Laparoscopy and Robotics

Comparing Off-clamp and On-clamp Robot-assisted Partial Nephrectomy: A Prospective Randomized Trial

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OBJECTIVE	To determine whether performing robot-assisted partial nephrectomy without warm ischemia "off-clamp" results in favorable postoperative renal functional outcomes compared with the on-clamp method.
METHODS	We conducted a prospective trial of 80 patients who underwent robot-assisted partial nephrectomy. They were randomized in a 1:1 ratio to undergo the procedure with renal artery clamping or without clamping. The groups were compared across demographics, operative information, perioperative outcomes, and postoperative renal function. We assessed renal function by estimated glomerular filtration rate and renal scintigraphy both preoperatively and at 3 months postoperatively.
RESULTS	Patients in the on-clamp and off-clamp groups were similar in age, gender, body mass index, comorbidities, clinical tumor size, nephrometry score, and laterality. Off-clamp procedures were lengthier at an average 178.0 minutes vs 156.0 minutes for on-clamp (P = .011). Estimated blood loss, rates of pelvicalyceal repair, postoperative complications, and positive margins were not different. At a median 3-month follow-up, no significant differences were seen in change in postoperative estimated glomerular filtration rate or percent split renal function between both groups.
CONCLUSION	In this prospective study, off-clamp robot-assisted partial nephrectomy resulted in similar perioperative outcomes compared with the on-clamp technique. No benefit was demonstrated in the preservation of renal function. Urologists may safely employ either an on-clamp or off-clamp strategy depending on surgeon preference and patient-specific factors including baseline renal insufficiency, multiple masses, or solitary kidney. UROLOGY 126: 102−109, 2019. © 2019 Elsevier Inc.

Nephron-sparing surgery is a broadly accepted treatment strategy in the management of clinical T1 renal masses.[1] By preserving normal renal parenchyma, most surgeons view this approach as preferable to radical nephrectomy—particularly in patients with preexisting chronic kidney disease, multiple or bilateral renal masses, or a solitary kidney. Such patients are uniquely suited to undergo nephron preservation to avoid the development or worsening of renal insufficiency postoperatively, and patients with otherwise healthy kidneys also may stand to benefit given the implications that chronic kidney disease may have on overall morbidity and mortality.[2,3]

Robot-assisted partial nephrectomy (RAPN) allows for minimally invasive nephron sparing. As the availability of robotics expands, so, too, does the utilization of RAPN as a favored nephron-sparing procedure compared with open and laparoscopic partial nephrectomy.[4] Irrespective of approach, most surgeons perform partial nephrectomy under conditions of renal ischemia achieved by placing a temporary clamp on the renal artery prior to resection of the mass. This reduces bleeding from the adjacent renal parenchyma during resection thus improving visualization of the tumor margin, lowering intraoperative blood loss, and facilitating renorrhaphy. While ischemia affords these benefits, many studies suggest that warm ischemia, in particular, leads to short- and long-term impairment in renal function.[5,6] For this reason, strategies such as selective vascular or parenchymal clamping have been implemented to minimize the amount of normal renal parenchyma subjected to warm ischemia.[7-10] These induce a localized regional ischemia only to the area of interest during resection. Furthermore, the duration of warm ischemia time (WIT) is modifiable factor that influences postoperative renal function.[5,11,12] To this end, some surgeons endorse early unclamping in which the clamp is removed after the mass is excised but before or during renorrhaphy, or "on-demand" clamping such that a clamp is applied to

the renal artery only if significant bleeding is encountered during resection.[13,14] Indeed, reducing both the amount and duration of renal warm ischemia is an objective to which many surgeons adhere.

Several authors have investigated whether avoiding ischemia altogether permits one to perform a feasible and safe operation.[7,15-17] As we and others have reported, performing RAPN without any ischemia "off-clamp" is not only possible, it is a preferred approach by some surgeons who have observed lower estimated blood loss (EBL) and a favorable morbidity profile.[18] However, only a slight benefit to postoperative renal function was shown in one of our previous studies,[19] and we saw no significant benefit in 2 subsequent larger studies.[16,18] Those investigations were hindered by retrospection and imprecision by utilizing estimated glomerular filtration rates (eGFR). We hypothesize that off-clamp RAPN results in less renal functional loss compared with on-clamp and sought to more accurately compare postoperative renal function by incorporating pre- and postoperative renal scintigraphy in addition to eGFR.

MATERIALS AND METHODS

Patients
After Institutional Review Board approval, we performed a prospective randomized trial of patients who underwent RAPN by a single surgeon (RSF) at Washington University School of Medicine (St. Louis, MO) from 2013 to 2017. In total, 80 patients with a small renal mass were enrolled in the study via an informed consent process. Patients were offered inclusion into the study if they were 18 years of age or older and able to sign consent, had a Karnofsky Performance Status greater than or equal to 40, and had an organ-confined renal mass suspicious for malignancy and deemed amenable to RAPN by the surgeon. Patients were excluded if they were unwilling to participate or did not meet the inclusion criteria. Forty patients were randomized to the on-clamp group and 40 to the off-clamp group. The surgeon has extensive experience in robotic surgery and has performed more than 300 off-clamp RAPNs.

Surgical Technique
The off-clamp RAPN technique has been described previously.[17,18] Patients are placed in the standard flexed lateral decubitus position. Five trocars are placed; two 12 mm trocars are placed in the upper quadrant for the camera and assistant, and three 8 mm robotic trocars are placed for a 4-arm robotic setup. The subcostal robotic trocar is placed in the midclavicular line, and the lower quadrant trocars are placed in the anterior axillary line (DaVinci Si System, Intuitive Surgical Inc., Sunnyvale, CA). Dissection of the kidney and hilar vessels is performed similarly in the off-clamp and on-clamp scenarios. Intraoperative ultrasonography is used to delineate the tumor margins. The margin of resection is scored on the renal capsule with electrocautery maintaining a small margin of normal tissue. The resection is continued deeper by applying precise retraction of the tissues and application of electrosurgical energy to avoid charring and maintain a bloodless field. When bleeding is encountered, this can almost always be controlled by precise application of electrosurgical energy. The resection is completed by working circumferentially around the mass while gently lifting the mass away from the kidney and avoiding deep dissection in any one area. If brisk bleeding is encountered, additional strategies may be employed to assist with hemostasis. These include application of pressure using the ProGrasp, hemostatic agents such as Surgicel (Ethicon, Cincinnati, OH), or placement of a clamp on the main renal artery. In the majority of cases, hemostasis is maintained with electrosurgical energy alone, and these additional measures are not necessary.

The approach to on-clamp RAPN is conventional and employs the same positioning, trocar placement, and working instruments. The mass is similarly circumscribed with electrocautery with the aid of intraoperative ultrasonography. After clamping the main renal artery with a bulldog or the second ProGrasp, sharp excision of the mass is performed while maintaining a small margin around the mass. Intravenous mannitol is not administered prior to clamping.

Collecting system defects are closed with a running stitch of 2-0 V-Loc (Medtronic, Minneapolis, MN) into an inner-layer corticomedullary closure. The renal capsule is reapproximated using a sliding-clip technique with interrupted 0 Vicryl and Hem-o-lok clips (Teleflex Medical, Research Triangle Park, MC), secured in place by Lapra-Ty clips (Ethicon Endosurgery, Cincinnati, OH).[20]

Data Collection and Statistics
Data were collected prospectively in an electronic database. Parallel group design with a randomization allocation ratio of 1:1 to off-clamp RAPN (study treatment) and on-clamp RAPN was utilized. Randomization was performed using a computerized randomization program. The randomized technique was assigned to a study ID and placed in a sealed envelope. At the time of consent, the envelope with the associated study ID was assigned to the participant. At the time of surgery, the study coordinator opened the envelope and provided the randomized technique by telephone to the surgeon (RSF), as the study coordinator was not present in the operating room. The surgeon and other study staff were blinded to the randomization technique. Randomization occurred just prior to the start of resection of the renal mass. The resection was performed using the technique to which the patient was randomized. The on-clamp and off-clamp groups were compared across demographics, operative information, perioperative outcomes, and postoperative renal function. We assessed global renal function by eGFR and differential renal function by renal scintigraphy both preoperatively and at 3 months postoperatively. Estimated GFR was calculated using the Modification of Diet in Renal Disease formula. Mercaptoacetyltriglycine (MAG3) renal scintigraphy was performed and interpreted by nuclear medicine radiologists. Univariate comparisons were made between the off-clamp and on-clamp groups using the Wilcoxon rank-sum and chi-square tests for quantitative and qualitative data, respectively. Fisher's exact test was substituted for the chi-square test for contingency tables with a cell less than or equal to 5. Multivariable linear models were used to analyze the relationship between off-clamp treatment and percent change in differential renal function and eGFR controlling for potential confounding variables. Relationships were considered significant in circumstances of $P \leq .05$. All statistics were performed using R version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

A priori power analysis was performed based on a pilot set of data to determine a sufficient sample size to detect statistical differences in the change in eGFR between off-clamp and

Table 1. Patient and operative characteristics, preoperative and postoperative renal function by clamp status during RAPN

Variable	On-Clamp (n = 40)	Off-Clamp (n = 40)	P Value
Age in y, mean (SD)	59.4 (11.2)	56.6 (9.8)	.212
Gender, %			.104
Male	72.5	55.0	
Female	27.5	45.0	
BMI in kg/m^2, mean (SD)	31.6 (5.9)	32.4 (6.3)	.345
CCI, %			.203
CCI = 0	52.5	40.0	
CCI = 1	30.0	25.0	
CCI ≥ 2	17.5	35.0	
Clinical tumor size in cm, mean (SD)	3.1 (1.4)	2.9 (1.2)	.665
Nephrometry score, mean (SD)	7.3 (2.0)	6.8 (2.0)	.269
Laterality, %			.179
Left	40.0	55.0	
Right	60.0	45.0	
Operative time in minutes, mean (SD)	156.0 (40.6)	178.0 (44.4)	**.011**
Warm ischemia time in minutes, mean (SD)	19.1 (7.5)	0 (−)	**<.001**
Pelvicalyceal repair, %	57.5	52.5	.653
Estimated blood loss in mL, mean (SD)	178.5 (207.5)	184.1 (193.3)	.815
30-d complication rate, %	17.5	20.0	1.000
30-d major complication rate, %	7.5	5.0	1.000
Malignant pathology, %	80.0	82.5	.908
Positive margin rate, %	5.9	6.3	1.000
Preoperative eGFR in mL/min/1.73m^2, mean (SD)	92.0 (21.6)	85.8 (21.0)	.424
Postoperative eGFR in mL/min/1.73m^2, mean (SD)*	81.8 (19.3)	76.0 (23.3)	.643
Percent change in eGFR, mean (SD)*	−9.4 (14.8)	−10.7 (17.5)	.982
Preoperative % split renal function, mean (SD)[†]	49.4 (4.9)	47.9 (6.3)	.322
Postoperative % split renal function, mean (SD)[‡]	44.0 (8.3)	42.5 (7.7)	.226
Percent change in % split renal function, mean (SD)[‡]	−11.8 (13.0)	−11.2 (13.7)	.400

BMI, body mass index; CCI, Charlson co-morbidity index; eGFR, estimated glomerular filtration rate; SD, standard deviation.
* Missing 3 postoperative eGFR from the On-Clamp group and 6 from the Off-Clamp group.
[†] Missing 1 preoperative renal scan from the Off-Clamp group.
[‡] Missing 1 postoperative renal scan from the On-Clamp group and 7 from the Off-Clamp group.

on-clamp procedures. The true difference between the treatments was hypothesized to be 7.0 mL/min/1.73m^2 with a standard larger drop in postoperative eGFR for the on-clamp treatment (approximately equivalent to an 8.2% larger drop in percent change in eGFR) with standard deviation of 10.8. A sample size of 80 was determined to be sufficiently powered with estimated power of greater than 80%.

RESULTS

Table 1 shows the results of all 80 patients who underwent RAPN during the study period as treated. Incomplete data occurred in some patients for postoperative serum creatinine and/or renal scintigraphy, which precluded the determination of their individual postoperative changes in eGFR or differential renal function, respectively. Measurement of creatinine occurred from 2.0 months to 5.8 months postoperatively; 95% of measurements occurred between 2.3 months and 4.5 months postoperatively. Both the on-clamp and off-clamp cohorts were similar in age, gender, body mass index, comorbidities, clinical tumor size, R.E.N.A.L. nephrometry score,[21] and tumor laterality. One patient was moved from the on-clamp cohort to off-clamp due to a randomization error, and one patient was converted from off-clamp to on-clamp intraoperatively due to excessive bleeding during mass resection. An intention-to-treat analysis did not reveal any significant differences despite these changes (Table 2).

Off-clamp procedures tended to take longer (178.0 vs 156.0 minutes, P = .011). All positive margins occurred in malignant tumors—6 clear cell renal cell carcinoma and 1 papillary renal cell carcinoma. Within the follow-up period, no local recurrences were identified, one patient had radiographic evidence of bone and lung metastasis, and no patients underwent a completion nephrectomy.

No significant differences were observed in either major or minor complication rates between the 2 groups. In the on-clamp group, complications of Clavien grade III or higher included pseudoaneurysm (2 patients), fever (1 patient), postoperative bleeding requiring blood transfusion (1 patient), urinary retention requiring intervention (2 patients), wound dehiscence (1 patient), and sepsis (1 patient). In the off-clamp group, complications of Clavien grade III or higher included postoperative bleeding requiring blood transfusion and embolization (1 patient), and death secondary to acute pulmonary embolus on the first postoperative day (1 patient).

Mean preoperative eGFR was similar in both groups, and there was no observed difference in postoperative eGFR (P = .643), nor percent change in eGFR (P = .982). Moreover, percent split renal function of the operated kidney revealed no difference preoperatively (P = .322) or at 3 months postoperatively (P = .226) between the 2 groups (Table 1, Fig. 1). When controlling for potential confounding variables, no detectable difference was observed in percent change in eGFR nor percent change in split renal function (Table 3).

Table 2. Intention to treat: multivariate linear model estimating percent change in eGFR and split renal function

Variable	Estimate	95% CI - Lower	95% CI - Upper	P Value
Percent change in eGFR				
Intent: off clamp vs on-clamp	0.0%	−7.1%	7.1%	.991
Nephrometry score	−1.1%	−3.2%	1.0%	.308
Clinical tumor size (1 cm increase)	2.1%	−0.8%	5.1%	.157
Age	−0.7%	−1.0%	−0.4%	**<.001**
Male vs female	5.1%	−1.9%	12.2%	.150
BMI	0.1%	−0.4%	0.7%	.570
Pelvicalyceal repair	3.0%	−4.9%	10.9%	.453
Preoperative eGFR	−0.4%	−0.6%	−0.2%	**<.001**
Operative time (1 min increase)	−0.1%	−0.2%	0.0%	**.010**
CCI = 1 vs CCI = 0	4.1%	−3.5%	11.8%	.287
CCI = 2 vs CCI = 0	−4.1%	−12.4%	4.2%	.329
Percent change in split renal function				
Intent: off clamp vs on-clamp	1.6%	−4.9%	8.2%	.621
Nephrometry score	−2.3%	−4.2%	−0.5%	**.013**
Clinical tumor size (1 cm increase)	−1.8%	−4.6%	1.0%	.206
Age	0.3%	0.0%	0.6%	**.049**
Male vs female	0.8%	−5.8%	7.3%	.818
BMI	−0.1%	−0.6%	0.4%	.738
Pelvicalyceal repair	−0.8%	−7.5%	5.9%	.816
Preoperative eGFR	0.0%	−0.1%	0.2%	.585
Operative time (1 min increase)	0.0%	−0.1%	0.1%	.610
CCI = 1 vs CCI = 0	2.8%	−4.3%	9.9%	.439
CCI = 2 vs CCI = 0	−10.4%	−18.0%	−2.9%	**.008**

BMI, body mass index; CCI, Charlson comorbidity index; CI, confidence interval; eGFR, estimated glomerular filtration rate.
Bolded values indicate a significant relationship (P ≤.05).

As statistical significance was not achieved, a post-hoc power analysis was performed to update the priori power analysis baseline hypothesis and determine what might be a reasonably true difference in percent change in eGFR between the clamping techniques that the observed sample was not able to detect. The observed standard deviation was higher than hypothesized (14.7 vs 10.8). That, combined with 9 observations not providing usable eGFR results, led to a noticeable reduction of proposed power. However, the lack of statistical significance is primarily due to the fact that the observed difference in change in postoperative GFR between on-clamp and off-clamp was much less than hypothesized. On univariate analysis, off-clamp was observed to have a 1.3% larger drop in eGFR vs a hypothesized 8.2% smaller drop.

An examination of the confidence interval reveals that there is a 95% chance that the true difference in percent change in eGFR is anywhere between a 9.0% smaller drop in favor of the on-clamp technique to a 6.4% smaller drop in favor of the off-clamp technique provided the sample is truly representative of the population. When controlling for other patient and surgical factors in the multivariable model, these estimates change to 7.4% in favor of on-clamp to 7.1% in favor of off-clamp. Based on equivalence testing, we can be confident the true difference in percent change in eGFR does not exceed 10% in favor of either technique (P = .01).

COMMENT

Operative technique in RAPN is a matter of wide variability and debate. Strategies differ among surgeons with respect to the establishment of renal ischemia, resection, and renorrhaphy. These nuances have implications in postoperative outcomes and renal function. Furthermore, when considering the amount of preserved renal parenchyma,[22] R.E.N.A.L. nephrometry score,[23] WIT, and baseline renal function as other potential influences, studies that examine the preservation of renal function after RAPN are tasked with teasing out the relative importance of these variables.

The present study evaluates the role of zero ischemia via off-clamp RAPN in patients with similar baseline renal function and compares peri- and postoperative outcomes including global and differential renal function by eGFR and renal scintigraphy, respectively. To the best of our knowledge, we report the only prospective randomized trial that compares off-clamp to on-clamp RAPN to date. While we continue to observe acceptable morbidity with the off-clamp approach, this study joins others that have not demonstrated a meaningful advantage in preserving renal function in partial nephrectomy.[18,24,25] This observation lends credence to the notion that WIT of sufficiently short duration does not significantly impair renal function.[11,12] Our mean WIT of 19.0 minutes in on-clamp patients falls below suggested thresholds reported in the literature of about 25 minutes.[11] Still, others contend that WIT of any duration is harmful and should be minimized as much as possible, and we support this concept.[5,6,22]

Some retrospective studies report a statistical benefit to renal function using off-clamp RAPN, but they are limited by relatively small sample sizes, short-term follow-up, sole use of eGFR to measure renal function,[15,19,26] and variability in surgeon and technique across institutions.[15] A 14-study meta-analysis by Trehan that examined open
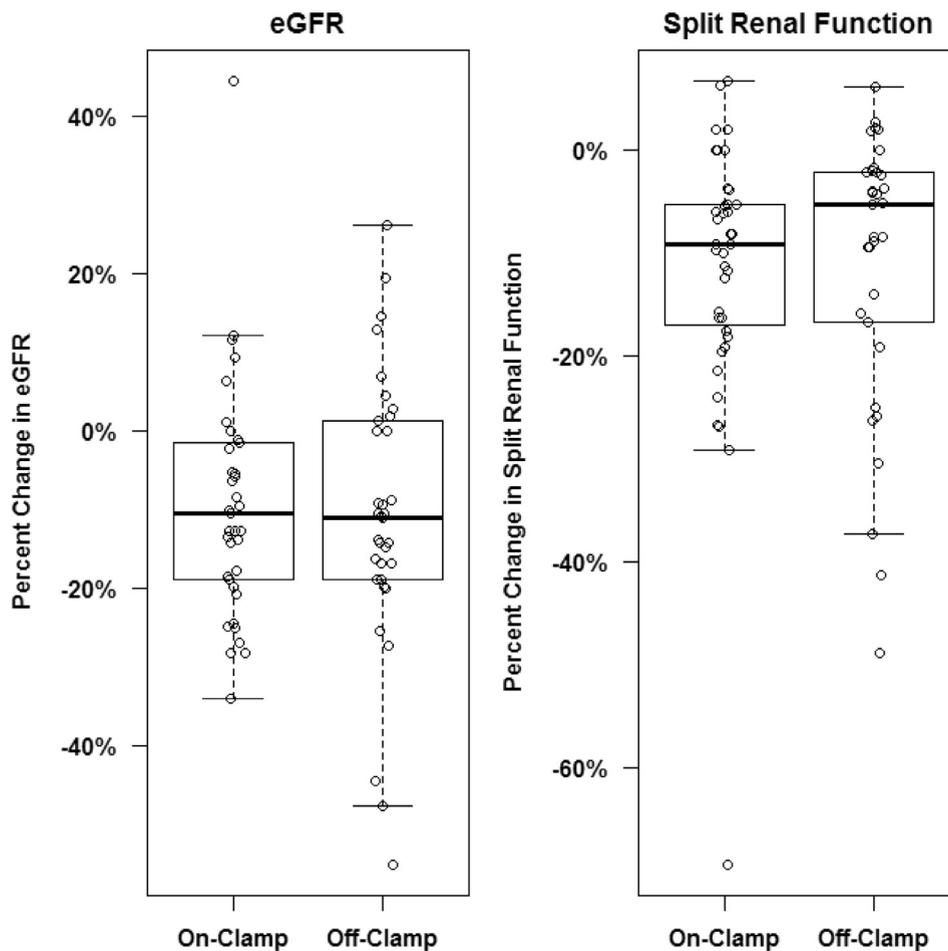
Figure 1. Percent change in eGFR and split renal function by clamp status during RAPN. eGFR, estimated glomerular filtration rate.

Table 3. Multivariate linear model estimating percent change in eGFR and split renal function

Variable	Estimate	95% CI - Lower	95% CI - Upper	P Value
Percent change in eGFR				
Off-clamp vs on-clamp	−0.2%	−7.4%	7.1%	.959
Nephrometry score	−1.1%	−3.2%	1.0%	.307
Clinical tumor size (1 cm increase)	2.1%	−0.9%	5.1%	.160
Age	−0.7%	−1.0%	−0.4%	**<.001**
Male vs female	5.1%	−2.0%	12.1%	.155
BMI	0.1%	−0.4%	0.7%	.569
Pelvicalyceal repair	3.0%	−4.9%	10.9%	.453
Preoperative eGFR	−0.4%	−0.6%	−0.2%	**<.001**
Operative time (1 min increase)	−0.1%	−0.2%	0.0%	**.010**
CCI = 1 vs CCI = 0	4.1%	−3.5%	11.7%	.288
CCI = 2 vs CCI = 0	−4.1%	−12.4%	4.3%	.333
Percent change in split renal function				
Off-clamp vs on-clamp	1.3%	−5.5%	8.0%	.709
Nephrometry score	−2.3%	−4.2%	−0.5%	**.014**
Clinical tumor size (1 cm increase)	−1.8%	−4.6%	1.0%	.199
Age	0.3%	0.0%	0.6%	**.049**
Male vs female	0.6%	−5.9%	7.2%	.845
BMI	−0.1%	−0.6%	0.4%	.721
Pelvicalyceal repair	−0.8%	−7.5%	6.0%	.822
Preoperative eGFR	0.0%	−0.1%	0.2%	.583
Operative time (1 min increase)	0.0%	−0.1%	0.1%	.565
CCI = 1 vs CCI = 0	2.7%	−4.4%	9.8%	.450
CCI = 2 vs CCI = 0	−10.6%	−18.2%	−2.9%	**.007**

BMI, body mass index; CCI, Charlson comorbidity index; CI, confidence interval; eGFR, estimated glomerular filtration rate.
Bolded values indicate a significant relationship ($P \le .05$).

and laparoscopic partial nephrectomy showed a trend toward increased EBL and transfusion rates with off-clamp RAPN, but a lower decrease in eGFR in these patients. They highlighted several limitations including short-term follow-up, lack of randomization, and selection bias (eg, patients in the off-clamp groups had smaller tumors).[27] We curtailed similar biases in our previous studies through propensity-score matching but concede that this is an imperfect solution.[18,19]

More recently, Simone et al performed a 52-paper literature review that included open and laparoscopic partial nephrectomy as well as off-clamp and selective ischemia techniques. They, too, noted an increase in EBL and transfusion rates associated with these strategies but underscored a lack of prospective randomized studies and short follow-up periods as limitations in the current literature. Their findings suggested that patients with lower renal function in which a prolonged ischemia time is anticipated may benefit most from off-clamp procedures.[28] As one of few studies that employed renal scintigraphy, Porpiglia et al performed a prospective nonrandomized trial that evaluated renal function in off-clamp and on-clamp laparoscopic partial nephrectomy patients in a consecutive series. They similarly found that those with the lowest baseline renal function appeared to have less functional loss from a zero-ischemia procedure.[29]

Some of our results contradict prior observations. We previously reported a shorter operative time and lower EBL in association with off-clamp RAPN; these findings were both encouraging and unforeseen.[18] The present study reports a longer operative time in the off-clamp group ($P = .011$), and no difference in EBL ($P = .815$). As mentioned earlier, many authors observe a higher EBL with off-clamp RAPN—an intuitive finding that speaks to the technical challenges associated with the approach.[15,25,26,28,30] Indeed, we reported a higher EBL earlier in the development of our technique.[19] Our longer operative time for off-clamp cases may be due to the meticulous dissection needed to maintain a dry operative field. Nevertheless, this finding also conflicts with one of our previous studies[18] and a multi-institutional analysis by Kaczmarek et al.[15]

Our current approach to RAPN considers each patient and renal mass similarly. We routinely start all resections off-clamp unless the unusual need arises to clamp the renal artery on-demand to aid hemostasis. This requires adequate dissection of the hilar vessels prior to starting the resection. While we observe favorable outcomes using this method, we accept that there is insufficient evidence that off-clamp RAPN provides any consequential benefit to renal function. Although the present study cannot claim such a benefit, if any benefit does exist, equivalence testing suggests that the difference in percent change in eGFR is likely less than 10% as stated previously. In the absence of any overwhelming potential functional advantage, we surmise that performing RAPN off-clamp is not an imperative but rather an optional approach. A surgeon may consider an off-clamp procedure based on their level of comfort with the technique or in specific cases in which clamping the renal artery may theoretically result in an increased risk of kidney injury (eg, solitary kidney or chronic kidney disease) or a prolonged clamp time (eg, multiple renal masses). In our experience, off-clamp RAPN is safe and reasonable for most patients.

This study has an inherent statistical advantage over retrospective analyses, but we acknowledge some limitations. First, while the precision of renal function assessment was improved by utilizing renal scintigraphy in addition to eGFR, a longer follow-up period would bolster the durability of our findings. Second, missing data prevented analysis in 9 patients; as discussed previously, this did not result in a significant alteration of the results. Third, maintaining a parenchymal margin during resection is but one way to perform RAPN, and inadvertent variations in this margin will influence the percentage of parenchymal loss. Estimated GFR and renal scintigraphy may not adequately address this issue, and specific calculations of preserved parenchyma may provide additional clarity. Moreover, maximizing preserved renal parenchyma by tumor enucleation may favor postoperative renal function; further studies should evaluate this and other facets of surgical approach including suturing and renorrhaphy technique. Last, we examined patients with 2 kidneys and normal renal function. As others have suggested, off-clamp RAPN may benefit those with a solitary kidney or baseline renal insufficiency more demonstrably.[28,29] Further studies that assess off-clamp RAPN in these patients are needed.

CONCLUSION

In patients with normal renal function, there is insufficient evidence to suggest that off-clamp RAPN results in less renal functional loss when compared with the on-clamp technique. Other perioperative outcomes are comparable.

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EDITORIAL COMMENT

In this interesting study, the authors report their results from an 80-patient prospective randomized controlled trial comparing perioperative outcomes in patients undergoing robot-assisted partial nephrectomy, either on-clamp with warm ischemia or off-clamp.[1] The authors should be commended on publishing the first prospective randomized controlled trial comparing on-clamp and off-clamp RAPN. The results of their study demonstrate no difference in perioperative outcomes including estimated blood loss, complications, or positive surgical margins between the different clamping techniques.[1] Additionally, there was no difference in postoperative renal function as measured by estimated glomerular filtration rate and renal scintigraphy at 3-month follow-up.[1] These results provide level-one evidence which contradicts previous reports demonstrating improved renal function with an off-clamp technique, and questions urologic dogma that short-warm ischemic time has a detrimental effect on the kidney and postoperative renal recovery.[2,3]

Nephron sparing surgery has become the mainstay of treatment for clinically staged T1 renal masses, which are amendable to this approach, given the superior outcomes in renal function compared with radical nephrectomy.[4] This is especially important when considering the implications of long-term cardiovascular and overall survival benefits that are associated with preventing chronic kidney disease.[5] However, the ideal operative technique for maximizing renal preservation in partial nephrectomy has yet to be determined and remains widely debated. The importance of preserving renal function is especially important for patients at higher risk of developing chronic kidney disease; such as those with baseline renal insufficiency, a solitary kidney, or multiple renal masses.[6,7] This subset of patients is likely to be most vulnerable to renal insults and thus benefit the most from an off-clamp technique. Unfortunately, only patients with 2 kidneys, normal preoperative renal function, and a solitary renal mass were included in the present study; this may explain why the authors failed to demonstrate a difference in postoperative renal function outcomes.

In addition, the patients in the on-clamp arm were only exposed to a short duration of warm ischemia (mean 19 minutes), which may minimize the difference in postoperative renal function observed. Furthermore, the authors only report on short-term renal function at 3 months postoperatively. It is likely that several factors including operative clamping technique may have an important impact on long-term renal function. The predictors of renal function outcomes following partial nephrectomy have been shown to be different in the early postoperative period compared with longer term follow-up.[8] The present study provides high-level evidence that performing a partial nephrectomy utilizing an off-clamp technique does not provide any measurable benefit in early postoperative renal outcomes. However, these results contradict some previously

published reports and challenge our understanding of the pathophysiological impact of renal ischemia.[2,3] Consequently, further well-designed prospective studies comparing clamping techniques, which include patients at high risk for postoperative renal insufficiency with longer term follow-up data, are required before a consensus regarding the ideal clamping technique can be reached.

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AUTHOR REPLY

Indeed, the benefit of performing nephron sparing surgery off-clamp remains controversial. The present findings are meaningful to the extent that, at least in the short term, the off-clamp approach does not appear to result in vastly superior renal functional preservation in most patients; surgeons who perform RAPN on-clamp clearly need not avoid doing so in reaction to this study. However, the findings should be considered in the context of the abovementioned limitations including a relatively short follow-up period and the enrollment of patients with normal baseline renal function. Furthermore, if warm ischemia times are minimized to the extent reported herein, the choice between on-clamp and off-clamp in terms of functional preservation may ultimately prove to be inconsequential. The path is clear for future prospective trials to further examine this potentially underutilized technique in patients more susceptible to renal functional loss.

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