 and January 2017 were evaluated in two university hospitals. All procedures were performed by surgeons with at least 5 years' experience in urooncological surgery and all surgeons performed the same technique. Patients with chronic renal failure (CRF) and bilateral renal tumors, and patients who underwent laparoscopic or robot assisted surgery using warm or cold ischemia were not included in the study. A total of 112 patients were excluded from the study when evaluated according to the exclusion criteria. Thus, 132 patients who underwent open surgery and off-clamp technique were included.

2.2. Radiological evaluation and nephrometry scoring

All patients underwent contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) preoperatively. Two urologists and one radiologist evaluated contrast - enhanced CT or MRI to assess the anatomic complexity of the renal tumor. All patients were analyzed separately with RENAL (radius for tumor size as maximal diameter, exophytic/endophytic tumor properties, nearness to deepest portion of tumor collecting system or sinus, anterior/posterior descriptor and location relative to polar line), PADUA (preoperative aspects and dimensions used for an anatomical) and C-index (centrality index method) scoring systems.

According to the RENAL scoring system, each parameter takes a score of one to three according to the anatomy of the tumor and is reported as the total score. According to total scores, patients with an RENAL nephrometry score of four-six are considered as in low complexity group, patients with a score of seven-nine are considered as in medium complexity group and patients with a score of 10—12 are considered as in high-complexity group.[4] According to the PADUA scoring system, renal tumors score between six and 14 in relation to their anatomical location and are considered to be six-seven as low, eight-nine as intermediate and >10 as higher complexity.[5] The C-index scoring system has a calculation method different from other scoring systems. The C-index measures the ratio of the tumor size and the distance between the center of the kidney to the center of the renal mass. Complexity of renal masses are deemed low if the C-index is greater than 2.5, and high if the C-index is lower than 2.5[6]

2.3. Evaluation

Preoperative demographic data, estimated glomerular filtration rate (e-GFR) and hematocrit (Hct) changes, operation time, tumor volume and hospitalization time from patients were evaluated separately and statistically for each of the three scoring systems. For the change in Hct level, the difference between the baseline Hct level in preoperative period and the postoperative first day level was used; while for e-GFR change, the difference between the preoperative value and the value calculated according to the nadir level of serum creatinine (cr) at postoperative 3rd or 4th month was calculated. The e-GFR mean value was calculated according to glomerular filtration rate-modification of diet in renal disease (GFR-MDRD). Tumor volume was determined for all patients using ellipsoid volume calculation (Ellipsoidvolume $=$ L x W x H x $\pi/6$).

Complications were classified intraoperatively and postoperatively, and modified Clavien-Dindo system was used to grade these complications.

2.4. Surgical technique

All operations were performed with retroperitoneal approach at dorsal lithotomy position and under general anesthesia. The surgeons created a cleavage between the tumor and the renal parenchyma with a sharp and blunt dissection combination, and then suppressed the area of the demarcation line with the fingers of the hand (renal squeeze). While small intrarenal vessels were controlled by electrocautery, large vessels were controlled with pediatric hemostats and tied with four-zero polyglycolic suture (Vicryl®). After removing the specimen, bleeding vessels are over sewn with a four-zero polyglycolic suture (Vicryl®). Margins are evaluated by frozen section. If frozen sections are positive, deeper resection is performed.

3. Statistical analysis

Statistical analysis of the study was conducted in the R 3.1.2 package program. The descriptive statistics of the continuous variables included in the study are shown as mean, standard deviation, median, minimum and maximum values, and categorical variables as frequency and percentage. Normal distribution of continuous variables was analyzed by Shapiro Wilk test. ANOVA was used for 3 and more group comparisons of normal distribution variables, and independent sample t test was used for two group comparisons. Also, Mann Whitney U test was used to compare two groups of variables with no normal distribution and Kruskal–Wallis test was used in 3 and more group comparisons. Bonferroni corrected Mann Whitney U test was used for the comparison of the two subgroups in meaningful variables. Pearson and Yates chi-square tests were used to compare categorical variables between groups. Relations between continuous variables were examined by Spearman correlation analysis. Comparisons below 0.05 were considered statistically significant in all statistical analyzes in the study.

4. Results

Our study consisted of 132 patients with a mean age of 53.9 $\pm$ 13.9 with 69 male and 63 female. The mean body mass index (BMI) was calculated as 25.4 $\pm$ 3.25 (20.1–36.1) kg/m^2 and the mean tumor volume as 37.1 $\pm$ 34.8 mm^3. When the patients were evaluated according to the tumor stages, 65 patients were classified as T1a, 63 patients as T1b and four patients as T2. Statistically significant difference between mean tumor volume values were found in RENAL and PADUA groups ($p < 0.005$). Moreover, statistically significant difference between the risk groups in RENAL and PADUA scoring were found ($p < 0.005$) according to tumor T stage. Mean body mass index (BMI), gender and tumor laterality results were not statistically different between the groups. The results of comparing the preoperative data of the patients are shown in Table 1.

When the operative and postoperative results of our patients were assessed on the basis of risk groups, it was found that as RENAL and PADUA scores increased statistically as well as the duration of operation and hospitalization also increased statistically **($p<0.001$)**. Among the risk groups of RENAL and PADUA scoring systems, a statistically significant difference was found between mean hematocrit change and transfusion rates **($p<0.05$)**. Statistically significant difference was only found between risk groups of RENAL scoring system in e-GFR reduction **($p<0.05$)**. After postoperative pathological examination, the most common diagnosis was clear cell carcinoma (62.8%) and no statistically significant difference was found in the comparison of histopathologic results between all three groups. The operative and postoperative results of the disease and the results of the pathological diagnosis are shown in Table 2.

When the patients were evaluated, complications were detected in a total of 16 patients (12.2%). When these complications were analyzed according to Clavien-Dindo system, grade IVa was observed in two patients, grade IIIb in four patients, grade II in one patient and grade I complication in nine patients. Two patients with grade IVa complication are solitary kidney patients requiring dialysis in the postoperative period. One of these patients was taken to the dialysis program due to chronic kidney disease and the other patient's level of creatinine remained constant at a level that did not require dialysis. The patient who was evaluated as chronic renal failure after the surgery has unfavorable factors such as age, diabetes, hypertension, elevated operation time and solitary kidney. These factors might be explain the Clavian 4a complication. Of the grade IIIb patients, one had pleural injuries, one had vena cava inferior injuries, and two had collector system opened. These patients were intervened intraoperatively and no additional surgery was performed. There was no statistically significant difference between the groups in the complications of all three classification systems **($p > 0.005$)**. Statistical analysis of postoperative complications according to subgroups is shown in Table 2.

There were two patients with positive surgical margins, one of them had recurrent tumor and had radical nephrectomy. The remaining patient is still under follow-up. None of our patients had died during follow-ups. The median follow-up time of the patients was 24 months.

When the duration of hospitalization, duration of operation, changes in Hct and e-GFR were assessed according to the Spearman correlation test, while it was determined that RENAL and PADUA results correlated positively with all values, positive correlation with C-index was found Hct and e-GFR variation rates (Table 3).

5. Discussion

The PN is an organ preservative oncological surgical modality. Equivalent to oncologic targets such as surgical margin negativity and disease-free survival; the aim of protecting the renal functions at the highest level is the main element of this treatment. The extent to which the postoperative renal function is preserved relative to the preoperative level varies depending on many factors. One of the most important of these factors, the warm ischemia time (WIT) has been an important controversy since PN was first made. Indeed, increase in every one minute in prolonged WIT had a 5% and 6% risk of developing acute renal

Table 1 Demographics and clinical data.

	RENAL			*P*	PADUA			*P*	C-İndex		*P*
	Low (n:82)	Med (n:37)	High (n:13)		Low (n:63)	Med (n:46)	High (n:23)		Low (n:70)	High (n:62)	
Age (year)	53,22 ± 13,95	56,49 ± 14,18	51,08 ± 12,99	0,362[c]	51,76 ± 12,63	55,89 ± 15,13	55,91 ± 14,54	0,235[c]	52,96 ± 13,84	55,02 ± 14,05	0,399[c]
BMI (kg/m^2)	25,45 ± 3,37	25,70 ± 3,02	24,82 ± 3,30	0,816[c]	25,65 ± 3,36	25,23 ± 3,13	25,40 ± 3,31	0,807[c]	25,60 ± 3,25	25,30 ± 3,26	0,600[c]
Tumor vol (mm3)	19.8	30.6	110.2	<**0,001**[a]	15.7	30.2	77.9	<**0,001**[a]	24.1	28.9	0,804[a]
Sex:											
Man	47 (%57,3)	16 (%43,2)	6 (%46,2)	0,326[b]	36 (%57,1)	22 (%47,8)	11 (%47,8)	0,564[b]	40 (%57,1)	29 (%46,8)	0,234[b]
Woman	35 (%42,7)	21 (%56,8)	7 (%53,8)		27 (%42,9)	24 (%52,2)	12 (%52,2)		30 (%42,9)	33 (%53,2)	
Grade:											
T1A	50 (%62,5)	15 (%41,7)	0 (%0)	<**0,001**[b]	44 (%71,0)	18 (%42,9)	2 (%9,1)	<**0,001**[b]	35 (%52,2)	29 (%49,2)	0,730[b]
T1B	30 (%37,5)	21 (%58,3)	13 (%100)		18 (%29,0)	24 (%57,1)	20 (%90,9)		32 (%47,8)	30 (%50,8)	
Laterality:											
Right	42 (%51,2)	20 (%54,1)	6 (%46,2)	0,883[b]	34 (%54,0)	23 (%50,0)	11 (%47,8)	0,852[b]	33 (%47,1)	35 (%56,5)	0,286[b]
Left	40 (%48,8)	17 (%45,9)	7 (%53,8)		29 (%46,0)	23 (%50,0)	12 (%52,2)		37 (%52,9)	27 (%43,5)	

$p < 0.05$ is considered to be statistically significant.
[a] Kruskal Wallis test.
[b] Pearson Chi-square test.
[c] Mann Whitney U.

Table 2 The comparison of preoperative and postoperative results of the patients according to scoring systems.

	RENAL			*P*	PADUA			*P*	C-İndex		*P*
	Low (n:82)	Med (n:37)	High (n:13)		Low (n:63)	Med (n:46)	High (n:23)		Low (n:70)	High (n:62)	
Tumor vol (mm3)	19.8	30.6	110.2	<**0,001**[a]	15.7	30.2	77.9	<**0,001**[a]	24.1	28.9	0,804[a]
Operation time (min)	148,43 ± 31,10	163,27 ± 23,55	206,85 ± 17,19	<**0,001**[a]	145,86 ± 29,54	159,46 ± 28,90	190,30 ± 27,23	<**0,001**[a]	159,44 ± 35,04	157,10 ± 30,43	0,765[a]
Hct decrease	4,34 ± 3,00	5,42 ± 3,03	6,99 ± 2,48	**0,005**[a]	4,38 ± 2,62	4,84 ± 3,16	6,48 ± 3,55	**0,022**[a]	5,35 ± 2,61	4,40 ± 3,46	0,052[a]
e-GFR decrease	6,45 ± 5,16	6,78 ± 4,56	11,66 ± 4,23	**0,002**[a]	6,22 ± 5,03	7,15 ± 4,93	9,14 ± 5,31	**0,054**[a]	7,34 ± 5,15	6,73 ± 5,10	0,394[a]
Hospitalisation (day)	4,76 ± 1,48	5,57 ± 1,43	6,31 ± 1,55	**0,001**[a]	4,54 ± 1,55	5,50 ± 1,11	6,04 ± 1,69	<**0,001**[a]	5,23 ± 1,50	5,03 ± 1,62	0,542[a]
Transfusion (unit)	0,28 ± 0,60	0,30 ± 0,57	1,08 ± 1,12	**0,004**[a]	0,19 ± 0,47	0,35 ± 0,64	0,87 ± 1,01	**0,001**[a]	0,40 ± 0,77	0,32 ± 0,59	0,858[a]
Complication											
No	73 (%89,0)	33 (%89,2)	10 (%76,9)	0,444[b]	58 (%92,1)	38 (%82,6)	20 (%87,0)	0,324[b]	60 (%85,7)	56 (%90,3)	0,588[b]
Yes	9 (%11,0)	4 (%10,8)	3 (%23,1)		5 (%7,9)	8 (%17,4)	3 (%13,0)		10 (%14,3)	6 (%9,7)	

$p < 0.05$ is considered to be statistically significant.
[+]Mann Whitney U.
[a] Kruskal Wallis test.
[b] Pearson Chi-square test.

Table 3 Spearman correlation index.

	Hosp.	Operation time	Hct decrease	e-GFR decrease
RENAL	r = 0,341	r = 0,402	r = 0,229	r = 0,220
	p < 0,001	p < 0,001	p = 0,008	p = 0,011
C-Index	r = 0,055	r = −0,079	r = 0,173	r = 0,243
	p = 0,531	p = 0,369	p = 0,047	p = 0,005
PADUA	r = 0,417	r = 0,468	r = 0,233	r = 0,243
	p < 0,001	p < 0,001	p = 0,007	p = 0,005

failure and following chronic kidney failure, respectively, reported by Thompson et al in their study of 362 PN in the solitary kidney.[10] In PN, concerns about the effect of warm ischemia-related renal functions on short and long term ischemic damage have recently brought the off-clamp PN technique into question.

Off-clamp PN is usually applied to small-sized and exophytic tumors in the urological literatüre.[11] When this perspective is considered, it can be said that these tumors are in a low risk group according to the scoring systems currently used to evaluate the complexity of the kidney masses. Not surprisingly, off-clamp PN is a difficult surgical procedure because of the disadvantages such as the negative surgical margin due to the tumor bed bleeding and the difficulty of effective renal repair. Shah et al reported that 61% of the off-clamp PN series that they applied laparoscopically had exophytic or lateral lesions, average RENAL nephrometry score was reported as 6.7, and mean tumor diameter was reported as 3.0 cm.[7] In a similar study, Rosen et al found that after their robotic off-clamp PN studies; RENAL nephrometry score was reported as 6, exophytic mass ratio> 50% over was reported as 45.7% and mean tumor size was reported as 2.7 cm.[12] In our study, we evaluated our patients according to three renal scoring systems; RENAL, PADUA, C-index scores were calculated as 6.1, 7.9 and 2.3 respectively. 23.6% of the tumors were in the middle and 13.7% were in the upper pole. When assessed according to the risk score, the high-risk tumor ratios in the RENAL, PADUA and C-index scoring systems were 9.9%, 17.4% and 47%, respectively. These data are generally similar when compared with the off-clamp PN series in the literature.

To date, more than 10 different anatomic nephrometry scores have been published and the majority of scoring aims to predict general complications with surgical complexity.[13] The main disadvantage of these scorings is the presence and use of various scores that limit the transfer and reproducibility of the findings.[14] Although some of the scores are not very popular due to their complexity or inaccuracy, the presence of a few scoring systems that have already proven to perform well in the measurement of the tumor complex has led to a difficult choice of urologists.[13,15] The 4 scoring system reported by Kriegmair et alindicated that although RENAL, PADUA and NePhRO scoring systems were more useful than the C-index scoring system, the four scoring system reported successful prediction of tumor complexity and surgical outcome.[16] According to our observation, our study is the first to evaluate tumor complexity and surgical outcomes in patients who underwent off-clamp PN. In our study, a statistically significant difference was found between the tumor volume, operation time, postoperative transfusion rate, duration of hospitalization, decreased hematocrit and reduction of e-GFR levels between the low, medium and high risk groups according to the RENAL scoring system. In the PADUA scoring system, there was a statistically significant difference between the groups in terms of tumor volume, duration of operation, postoperative transfusion rate, duration of hospitalization and hematocrit reduction. However, no statistical difference was found between the groups in the C-Index. In this context, all three scoring sytem successfully predicted the surgical complexity ve surgical outcomes however, in our study the RENAL scoring system predicted eGFR alteration more successfully than the other scoring systems.

There is a continuing debate in the literature as to whether partial nephrectomy should be done with or without ischemia, especially in appropriate cases. Shah et al found no statistically significant difference in e-GFR between the ischemic and non-ischemic groups in their long-term outcome study of patients with laparoscopic partial nephrectomy. However, it has been stated that the contralateral normal kidney may be caused by the compensatory effect.[7] In this sense, the studies in the solitary kidney model are obviously only able to reflect changes in renal function. Data from Wszolek et al suggested the superiority of the off-clamp group in preserving postoperative renal functions in solitary renal patients and reported that PN should be performed in these patients, if possible, without vascular clamping.[17] In our study, the decrease amount in e-GFR in RENAL, PADUA and C-Index scoring groups was considerably lower compared to the series of ischemic PN series in the literatüre.[16,18] Indeed, even in high-risk groups of RENAL, PADUA and C-Index scoring systems, the amount of reduction in e-GFR is 11.66 ± 4.23, 9.14 ± 5,31, and 6.73 ± 5.10 mL/min/1.73 m^2, respectively, compared with those with ischemia. The patients classified with C-Index had better e-GFR outcome however, the comparison of within C-Index groups shown insignificant difference. In addition, the correlation analyses of the C-Index scoring system shown weak correlation with Spearman correlation index analysis.

In the meta-analysis performed by Trehan et al although there was no statistically significant difference in the duration of operation, tumor size, estimated blood loss, transfusion rate, general and urological complications between ischemic and non-ischemic PN groups, statistically significant superiority of non-ischemic PN was reported in terms of preservation of renal function.[19] Simmons et al reported that in 301 PN-series patients with ischemia, the overall intraoperative complication rate was 3% and the postoperative complication rate was 9%.[20] Borgman et al reported a mean operation time of 194 ± 62 min in the open PN series with ischemia,[21] whereas in our series the mean operation time was calculated as 157.5 ± 29.1 min. It is plausible that this difference is caused by the renal pedicle dissection without wasting time as done by Ficarra et al in the application of non-ischemic renal squeeze technique.[5] In our study, the overall intraoperative and postoperative complication rate was found to be 12.2% and the complication rate was found to be similar to other studies in the literatüre.[20,21] Under this circumstance it can be suggested

that, the acceptable complication rate of off-clamp PN in terms of protection of renal function can be performed in all renal tumors with low morbidity.

We think that our study is valuable because current renal scoring systems are the first to be compared in the off-clamp PN series, despite the retrospective design, limited number of patients and the absence of long-term follow-up.

5. Conclusion

In our study, all three scoring sytem successfully predicted the surgical complexity ve surgical outcomes and our results indicate that off-clamp PN has similar success and complications rates when compared to the literature. The off-clamp PN must be kept in mind to maintain postoperative renal functions eligible patients.

Ethics

Ethics committee approval was obtained.

Financial disclosures

N/A.

Competing interests

The authors declare no competing financial or personal interests.

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