Comparison of clinical outcomes by clamping modalities during robotic-assisted laparoscopic partial nephrectomy

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Comparison of clinical outcomes by clamping modalities during robotic-assisted laparoscopic partial nephrectomy

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<TABLE OF CONTENTS>

LIST OF TABLES

ABSTRACT

Comparison of clinical outcomes by clamping modalities during robotic-assisted laparoscopic partial nephrectomy

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Purpose

To evaluate perioperative and functional outcomes of robotic-assisted laparoscopic partial nephrectomy (RAPN) with different clamping techniques and compare effectiveness relative to main artery clamped RAPN.

Patients and Method

Patients were retrospectively analyzed from 2006 to 2016 in patients undergoing robotic-assisted laparoscopic partial nephrectomy at Severance Hospital. The peri-operative data of patients without impaired renal function undergoing RAPN performed with different clamping techniques were retrospectively analyzed (group 1: off-clamp, n = 57; group 2: selective clamp, n = 58; group 3: main artery clamp, n = 158). We performed logistic regression analysis to identify possible factors that could affect the occurrence of acute kidney injury (AKI). Multivariate linear regression analysis was performed to find the factors related to the amount of change in postoperative estimated glomerular filtration rate (eGFR). Additionally, propensity score matching analysis was performed to reduce the selection bias.

Results

A total of 273 patients were enrolled in the study, who had eGFR> 60 and had two normal kidneys. Baseline characteristics were not significantly different among the groups. The off-clamp group tumors were smaller and less complex than the other two groups(1.9cm vs. 3.15cm vs. 3.35cm, p = <0.001). Postoperative complication rates among the three groups were not significantly different. Also, the rates of positive surgical margin, recurrence, and mortality were not significantly different. The incidence of postoperative AKI was higher in the MAC group than in the off-clamp group or SAC group(7.0% vs. 12.0% vs. 24.7%, p=<0.005). Compared to MAC group, off-clamp group and SAC group had lower eGFR changes in 3 months postoperatively. In logistic regression analysis, tumor complexity and clamping methods were predictive of AKI. In linear regression analysis, age, preoperative eGFR, tumor size, EBL, and persistent AKI were significantly associated with eGFR change after 3 years postoperatively. In the propensity score-matched groups, the off-clamp group compared to the MAC group, the incidence of transient AKI and persistent AKI was significantly lower (p=0.009, p=0.022). After matching the SAC group and the MAC group, the persistent AKI was lower in the SAC group (3.6 vs. 14.5%, p = 0.048).

Conclusion

Our study findings show no difference in Oncological outcome, complication rates or long-term renal functional outcomes among the groups. However, off-clamp and SAC techniques showed a lower incidence of AKI, including persistent AKI, than MAC. Also, since persistent AKI may be strongly associated with long-term renal function changes, further studies are needed to investigate its impact.

Key words : renal cell cancer, robotic-assisted partial nephrectomy, clamping technique

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I. INTRODUCTION

Over the past 30 years, the incidence of incidental small renal mass has considerably increased. For the treatment of clinical T1 renal masses, the current guidelines recommend partial nephrectomy.[1] Partial nephrectomy can preserve renal function compared to radical nephrectomy, providing equivalent effective cancer control for T1 tumor. Furthermore, considerable efforts have been made to improve partial nephrectomy techniques for securing both oncological and functional outcomes. The ischemic time caused by clamping of renal artery during tumor excision and renorrhaphy, part of partial nephrectomy, is one of the modifiable factors that affect functional outcomes. In particular, a prolonged ischemic time has been found to be associated with a functional decline in the kidneys[2], potentially leading to irreversible and significant renal injury.

During renal mass excision and reconstruction of the renal parenchyma, renal artery clamping was considered necessary to obtain the operation field. Main artery clamping (MAC) is a technique of inducing ischemia of the entire kidney, providing a possibility of a long-term decrease in renal function after surgery.

The renal function after partial nephrectomy with ischemic time within 25 minutes caused reversible and transient renal dysfunction, but occasionally progressed to

CKD.[3-6] The ischemic injury can lead to the risk of losing renal function to the patients with solitary kidney and those with CKD of Grade 3 or higher.[7,8]

To attend to these concerns, novel techniques have been devised to minimize or eliminate renal ischemia during partial nephrectomy. Among those techniques, the off-clamp technique is used to excise the tumor without clamping to eliminate the ischemia and to seal the resection site.[9] It is mainly applied to the exophytic mass.[10] Additionally, the selective artery clamp (SAC) technique is applied to the mass of the hilar region by clamping only the branch of the renal artery to minimize ischemia around a renal mass.[11,12] However, the results of the studies comparing these techniques and functional outcomes of MACs remain controversial.[10,12-14] Recently, in view of the recovery of renal function after partial nephrectomy, urological literature has also become more interested in postoperative acute kidney injury (AKI). Recent retrospective studies reported the importance of AKI as a predictor of long-term renal function after partial nephrectomy.[5,15-17]

In this context, the purpose of the present study was to perform a retrospective comparison of the patients who had undergone robotic-assisted laparoscopic partial nephrectomy (RAPN) performed using the off-clamp, selective artery clamp, and main artery clamp techniques with the focus on comparing their oncological and functional outcomes. Our second aim was to find predictors of postoperative AKI and factors that predict long-term renal function.

II. MATERIALS AND METHODS

1. Patient population & Characteristics

A prospectively maintained institutional review board-approved database was used to identify 299 patients from a tertiary institute who had undergone RAPN by a single, expert surgeon (K.H.R), in a tertiary institute between 2006 and 2016. Three groups were arranged according to the clamping method of renal vessel used during the tumor excision: the off-clamp, the selective artery clamp, and the main artery clamp groups. Clamp technique was chosen based on the surgeon's preference and clinical judgment. The inclusion criteria were the availability of clinical data for over 12 months after surgery and resection of a single renal mass with normal kidney. The patients with baseline estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73/m^2 (n = 18), or conversion to radical nephrectomy (n = 8) were excluded from the analysis. Perioperative and postoperative outcomes, including the operative complications, the operative time and warm ischemic time, the length of hospital stay (LOS), the estimated blood loss (EBL), and eGFR were analyzed and compared among the three groups. Tumor complexity was assessed using the R.E.N.A.L (Radius; Exophytic / Endophytic; Nearness: Anterior / Posterior Location) scoring system.[18] Tumour complexity was stratified as low (RENAL score 6–7), intermediate (RENAL score 8–9), or high (RENAL score ≥ 10). Surgical specimens were examined by two expert uropathologists in a standard form. The serum creatinine levels were routinely measured at every postoperative follow-up. The eGFR was calculated using the following Chronic Kidney Disease Epidemiology Collaboration equation: 141 × minimum (creatinine/ κ , 1)α × maximum (creatinine/ κ , 1)-1.209× 0.993age× 1.018 (if female) × 1.159 (if black), where κ is 0.7 for women and 0.9 for men, and α is − 0.329 for women and − 0.411 for men.[19] The percentage change in eGFR was calculated according to the following formula : 100 x [(Preoperative eGFR -

Postoperative eGFR) / Preoperative eGFR]. Acute kidney injury(AKI) was defined as a change in preoperative GFR > 25% within 72 hrs after surgery, or stage 1 of the Risk, Injury, Failure, Loss of Kidney Function, and End-stage Kidney Disease (RIFLE) criteria.[17] Transient AKI was defined as AKI resolved within 3 days after surgery.[17] Persistent AKI was defined as AKI lasting longer than 3 days after surgery. All complications were categorized according to the Clavien–Dindo classification.

2. Surgical Technique

The MAC technique was typically performed and the renal artery was clamped using a standard bulldog clamp after dissection. For the off-clamp technique, clamping of the renal artery was not performed during tumor excision and renorrhaphy. Only the tumor feeding branch of the renal artery found by preoperative imaging was identified and skeletonized, the selected artery clamping was applied.[11,20] In order to clarify the devascularization of only the tumor and the margin, either robotic near-infrared imaging after intravenous administration of indigo-cyanine green or color Doppler ultrasonography was used.

3. Statistical analyses

Demographic and peri-operative data were analyzed using descriptive statistics. Frequencies were expressed as percentages and continuous data were presented as median and interquartile ranges (IQR). Differences among the three groups were compared either by using the non-parametric Kruskal-Wallis H test and the Mann-Whitney test for continuous variables or the chi-squared test for categorical variables. For all statistical analyses, a two-sided p-value < 0.05 was considered to indicate statistical significance. Logistic regression was used for univariate and multivariate analysis for predictive factors for AKI. Multivariate linear regression analysis was used to identify relevant factors for postoperative eGFR changes. All

analyses were performed using SPSS statistical package 23 (SPSS Inc., Chicago, IL, USA). The off-clamp technique and the SAC technique were applied to selected patients. The propensity score matching analysis was performed to reduce the selection bias for comparison with the MAC technique. The nearest-neighbor 1-to-1 propensity score matching was performed using the MatchIt package of R version 3.1.3. The MAC group versus the SAC group and the MAC group versus the off-clamp group were propensity-score-matched on age, gender, body mass index (BMI), preoperative eGFR, clinical tumor size, and R.E.N.A.L. score.

III. RESULTS

1. Patient characteristics

A total of 273 patients with eGFR> 60 and two normal kidneys were enrolled in the study. The patients were divided into the off-clamp group (n = 57), the SAC group (n = 58), and the MAC group (n = 158) according to the artery clamping method during RAPN. In the baseline characteristics, age, BMI, and laterality, no significant differences among the groups were observed. The American Society of Anesthesiologists (ASA) class showed significant differences between the off-clamp group and the MAC group (p = 0.01) and between the SAC group and the MAC group (p = 0.34). However, no differences among the groups in the patients with ASA class 3 or higher were observed (p = 0.053). The off-clamp group had a smaller and lower complexity as compared to the other two groups, and there were no differences between the SAC group and the MAC group. The off-clamp group had a higher rate of exophytic mass and a lower ratio of malignancy. No significant differences between the SAC group and the MAC group were found. With regard to tumor characteristics, there was no difference between the SAC group and the MAC group, but the off-clamp group had a higher proportion of exophytic mass.

2. Perioperative outcome

Preoperative and postoperative results, operative time, EBL, and LOS were significantly different among the groups (Table 2). The off-clamp group and the SAC groups had a shorter operative time than the MAC group. No significant difference in EBL between the SAC group and the MAC group was observed, and the off-clamp group had a lower EBL as compared to the other two groups. The median clamp time of the MAC group was 27 min and that of the SAC group was 19.5 min. Clavien-Dindo postoperative complications of the three groups were not significantly different. Finally, the positive surgical margin, recurrence, and

mortality rates were not significantly different in the three groups. In the median follow-up period, the MAC group was the longest among the three groups.

3. Renal function outcome

The results of preoperative and postoperative renal function and postoperative AKI incidence are shown in Table 3. Preoperative serum creatinine was lower in the off-clamp group than in the other two groups; however, no significant differences in eGFR among the three groups were found. But, the incidence of postoperative AKI was higher in the MAC group than in the off-clamp group and the SAC group. The incidence of transient AKI and persistent AKI was also higher in the MAC group, but there was no statistically significant difference between the SAC group and the MAC group in persistent AKI. The postoperative eGFR was significantly higher in the off-clamp group than in the MAC group until 1 year postoperatively, and the SAC group was significantly higher up to 6 months postoperatively. The percent change eGFR after surgery was lower in the off-clamp and SAC groups until 3 months after surgery.

Table 1. Patient and tumor characteristics

Variable	Group 1: Off-clamp	Group 2: Selective artery clamp	Group 3: Main artery clamp	P value (Group 2 vs. 3)
Patients, no	57	58	158	
Median (Range) age, years	53 (44-61)	50 (43-59)	51 (44-59)	0.627(0.569)
Sex: female (%) / male (%)	28 (49.1) / 29 (50.9)	17 (29.3%) / 41(70.7)	59 (37.3) / 99 (62.7)	0.088(0.274)
Median (Range) BMI, kg/m^2	24.2 (22.05-26.37)	24.9 (22.3-27.2)	24.4 (22.5-26.6)	0.414 (0.381)
ASA class, n (%)				0.002 (0.034)
1	21 (36.8)	24 (41.4)	98 (62.0)	
2	28 (49.1)	33 (56.9)	47 (29.7)	
3	8 (14.0)	1 (1.7)	13 (8.2)	
Tumor sides: Left (%) / Right (%)	25 (43.9) / 32(56.1)	32 (55.2) / 26 (44.8)	80 (50.6) / 78 (49.4)	0.473 (0.555)
Median (range) tumor size, cm				
Clinical	1.9 (1.4-2.6)	3.15 (2.3-4.1)	3.35 (2.0-4.9)	<0.001(0.679)
Pathological	1.6 (1.3-2.5)	3.1 (2.1-4.0)	3.0 (1.9-4.2)	<0.001(0.824)
Median (range) tumor complexity score				<0.001(0.170)
Low	34 (59.6)	18 (31.0)	46 (29.1)	
Intermidiate	21 (36.8)	33 (56.9)	71 (44.9)	
High	2 (3.4)	7 (12.1)	41 (25.9)	
Tumor characteristic, n (%)				<0.001(0.148)
Endophytic	2 (3.5)	10 (17.2)	39 (24.7)	
Mesophytic	22 (38.6)	28 (48.3)	83 (52.5)	
Exophytic	33 (57.9)	20 (34.5)	36 (22.8)	
Pathological T stage, n (%)				0.013(0.126)
pT1a	38 (95.2)	41 (80.4)	96 (73.8)	
pT1b	2 (4.8)	10 (19.6)	28 (21.5)	
pT2a	0 (0)	0 (0)	4 (3.1)	
pT2b	0 (0)	0 (0)	2 (1.5)	
Malignant / Benign, n (%)	40 (70.2) / 17 (29.8)	51 (87.9) / 7 (12.1)	130 (82.3) / 28 (17.7)	0.043(0.319)

BMI = Body Mass Index; ASA = American Society of Anesthesiologists; R.E.N.A.L = radius,exophytic/endophytic properties, nearness of deepest tumor portion to collecting system or sinus, anterior/posterior and location relative to polar line score

Table 2. Perioperative and postoperative outcomes

Variable	Group 1: Off-clamp	Group 2: Selective artery clamp	Group 3: Main artery clamp	P value (Group 2 vs. 3)
Median (range) operating time, min	110 (95-150)	139 (102-175)	171 (134-206)	<0.001 (<0.001)
Median (range) EBL,ml	150 (100-300)	350 (150-550)	250 (100-500)	0.011 (0.247)
Median (range) clamp time, min	0	19.5 (17.0-23.0)	27.0 (20.0-32.0)	
Median (range) preoperative hemoglobin, g/dL	13.2 (12.3-14.5)	13.7 (12.6-15.0)	13.3 (12.3-14.8)	0.449 (0.230)
Median (range) postoperative hemoglobin, g/dL	12.2 (11.4-13.5)	12.5 (11.7-13.5)	12.2 (11.3-13.5)	0.239 (0.088)
Peri-operative transfusion, n (%)	1 (1.8)	2 (3.4)	6 (3.8)	0.767 (0.887)
Postoperative complications, n (%)				0.424 (0.871)
Clavien-Dindo I - II	5 (8.8)	9 (13.7)	26 (16.4)	
Clavien-Dindo III - V	2 (3.5)	3 (5.2)	6 (3.8)	
Positive surgical margin, n (%)	2 (5.0)	4 (7.8)	12 (9.2)	0.564 (0.887)
Median (Range) LOS, days	3 (3-5)	4 (3-6)	4 (3-6)	0.007 (0.683)
Recurrence, n (%)	0	1 (1.7)	8 (5.1)	0.140 (0.278)
Mortality, n (%)	0	0	5 (3.2)	0.158 (0.171)
Median (IQR) follow-up period, months	30.1 (13.5-52.4)	34.3 (19.6-50.7)	60.0 (30.4-79.2)	

EBL = Esitimated Blood Loss; LOS = length of hospital stay

Table 3. Renal function, acute kidney injury grade, and recovery from ischemia

Variable	Group 1: Off-clamp	Group 2: Selective artery clamp	Group 3: Main artery clamp	P value (group 2 vs. 3)
Preoperative SCr	0.73 (0.65-0.95)	0.88 (0.69-1.0)	0.87 (0.73-1.0)	0.028 (0.754)
Preoperative eGFR	97.7 (90.6-107.1)	99.0 (82.2-107.0)	92.8 (83.9-102.1)	0.099 (0.130)
Incidence of AKI				<0.001 (0.02)
No. AKI (%)				
RIFLE criteria				
Grade 0 (no AKI)	49 (86.0)	44 (75.9)	92 (58.2)	
Grade 1	4 (7.0)	11 (18.9)	63 (40.0)	
Grade 2	0	0	2 (1.3)	
Grade 3	0	0	1 (0.6)	
Transient AKI (%)	4 (7.0)	7 (12.0)	39 (24.7)	0.005 (0.045)
Perisistent AKI (%)	0	4 (6.9)	27 (17.0)	0.001 (0.059)
Postoperative eGFR				
1day	98.1 (82.2-106.5)	89.9 (71.7-104.2)	71.9 (62.2-87.3)	<0.001(<0.001)
3days	100.1(92.8-114.8)	99.4(85.3-111.3)	81.2(67.5-95.7)	<0.001(<0.001)
7days	96.3 (74.7-107.6)	89.0 (78.1-105.5)	74.9 (62.0-92.6)	<0.001(<0.001)
1month	92.6 (77.0-101.6)	92.9 (79.0-103.5)	79.2 (67.2-94.9)	<0.001 (0.001)
3months	92.2 (81.9-100.3)	91.5 (78.5-104.9)	80.8 (72.0-95.8)	0.003 (0.004)
6months	91.7 (73.4-101.7)	89.2 (76.6-100.9)	80.7 (70.8-91.8)	0.015 (0.033)
12months	93.1 (84.3-102.1)	90.3 (79.3-101.2)	85.8 (72.8-99.5)	0.045 (0.101)
24months	91.3 (81.4-97.5)	88.3 (76.6-102.3)	88.0 (76.5-96.8)	0.584 (0.630)
36months	89.3 (80.4-98.8)	90.7 (76.8-101.3)	90.8 (80.9-97.9)	0.834 (0.912)
Postoperative % Change eGFR,				
1day	0.0 (0-5.4)	6.0 (0-20.6)	21.5 (10.5-31.2)	<0.001(<0.001)
3days	0.0 (0-0.6)	0.0 (0-5.9)	10.9 (1.2-22.1)	<0.001(<0.001)
7days	2.2 (0-11.4)	4.0 (0-14.3)	18.2 (5.1-26.1)	<0.001(<0.001)
1month	4.2 (0-11.4)	1.3 (0-10.9)	11.5 (2.5-23.8)	<0.001(<0.001)
3months	4.7 (0-10.8)	2.4 (0-11.6)	8.7 (0.9-18.0)	0.008 (0.017)
6months	5.9 (2.6-10.1)	3.4 (0-15.3)	12.2 (0.7-20.6)	0.069 (0.072)
12months	3.5 (1.1-10.1)	6.6 (1.2-13.2)	6.4 (0-19.9)	0.411 (0.726)
24months	7.1 (1.7-10.9)	5.0 (0-14.4)	5.4 (0-15.0)	0.940 (0.863)
36months	4.5 (0.3-10.7)	6.0 (0-11.9)	3.1 (0-10.6)	0.608 (0.362)

SCr = Serum Creatinine; eGFR = estimated Glomerular Filtration Rate; AKI = Acute Kidney Injury; RIFLE criteria= Risk, Injury, Failure, Loss of Kidney Function, and End-stage Kidney Disease(RIFLE) criteria.

4. Logistic regression analysis of AKI

To identify possible factors that could affect the incidence of AKI, univariate and multivariate logistic regression analyses were performed (Table 4). In univariate logistic regression analysis, the incidence of AKI was associated with tumor size (OR 1.366, $p < 0.001$), tumor complexity (OR 2.434, $p < 0.001$), the use of off-clamp technique (OR 0.116, $p < 0.001$) and selective artery clamping technique (OR 0.359, $p = 0.006$), operation time (OR 1.007, $p = 0.001$), and EBL (OR 1.001, $p = 0.027$). In multivariate models based on the same variables, tumor complexity (OR 1.63, $p = 0.041$), off-clamp method (OR 0.184, $p = 0.003$), and selective artery clamp method (OR 0.402, $p = 0.02$) were independent predictors of AKI.

5. Multivariate Linear regression analysis of the change of eGFR

Multivariate linear regression analysis was performed to find the factors related to the amount of change in postoperative eGFR (Table 5). Age (β 0.231, $p = 0.001$), preoperative eGFR (β 0.190, $p = 0.001$), transient AKI (β 6.702, $p = 0.001$), and persistent AKI (β 14.373, $p = 0.001$) were associated at 6 months postoperatively. At 36 months postoperatively, age (β 0.225, $p = 0.003$), preoperative eGFR (β 0.212, $p = 0.001$), tumor size (β 1.351, $p = 0.013$), EBL (β 0.005, $p = 0.04$), and persistent AKI (β 6.448, $p = 0.017$) were significantly associated with the eGFR changes.

Table 4. Logistic regression analysis of Acute Kidney Injury

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.001	0.979-1.023	0.935	1.011	0.981-1.043	0.460
BMI	1.026	0.952-1.105	0.506	1.034	0.945-1.131	0.468
ASA score	0.758	0.494-1.164	0.205	0.761	0.459-1.263	0.291
Preoperative eGFR	0.996	0.979-1.013	0.616	1.010	0.986-1.034	0.440
Tumor size	1.366	1.168-1.597	<0.001	1.123	0.927-1.362	0.236
R.E.N.A.L. Complexity	2.434	1.641-3.609	<0.001	1.630	1.021-2.603	0.041
Surgical approach			<0.001			0.002
Main artery clamp	Ref.			Ref.		
Off-clamp	0.116	0.040-0.336	<0.001	0.184	0.059-0.568	0.003
Selective artery clamp	0.359	0.173-0.744	0.006	0.402	0.187-0.866	0.020
Operative time	1.007	1.003-1.011	0.001	1.004	1.000-1.008	0.070
EBL	1.001	1.000-1.001	0.027	1.000	0.999-1.001	0.501

BMI = Body Mass Index; ASA = American Society of Anesthesiologists; eGFR = estimated Glomerular Fillteration Rate; R.E.N.A.L = radius,exophytic/endophytic properties, nearness of deepest tumor portion to collecting system or sinus, anterior/posterior and location relative to polar line score; EBL = Estimated Blood Loss

Table 5. Multivariate Linear regression analysis on predictive factors for eGFR change on postoperative 6 months and 3 years after surgery.

	Postop. 6moths			Postop. 36months		
	β	95% CI	P value	β	95% CI	P value
Age	0.231	0.123,0.335	0.001	0.225	0.078,0.360	0.003
BMI	0.315	-0.224,0.783	0.239	-0.350	-0.750,0.062	0.090
ASA score	1.530	-0.987,4.511	0.261	0.416	-2.583,3.378	0.791
Preoperative eGFR	0.190	0.098,0.274	0.001	0.212	0.123,0.307	0.001
Tumor size	0.149	-0.775,0.972	0.723	1.351	0.076,2.293	0.013
R.E.N.A.L. Complexity	0.394	-1.756,2.469	0.690	1.037	-0.627,2.851	0.241
Surgical approach						
Main artery clamp	Ref.			Ref.		
Off-clamp	-2.512	-6.442,1.146	0.197	2.691	-1.911,6.409	0.193
Selective artery clamp	-0.961	-4.670,2.689	0.602	1.601	-2.521,5.182	0.429
Operative time	0.010	-0.12,0.031	0.353	-0.007	-0.028,0.016	0.491
EBL	-0.001	-0.004,0.002	0.540	0.005	0.001,0.011	0.040
Transient AKI	6.702	3.419,10.321	0.001	0.843	-2.427,4.207	0.609
Persistent AKI	14.373	9.766,19.065	0.001	6.448	1.203,11.559	0.017

BMI = Body Mass Index; ASA = American Society of Anesthesiologists; eGFR = estimated Glomerular Fillteration Rate; R.E.N.A.L = radius,exophytic/endophytic properties, nearness of deepest tumor portion to collecting system or sinus, anterior/posterior and location relative to polar line score; EBL = Estimated Blood Loss; AKI = Acute Kidney Injury

6. Propensity score matching – Off-clamp group vs. MAC group

After matching the off-clamp group and the MAC group, the following factors that were significantly different before matching were no longer such: ASA class (p = 0.462), tumor size (2.0 vs 2.3 cm; p = 0.106), characteristics (p = 0.533), and complexity (p = 0.928) (Table 6). In the propensity score-matched groups, the off-clamp group compared to the MAC group, the incidence of transient AKI and persistent AKI was significantly lower (Table 7). The percentage of change in eGFR was significantly lower up to 3 months postoperatively (4.8% vs. 13.1%, p < 0.001), and postoperative eGFR was statistically significant up to 7 days postoperatively.

Table 6. Patient and tumor characteristics after propensity score matching (Off-clamp group vs. MAC group)

Characteristic	Group 1: Off-clamp	Group 3: main artery clamp	P value
Patients, no	45	45	
Age, years	55 (46-61)	50 (47-61)	0.625
Sex: female (%) / male (%)	24 (53.3) / 21 (46.7)	20 (44.4) / 25 (55.6)	0.402
Median (Range) BMI, kg/m^2	24.0 (22.1-26.2)	23.9 (22.6-26.3)	0.654
ASA class, n (%)			0.462
1	19 (42.2)	23 (51.1)	
2	22 (48.9)	18 (40.0)	
3	4 (8.9)	4 (8.9)	
Tumor sides: Left (%) / Right (%)	18 (40) / 27 (60)	23 (51.1) / 22 (48.9)	0.293
Median (range) tumor size, cm			
Clinical	2.0 (1.5-2.8)	2.3 (1.9-3.0)	0.106
Pathological	1.6 (1.5-2.5)	2.2 (1.7-3.2)	0.083
Median (range) tumor complexity score			0.928
Low	20 (44.4)	20 (44.4)	
Intermidiate	18 (40.0)	19 (42.2)	
High	7 (15.6)	6 (13.3)	
Tumor characteristic, n (%)			0.533
Endophytic	21 (46.7)	20 (44.4)	
Mesophytic	22 (48.9)	19 (42.2)	
Exophytic	12 (26.7)	12 (26.7)	
Malignant, n (%)	33 (73.3)	33 (73.3)	>0.99
Warm ischemic time, min	-	23.0 (18.0-32.0)	
Median (range) operating time, min	110 (95-150)	167 (148-243)	<0.01
Median (range) EBL,ml	150 (100-500)	250 (200-500)	0.113
Postoperative complications, n (%)			0.183
Clavien-Dindo I - II	4 (8.8)	9 (20.0)	
Clavien-Dindo III - V	1 (2.2)	1 (2.2)	
Positive surgical margin, n (%)	2 (6.7)	1 (3.0)	0.559
Median (Range) LOS, days	3 (3-4)	4 (3-6)	0.09

BMI = Body Mass Index; ASA = American Society of Anesthesiologists; R.E.N.A.L = radius,exophytic/endophytic properties, nearness of deepest tumor portion to collecting system or sinus, anterior/posterior and location relative to polar line score; EBL = Esitimated Blood Loss; LOS = length of hospital stay

Table 7. Renal function, acute kidney injury grade, and recovery from ischemia after propensity-score matching (Off-clamp group vs. MAC group)

Variable	Group 1: Off-clamp	Group 3: main artery clamp	P value
Preoperative SCr	0.73 (0.65-0.97)	0.87 (0.70-0.97)	0.260
Preoperative eGFR	97.4 (84.0-104.4)	91.0 (84.3-103.0)	0.521
No. AKI (%)			<0.001
RIFLE criteria			
Grade 0 (no AKI)	41 (91.1)	26 (64.4)	
Grade 1	4 (8.9)	15 (33.3)	
Grade 2	0	1 (2.2)	
Grade 3	0	0	
Transient AKI (%)	4 (8.9)	11 (24.4)	0.009
Perisistent AKI (%)	0	5 (11.1)	0.022
Postoperative eGFR			
1day	97.1 (79.5-105)	79.4 (64-89.2)	<0.001
3days	99.1 (93.7-113.5)	85.5 (73.8-99.4)	<0.001
7days	96.3 (67-107.5)	77.8 (61.5-95.1)	0.025
1month	92.0 (77-101.4)	80.5 (66.4-95.3)	0.089
3months	91.8 (79.8-100.3)	81.1 (72.3-100)	0.194
6months	91.7 (73.4-101.4)	77.6 (68.3-97.8)	0.141
12months	93.1 (83.4-102.1)	84.5 (66.1-105)	0.196
24months	91.1 (80.1-98.5)	88.0 (76.5-99.5)	0.595
36months	87.5 (78.6-98.8)	90.3 (79.8-97.2)	0.555
Postoperative % Change eGFR			
1day	0 (0-6)	16.7 (4.4-29.5)	<0.001
3days	0 (0-0.7)	6.8 (0-20.8)	<0.001
7days	1.7 (0-7.3)	12.7 (4.1-28.9)	<0.001
1month	4.6 (0-11.7)	16.9 (1-27.7)	0.025
3months	4.8 (0-10.7)	13.1 (2.6-19.5)	<0.001
6months	6.1 (2.6-10.2)	15.7 (0-27.3)	0.106
12months	3.4 (1.1-10.2)	7.7 (0-28)	0.333
24months	6.3 (1.2-10.6)	4.2 (0-16)	0.678
36months	4.6 (0.3-10.8)	2.9 (0-9.3)	0.651

SCr = Serum Creatinine; eGFR = estimated Glomerular Filtration Rate; AKI = Acute Kidney Injury; RIFLE criteria= Risk, Injury, Failure, Loss of Kidney Function, and End-stage Kidney Disease(RIFLE) criteria.

7. Propensity score matching – SAC group vs. MAC group

No significant differences in age, BMI, tumor size, tumor complexity, and tumor characteristics including ASA class after propensity score matching of the MAC group and SAC clamp group were observed (Table 8). However, the SAC group had a shorter postoperative time (134min vs. 160min, p = 0.009) and a significantly higher EBL (300 ml vs. 200 ml, p = 0.015). The postoperative complication, PSM rates, and LOS were not significantly different between the two groups. The rates of AKI and transient AKI between the two groups were not different (Table 9), but the persistent AKI was lower in the SAC group (3.6% vs. 14.5%, p = 0.048). In addition, the SAC group showed a higher postoperative eGFR and a lower percentage of eGFR change by 1 month.

Table 8. Patient and tumor characteristics after propensity score matching (SAC group vs. MAC group)

Characteristic	Group 2: selective artery clamp	Group 3: main artery clamp	P value
Patients, no	55	55	
Age, years	52 (43-59)	50 (44-62)	0.813
Sex: female (%) / male (%)	16 (29.1) / 39 (70.9)	22 (40.0) / 33 (60.0)	0.231
Median (Range) BMI, kg/m^2	24.9 (22.4-27.3)	24.4 (22.8-26.9)	0.876
ASA class, n (%)			0.209
1	24 (43.6)	32 (58.2)	
2	30 (54.5)	20 (36.4)	
3	1 (1.8)	3 (5.5)	
Tumor sides: Left (%) / Right (%)	32 (58.2) / 23 (41.8)	26 (47.3) / 29 (52.7)	0.254
Median (range) tumor size, cm			
Clinical	3.2 (2.2-4.2)	3.0 (2.0-4.0)	0.309
Pathological	3.1 (2.1-4.0)	2.7 (1.8-3.7)	0.142
Median (range) tumor complexity score			0.433
Low	15 (27.3)	19 (34.5)	
Intermidiate	33 (60.0)	30 (54.5)	
High	7 (15.6)	6 (10.9)	
Tumor characteristic, n (%)			0.747
Endophytic	17 (30.9)	14 (25.5)	
Mesophytic	28 (50.9)	32 (58.2)	
Exophytic	10 (18.2)	9 (16.4)	
Malignant, n (%)	49 (89.1)	46 (83.6)	0.407
Warm ischemic time, min	-	25.0 (18.0-32.0)	
Median (range) operating time, min	134 (100-175)	160 (123-193)	0.009
Median (range) EBL,ml	300 (150-600)	200 (100-400)	0.015
Postoperative complications, n (%)			0.512
Clavien-Dindo I - II	7 (12.7)	9 (16.4)	
Clavien-Dindo III - V	2 (3.6)	3 (5.5)	
Positive surgical margin, n (%)	4 (8.2)	3 (6.5)	0.697
Median (Range) LOS, days	4 (3-6)	4 (3-6)	0.688

BMI = Body Mass Index; ASA = American Society of Anesthesiologists; R.E.N.A.L = radius,exophytic/endophytic properties, nearness of deepest tumor portion to collecting system or sinus, anterior/posterior and location relative to polar line score; EBL = Esitimated Blood Loss; LOS = length of hospital stay

Table 9. Renal function, acute kidney injury grade, and recovery from ischemia after propensity-score matching (SAC clamp group vs. MAC group)

Variable	Group 2: selective artery clamp	Group 3: main artery clamp	P value
Preoperative SCr	0.89 (0.69-1.0)	0.84 (0.70-1.01)	0.888
Preoperative eGFR	98.9 (82.2-106.8)	93.1 (85.5-104.3)	0.339
No. AKI (%)			0.074
RIFLE criteria			
Grade 0 (no AKI)	46 (83.6)	38 (69.1)	
Grade 1	9 (16.3)	17 (30.9)	
Grade 2	0	0	
Grade 3	0	0	
Transient AKI (%)	7 (12.7)	9 (16.4)	0.59
Perisistent AKI (%)	2 (3.6)	8 (14.5)	0.048
Postoperative eGFR			
1day	88.0 (71.6-103.4)	74.4 (61.6-86.1)	<0.001
3days	99.0 (83.8-111)	86.4 (63.4-98.3)	<0.001
7days	87.6 (77.1-104.8)	77.1 (60.7-91.3)	<0.001
1month	92.9 (78-102.8)	83.5 (66-96)	0.026
3months	91.5 (77.1-102.8)	87.0 (72.1-98)	0.099
6months	90.6 (76.1-101.2)	85.3 (70.3-91.8)	0.166
12months	88.8 (78.1-100.3)	85.7 (74.1-98.7)	0.400
24months	87.7 (76.2-101.6)	88.3 (75.8-100.2)	0.880
36months	90.7 (76.8-101.3)	92.6 (80.2-98.6)	0.966
Postoperative % Change eGFR			
1day	9.5 (0-20.7)	19.2 (10.8-31.3)	<0.001
3days	0 (0-6.5)	8.1 (0.3-21.9)	<0.001
7days	5.0 (0-15.1)	18.3 (6.3-27.4)	<0.001
1month	1.8 (0-12.7)	11.2 (2.1-24.6)	<0.001
3months	2.9 (0-12.5)	8.6 (1.6-14.2)	0.145
6months	3.4 (0-18)	10.1 (1.4-16.9)	0.303
12months	6.6 (2.2-13.4)	6.4 (0-15.7)	0.694
24months	6 (0-15.6)	4.2 (0-11.4)	0.305
36months	6.1 (0-12)	3.7 (0-8.3)	0.301

SCr = Serum Creatinine; eGFR = estimated Glomerular Filtration Rate; AKI = Acute Kidney Injury; RIFLE criteria= Risk, Injury, Failure, Loss of Kidney Function, and End-stage Kidney Disease (RIFLE) criteria.

IV. DISCUSSION

In the present study, the off-clamp group and the SAC group showed no significant differences as compared to the MAC group in the oncological outcome and complication rate. In the functional results, the off-clamp group and the SAC group had higher eGFR until 3 months after surgery. But there was no significant difference in results beyond 6 months compared with MAC group. These results are consistent with the findings of previous studies where patients who underwent the off-clamp or SAC technique have an oncological outcome equivalent to those who underwent the MAC technique.[9,10,12-14] Despite the renal function advantages of short-term follow up, the advantages of SAC and off-clamp compared to MAC did not find significance for longer than 6 months.

In a study comparing off-clamp RAPN and clamped RAPN, Kaczmarek et al. reported that, in the off-clamp group, a smaller decline in eGFR within 6 months after surgery, a shorter operative time, and a higher EBL were observed.[10] Barrett reported that the off-clamp group did not differ significantly from the eGFR within 9 months after surgery as compared to the clamped group.[14] Operative time and EBL are more favorable in the off-clamp group. However, since due to the short follow-up period, previous findings on the off-clamp group and the MAC group are not sufficient to clearly show the benefit of the off-clamp technique in evaluating the renal function.

In our study, operative time was shorter in the off-clamp technique, and postoperative GFR was consistent with these results. Additionally, we performed analysis of AKI and showed that transient AKI and persistent AKI were significantly lower in patients who underwent RAPN using the off-clamp technique. The off-clamp technique could save time by avoiding delicate dissection of the hilar region. EBL was not different between off-clamp group and MAC group after propensity score matching. this tendency is present in the recently reported studies.[14,21]

The SAC technique, also known as the zero ischemia technique, theoretically makes ischemia only around the tumor site to prevent ischemic injury. However, the results of studies showing that the functional outcomes of the SAC technique do not differ significantly from the MAC technique have been reported, so the usefulness of the SAC technique in two-kidney patients is controversial.[13,22] These different results may have affected various definitions of AKI, disease populations and clinical settings among studies.

The MAC technique is the standard process of partial nephrectomy, most patients with two kidney and normal renal function who underwent RAPN using MAC technique due to T1a renal mass recovered to new baseline values after a few months after surgery. However, CKD progression in patients who underwent partial nephrectomy reported in 4-6% of the previous studies[23,24], and recent studies reported a rate of AKI of 10-30%[5,13,24,25]. AKI can be associated with increased morbidity and mortality and AKI may predispose to CKD.[17,26] Postoperative AKI in partial nephrectomy is mainly due to loss of parenchymal volume and ischemia. In this context, the analysis of an incidence of AKI according to the clamping technique, which is one of the modifiable factors affecting renal function after RAPN, has clinical significance.

Recently, studies on AKI after RAPN have been reported in urology literature. Paulucci et al. recently performed the propensity score matching analysis on the patients who had undergone the SAC technique and MAC technique. They did not find any difference by comparing the rates of AKI.[13] In their study, the median size of tumor sizes in the 76 patients in the SAC group was 2.5 (2.0-3.5) cm, while the R.E.N.A.L score was 7.0 (6.0-8.0). The rate of eGFR percent change was 14.6% (0.5-22.8) and 10.4% (1.7-21.1) at 4-24 months after the operation, respectively.

However, the rates of AKI in our study were lower in the Off-clamp group and the SAC group than in the MAC group. Particularly, the incidence of persistent AKI was lower in the off-clamp group and SAC group than in the MAC group after

propensity score matching. Compared to the results of previous studies, the patients included in the present study had a larger tumor size and a higher tumor complexity. Studies of renal function after partial nephrectomy have resulted in inconsistencies in the results because of the short follow-up period and the absence of large-scale studies. The discordance in incidence of AKI between our study and previous research could be due to the complexity of AKI, the recent studies about AKI in urologic literature provides important context to our findings.

Kaouk et al. conducted a marginal effect analysis of the interaction of AKI, warm ischemic time (WIT), and excisional volume loss (EVL) in 1162 patients who underwent RAPN.[8] Below the EVL of 3mm margin for a 50% exophytic 3.5cm^3 tumor (which equal to 5.5cm^3 of EVL), the effect of WIT on rates of AKI after PN is insignificant. Above the EVL of 9cm^3, less than 25 minutes of WIT may also impair early renal function after surgery. They reported that the tumor complexity influence to in the synergistic effect of WIT and EVL on AKI. As tumor complexity increases, the effect of EVL on the rate of possibility of AKI increases significantly.

We also found that renal ischemia due to renal artery clamping and tumor complexity are predictive factors of AKI. For instance, a larger tumor size and a higher tumor complexity can increase the incidence of AKI. In the present study, age, preoperative eGFR, tumor size, EBL, and AKI were identified as predictors of renal function after RAPN. Postoperative change in renal function was associated with both transient AKI and persistent AKI at 6 months postoperatively. In particular, persistent AKI was the strongest predictive factor of postoperative GFR change at 36 months postoperatively (β 6.448, $p = 0.017$). It is possible that persistent AKI reflects the damage that cannot be recovered in the short term. In our study, persistent AKI was a strong predictive factor for long-term renal function, and the off-clamp and SAC technique was able to lower the rate of persistent AKI compared to the MAC technique. These results support the

applicability of the two techniques, although the MAC technique should be considered in a standard way in patients with two kidneys.

It is still unclear about the recovery after renal ischemia and patients with high risk of renal function deterioration after partial nephrectomy. The advance in this question would make it clear to understand and apply the off-clamp and SAC techniques.

The limitation of our study is that our data do not reflect preserved renal volume after surgery. Also, since the clamping technique was chosen according to the surgeon's preference, the bias could have affected our outcome. To overcome these limitations, we performed multivariate regression analysis and propensity score matching. However, the interpretation of results is limited because we analyzed the patients with two normal renal functions. Therefore, to confirm the results of the present study, a randomized study involving more patients is needed. Also, rather than estimating kidney function using creatinine, a more accurate evaluation of renal function, such as MAG3 renal scan, is required in the future.

V. CONCLUSION

In the present study, we show that the off-clamp and SAC techniques for RAPN are feasible and comparable to the MAC techniques in terms of oncologic outcomes and perioperative complication rates. Functionally, confined to those with two intact kidneys and GFR>60, there was no difference of renal function assessed after one year of surgery in the three techniques. However, the off-clamp and SAC techniques provided significantly less chance of AKI, including persistent AKI, than the MAC technique. Furthermore, persistent AKI following partial nephrectomy may be strongly associated with long-term renal function changes, which could be further validated by a larger-scale study.

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ABSTRACT (IN KOREAN)

로봇 보조 복강경하 부분 신절제술의 결찰 방식에 따른 임상 결과 비교

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김명수

본 연구에서는 신장암의 로봇보조하 신장부분절제술 시 신동맥의 결찰 방식에 따른 수술 후 신기능의 변화, 종양학적 결과, 수술 합병증에 관한 분석을 수행하였다. 2006 년부터 2016 년까지 세브란스 병원에서 로봇 보조 복강경 부분 신절제술을 받았으며, 신기능의 이상이 없는 환자들을 후향적으로 분석했다(비결찰군: n = 57, 선택 결찰군: n = 58, 전체 결찰군, n = 158). 2개의 정상 신장을 가진 273명의 환자들이 연구에 등록되었다. 환자들의 인구학적 특성에서 그룹 간에는 유의한 차이는 없었다. 비결찰군은 다른 두 군 (1.9 vs 3.15 vs 3.35㎝, p = <0.001)에 비해 종양 크기가 작고 종양복잡도가 낮았다. 세 군의 술 후 합병증은 유의한 차이가 없었다. 종양절제면 양성율, 종양학적 재발 및 사망률이 양군간에 유의한 차이가 없었다. 수술 후 급성신부전의 발생률은 전체결찰군이 비결찰군과 선택결찰군에서 보다 더 높았다 (7 대 12.0 대 24.7 %, p = 0.005). 수술 후 eGFR의 감소는 비결찰군과 선택 결찰군에서 수술 후 3 개월까지 전체 결찰군에 비해 낮

았다. 로지스틱 회귀 분석에서 종양의 복잡성과 혈관 결찰 방법이 수술 후 급성신부전를 예측하는 인자였다. 수술 3년 후의 eGFR 변화에 대한 선형 회귀 분석에서 연령, 수술 전 eGFR, 종양 크기, 실혈양 및 지속적 급성신부전이 eGFR 변화와 유의 한 관련이 있었다. 성향 점수 매치를 시행한 후에, 전체 결찰군에 비해 비결찰군에서 일시적 급성신부전 및 지속적 급성신부전 발병률이 유의하게 낮았다 ($p = 0.009$, $p = 0.022$). 선택 결찰군과 전체 결찰군을 성향점수매치 한 후 분석하였을때, 지속적 급성신부전은 선택 결차군에서 더 낮았다 (3.6 vs 14.5 %, $p = 0.048$). 본 연구 결과는 각 결찰 방식에 따른 군 간의 종양학적 결과, 합병증 발생률에서 유의한 차이가 없음을 확인하였다. 수술 후 신장 기능 결과는 수술 1 년 후부터 세 군 간의 차이를 발견할 수 없었지만, 비결찰군과 선택 결찰군은 전체 결찰군보다 일시적 급성신부전과 지속적 급성신부전의 발병율이 유의하게 낮았다. 더불어, 본 연구에서 수술 후 3 일 이상 지속되는 급성신부전은 장기간의 신장 기능 변화와 밀접하게 연관되어있는 것으로 나타났으며, 그 영향을 조사하기 위해 더 큰 규모의 추가 연구가 필요하다.

핵심되는 말 : 신장암, 로봇 보조 부분 신절제술, 신동맥결찰