



Impact of robotic partial nephrectomy with and without ischemia on renal functions: experience in 34 cases

İskemili ve iskemisiz robotik parsiyel nefrektominin renal fonksiyonlar üzerine etkisi: Otuz dört vakalık deneyim

Kemal Ener¹, Abdullah Erdem Canda², Serkan Altınova¹, Ali Fuat Atmaca², Erdal Alkan³, Erem Asil¹, Muhammet Fuat Özcan¹, Ziya Akbulut², Mevlana Derya Balbay³

ABSTRACT

Objective: In this study we aimed to compare renal functions in patients who underwent robotic partial nephrectomy (RPN) with on-clamp and zero- ischemia techniques.

Material and methods: Between 2009 and 2015, 12 off-clamp and 22 on-clamp RPN procedures were performed on a total of 34 patients in two centers. The main outcome parameters examined were serum creatinine, and estimated glomerular filtration rate (eGFR) during preoperative, immediate postoperative periods, and at postoperative 3rd months.

Results: There were no statistically significant differences between on-clamp and zero- ischemia groups regarding age, ASA score, BMI, PADUA and R.E.N.A.L. nephrometry scores, operation time and tumor size ($p>0.05$). Significant differences were found in the duration of hospital stay (3.8 ± 0.9 days vs. 3.0 ± 0.9 days) and amount of blood loss (85.9 ± 49.6 mL vs. 183.3 ± 176.2 mL) between the on-clamp and zero-ischemia groups ($p<0.05$). Statistically significant differences were found between preoperative and immediate post-operative periods, in terms of eGFR and serum creatinine levels in both groups. Moreover, statistically significant differences were found between preoperative and postoperative 3rd month periods, in the on-clamp group in terms of eGFR and serum creatinine levels. In the zero-ischemia group, the decrease in eGFR and serum creatinine levels at postoperative 3rd month relative to the preoperative period was not statistically significant.

Conclusion: Off-clamp RPN technique is superior, in short-term outcomes involving renal functions, compared to on clamp approach. However, long- term data regarding the renal functions should be evaluated to arrive at a definitive decision.

Keywords: Partial nephrectomy; renal cell carcinoma; robotic surgery; kidney function.

ÖZ

Amaç: Klempli ve sıfır-iskemi teknikleriyle robotik parsiyel nefrektomi (RPN) yapılan hastaların renal fonksiyonlarının karşılaştırılması amaçlanmıştır.

Gereç ve yöntemler: On iki hastaya klempsiz, 22 hastaya klempli olmak üzere, toplam 34 hastaya 2009-2015 yılları arasında RPN yapılmıştır. İncelenen ana parametreler, preoperatif, erken postoperatif ve postoperatif 3. aydaki serum kreatinin ve glomerüler filtrasyon oranı (eGFR) değerleridir.

Bulgular: Klempsiz ve sıfır iskemi grupları arasında, yaş, ASA skoru, vücut kitle indeksi (VKİ), PADUA ve R.E.N.A.L. nefrometri skorları, operasyon süresi ve tümör boyutu açısından istatistiksel olarak anlamlı bir fark bulunmamaktaydı ($p>0.05$). Hastanede kalış süresi ($3,8\pm0,9$ güne karşı $3,0\pm0,9$ gün) ve kanama miktarı ($85,9\pm49,6$ mL'e karşı $183,3\pm176,2$ mL) açısından klempsiz ve sıfır iskemi grupları arasında istatistiksel olarak anlamlı fark tespit edildi ($p<0,05$). Her iki grupta da preoperatif ve erken postoperatif dönemlerdeki eGFR ve serum kreatinin değerleri karşılaştırıldığında, istatistiksel açıdan anlamlı fark tespit edildi. Buna ilaveten, preoperatif ve 3. ay eGFR ve serum kreatinin değerleri karşılaştırıldığında, sadece klempli grupta bu değerlerde istatistiksel olarak anlamlı bir fark tespit edildi. Sıfır-iskemi grubunda ise, preoperatif döneme göre postoperatif 3. ayda gerçekleşen düşmenin istatistiksel olarak anlamlı olmadığı görüldü.

Sonuç: Klempsiz RPN tekniği klempli yöntemle göre kısa dönemdeki renal fonksiyonlar sonuçları açısından üstündür. Ancak, renal fonksiyonel sonuçlar yönünden kesin bir yargıya varmak için uzun dönem sonuçları değerlendirilmesi gerekmektedir.

Anahtar Kelimeler: Parsiyel nefrektomi; renal hücreli karsinom; robotik cerrahi; böbrek fonksiyonu

¹Clinic of Urology, Ankara Atatürk Training and Research Hospital, Ankara, Turkey

²Department of Urology, Yıldırım Beyazıt University School of Medicine, Ankara, Turkey

³Department of Urology, Memorial Şişli Hospital, İstanbul, Turkey

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Correspondence:
Kemal Ener
E-mail:
kemalener75@yahoo.com

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Introduction

Although the curative treatment of renal mass is radical nephrectomy (RN), partial nephrectomy (PN) has become the standard of care for tumors less than 4 cm in size.^[1] Equivalence of oncologic outcomes while superiority of functional outcomes of PN versus RN have been reported previously.^[2] However, with the era of minimally invasive approach in renal tumors, the relative inability to cool the kidney during tumor resection and renorrhaphy to reduce the ischemic injury, remains as a challenging issue.^[3] Several suggestions have been made in order to reduce the renal ischemic injury and preserve the renal function, including robotic surgery which may allow faster tumor resection and renorrhaphy, and selective application of PN without renal arterial clamping. After the introduction of the da Vinci robotic system (Intuitive Surgical, Sunnyvale, CA, USA), several reports showing the feasibility and safety of the procedure have been reported.^[4-10] The utilization of the robot in this field has facilitated the PN procedure, especially during the periods of renal parenchymal dissection, renorrhaphy and warm ischemia after the excision of the tumor.^[11] In this study, we present our experience with robotic partial nephrectomy (RPN) in 34 patients with (n=22) and without (n=12) renal arterial clamping, and evaluate the impact of these techniques on renal functions by analyzing estimated glomerular filtration rates (eGFRs).

Material and methods

This study was conducted in compliance with recognized international standards, including the principles of the Declaration of Helsinki involving Human Subjects, and each patient's consent for the use of their information was taken in writing. A total number of 34 patients underwent transperitoneal RPN transperitoneally, utilizing four-arm da Vinci-S robotic surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA) between 2009 and 2015. In order to determine the location and size of the mass, the patients were scanned with abdominal computed tomography (CT) or magnetic resonance imaging (MRI). R.E.N.A.L. nephrometry and PADUA scores of all patients were calculated by examining the CT and MRI scans.^[12,13] Intraoperative and perioperative (1-30 days) complications were evaluated with regard to the modified Clavien classification system.^[14] In addition, patients' age, gender, weight, body mass index (BMI), American Society of Anaesthesiology (ASA) score, radiologic tumor size, pathological tumor size, nuclear grade of the tumor according to Fuhrman grading system,^[15] and histological subtypes of the tumors in accordance with the classification of the World Health Organization^[16] were determined. Preoperative, immediate postoperative and postoperative 3rd month eGFRs of all patients were calculated using the Modification of Diet in Renal Disease (MDRD) formula.^[17]

Robotic partial nephrectomy procedures: All RPN procedures were performed transperitoneally, using the da Vinci surgical system (Intuitive Surgical, Sunnyvale, CA, USA) with patients placed in 60-degree flank position on the surgical bed. A 4-port or 5-port approach was performed including one port for robotic scope, 1 port for bedside assistant and 2 or 3 ports for robotic instruments. Pneumoperitoneum was maintained by CO₂ insufflation at 15 mmHg in all cases. During surgery, standard PN procedure was followed including mobilization of the colon, renal arterial dissection and identification with a vessel loop, visualisation of the tumor, and in on-clamp approaches, clamping renal artery with laparoscopic bulldog clamp, excision of the tumor by opening Gerota's fascia, renorrhaphy, and the removal of the clamp. All tumors were macroscopically dissected with the robotic scissors until normal parenchyma margin was visualized, and extracted tumors were placed in an endobag with their overlying adipose tissue. Bleeding sites on the tumor bed surface were cauterized using monopolar and bipolar energy. Renal parenchymal repair was accomplished, and internal renorrhaphy was performed with the use of a 30 cm 4-0 barbed suture with ½ circle needle with 17 mm radius (Covidien™, USA). Thereafter, an absorbable fibrin sealant patch (TachoSil®) was applied if required on the tumor surface for adequate hemostasis and an external renorrhaphy was performed with a 30 cm 3-0 barbed suture with a ½ circle needle with 26 mm radius (Covidien™, USA) suture. Absorbable Lapra-Ty® clips (Ethicon Endo-surgery, Inc., Cincinnati, OH, USA) applied reciprocally across the sutures outside the renal capsule. Intraabdominal pressure was decreased to 5 mmHg at the end of the procedure in order to check if adequate hemostasis had been achieved.

Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS Inc; Chicago, IL, USA) version 20. The minimum and maximum values of the mean and the standard deviation were used in summarizing the numeric parameters. Kolmogorov-Smirnov test was used to determine the distribution of the variables. Wilcoxon's signed-rank test was used as a non-parametric statistical method to compare parameters with a skewed distribution. Mann-Whitney U test was used to compare the variables among the zero-ischemia and on-clamp groups. Wilcoxon signed-rank test for paired data was used to compare the variables of renal functions detected at preoperative, immediate postoperative and postoperative 3rd months. The level of statistical significance was determined as p=0.05.

Results

A total of 34 patients had undergone RPN, between 2009 and 2015 using 12 off-clamp and 22 on-clamp resections performed in two centers. In the on-clamp group; of the 22 patients, 19 (86.4%) were male and 3 (13.6%) were female. Mean warm ischemia time was 22.0±4.5 mins. In the off-clamp group; of 12 patients, 11 (91.7%) were male and 1 (8.3%) was female.

Table 1. Comparison of patient characteristics, peri-, and postoperative outcomes of on-clamp and zero-ischemia robotic partial nephrectomy groups

	On-clamp (n=22)	Zero-ischemia (n=12)	p
Age (years)	54.4±10.1	53.0±8.2	0.639
ASA score	1.6±0.6	1.6±0.6	0.232
BMI (kg/m ²)	28.3±3.5	29.2±4.6	0.528
PADUA score	7.8±1.4	7.2±1.0	0.259
R.E.N.A.L nephrometry score	6.0±1.6	6.0±1.5	0.912
Operation time (minutes)	131.1± 16.1	122.5±2.4	0.156
Hospitalisation time (days)	3.8±0.9	3.0±0.9	0.02*
Blood loss (mL)	85.9±49.6	183.3±176.2	0.01*
Tumor size (cm)	3.2±0.9	3.3 ±1.1	0.95

Mann-Whitney U test. *statistically significant. BMI: body mass index; ASA: American Society of Anesthesiologists

There were no statistically significant differences between on-clamp and zero-ischemia groups regarding age, ASA score, BMI, PADUA and R.E.N.A.L. nephrometry scores, operation time and tumor size ($p>0.05$) (Table 1). Significant differences were found as for duration of hospital stay and amount of blood loss between the on-clamp and zero- ischemia groups ($p<0.05$). Comparisons of the patient characteristics, peri-, and postoperative outcomes of the groups are shown in Table 1.

The paired data of the variables showing the renal functions during the preoperative period were compared separately with those of the immediate postoperative period, and postoperative 3rd month variables (Table 2, and 3). In both groups, immediate postoperative serum creatinine levels increased, and postoperative 3rd month serum creatinine levels decreased, compared with those of the preoperative period. Also, eGFR decreased in the immediate postoperative period, and at postoperative 3rd months compared with the preoperative period, in both groups. Statistically significant intergroup differences were found between preoperative and immediate postoperative periods, and pre-and postoperative 3rd months, in terms of eGFR and serum creatinine levels. Moreover, statistically significant differences were found between preoperative period, and post-operative 3rd months, in the on-clamp group in terms of eGFR and serum creatinine levels. In the zero-ischemia group, the decrease of eGFR and serum creatinine levels at the postoperative 3rd months relative to the preoperative period was not statistically significant.

Table 2. Comparison of serum creatinine levels between pre-operative, immediate post- operative and post-operative 3rd month periods in on-clamp and zero ischemia groups

	Pre- operative creatinine	Immediate post- operative creatinine	p	Pre- operative creatinine	Post- operative 3 rd month creatinine	p
Zero-ischemia group (n=12)	0.84±0.6 (0.6-3.1)	0.94±0.6 (0.6-4.1)	0.003*	0.84±0.6 (0.6-3.1)	0.82±0.8 (0.6-3.6)	0.44
On-clamp group (n=22)	0.93±0.2 (0.6-1.6)	1.20±0.3 (0.6-2.0)	0.00*	0.93±0.2 (0.6-1.6)	0.91±0.3 (0.7-1.6)	0.01*

Wilcoxon Signed-Rank Test. *statistically significant

Table 3. Comparison of eGFR between pre-operative, immediate post-operative periods, and at post-operative 3rd months in on-clamp and zero- ischemia groups

	Pre- operative eGFR	Immediate post- operative eGFR	p	Pre- operative eGFR	Post- operative 3 rd month eGFR	p
Zero-ischemia group (n=12)	92.9±29.8 (20-134)	82.8±28.0 (15-126)	0.003*	92.9±29.8 (20-134)	90.0±27.6 (18-118)	0.64
On-clamp group (n=22)	83.9±21.5 (32-115)	64.4±18.0 (26-102)	0.00*	83.9±21.5 (32-115)	79.7±21.4 (32-109)	0.05*

Wilcoxon Signed-Rank Test. *statistically significant. eGFR: estimated glomerular filtration rates

There were no intraoperative complications in any patients. During the perioperative period (1-30 days), complications occurred in only two patients (Clavien Grade 1 due to the necessity of blood transfusion and radiological examination) in the on-clamp group, while no complications were seen in the remaining 32 patients (Clavien grade 0). None of the patients required readmission for any reason after being discharged. The fourth arm of the robot was utilized in 17 (14 on-clamp, 3 zero-ischemia) patients.

Discussion

Since its first introduction in 2004,^[18] RPN has been presented as an alternative to laparoscopic PN which required advanced instrumentation skills. Robotic surgery stands out by decreasing the effects of tremor, providing 3-dimensional magnified view and surgeon comfort, and fulfils the needs of laparoscopic surgery with these advantages. In studies on the pathophysiology of acute ischemic renal failure, ischemia was found to lead to a reduction in the effective GFR and acute kidney damage through three main mechanisms, including persistent vasoconstriction, obstruction of the tubules, and reperfusion injury which occurs after blood flow is restored.^[19,20] The limit of warm ischemia time before occurrence of renal ischemic damage is still a debated issue, but there is no doubt that any amount of injury might be seen in the PN procedures performed with temporary renal arterial clamping. Zero ischemia approach avoids complete renal ischemia with an anticipated positive impact on postoperative renal function. The advantage of robotic technology that enables the surgeon to perform easier tissue reconstruction and intracorporeal suturing also facilitates the procedure allowing realization of the surgery in a shorter duration of operation time which may contribute to preserve the kidney function.

In a recent prospective study, 21 patients have undergone robotic zero- ischemia PN.^[21] The procedure was successful in terms of oncologic and functional results in all cases, including 7 patients with hilar tumors. The authors concluded that zero-ischemia RPN is a safe procedure and elimination of warm ischemia may optimally preserve renal function. In this study, there was no statistically significant difference in renal functions detected at baseline on the day of discharge. In another study, it has been indicated that RPN without ischemia is a feasible method in patients with a solitary tumor or with multiple tumors in one kidney, which therefore, necessitates a longer ischemia period.^[22] Similar to our study, in this study conducted on a total of twenty-two patients, although immediate postoperative eGFR values decreased in relative to the preoperative period, it was observed that the values assessed at the 6th postoperative month were the same with the preoperative values. For eleven patients in the off-clamp group in our study, our most important preference criteria for performing this method was that the tumor was mostly exophytically located. In the remaining one patient, underlying nephropathy was evaluated as an indication for PN without ischemia. Ultimately, although immedi-

ate postoperative kidney functions were impaired in both groups, the postoperative 3rd month values returned to preoperative values only in the zero-ischemia group. Especially in patients with underlying chronic nephropathy, for whom functional kidney reserve is more essential, we are of the opinion that the implementation of this method must be encouraged. Nonetheless, even if the patient has no renal disease, it is obvious that this method is the first method of choice in patients with exophytic masses, considering that every patient with renal tumors who are undergoing renal surgery can be a potential candidate for renal failure.

Generally, blood transfusion is not performed during the postoperative period if hemoglobin levels do not decrease under 10 g/dL or the need for transfusion does not develop clinically. In our study, even if the amount of bleeding was more in patients without hilar clamping, in comparison to the patients with hilar clamping, in the non-clamping group the need for transfusion or a significant complication according to Clavien complication scale did not occur. It has been suggested that a controlled hypotension can be achieved during surgery performed with the off-clamp method for which the bleeding is expected to be of greater amount.^[23] However, this method has not been widely accepted due to the damage it can cause in the contra lateral kidney.

In our series, the operation time and duration of hospital stay were longer in the on-clamp group which might be related to the surgical experience and learning curve as initial cases did not include off-clamp patients.

Lack of any difference between our study groups in terms of the PADUA and R.E.N.A.L nephrometry scores which evaluate the tumor size and complexity of the tumor, provides strong evidence regarding the effect of the methods performed on kidney functions. However, the small number of patients included in our study and inability to evaluate the kidney functions in the long term prevent us from stating a definite opinion on this controversial subject.

The number of studies on the topic of zero ischemic PN is increasing in the literature. The outcomes of various selected zero-ischemia robotic and laparoscopic PN studies are summarized in Table 4. In a recent, retrospective, multi-institutional study, perioperative and functional outcomes of RPN, with (n=283) and without (n=49) hilar clamping were evaluated.^[24] The off-clamp group had a smaller tumor size, a significantly shorter operative times, increased blood loss, and a smaller decrease in eGFR. The authors concluded that, zero- ischemia RPN is a safe and feasible minimally invasive surgical option in patients with small renal masses. Adequate surgical experience reduces the risk of progression to renal insufficiency and enables better preservation of renal function. In a retrospective review, perioperative outcomes of off-clamp (n=150) and on-clamp (n=289) cases were evaluated.^[25] Renal masses in the off-clamp group

Table 4. The results of selected zero- ischemia robotic and laparoscopic partial nephrectomy series in the literature

Authors (Reference no)	Year	Number of patients	OT (min)	EBL (mL)	Size (cm)	Method	Complication	eGFR (mL/min/ 1.73 m ²)
Kaczmarek et al. ^[24]	2013	49	155	210	2.5	R	No Clavien 3-5 complication	Better in the off-clamp group
George et al. ^[25]	2013	150	137	338	2.7	L	Lesser complication rates (10%) compared with the on-clamp group (20%)	Better in the off-clamp group, - 5.8%
Novak et al. ^[22]	2012	28	183	274	2.1	R	4.5%	Better in the off-clamp group, 86.5 mL/min
Papalia et al. ^[26]	2012	78 43	57.8 58.3	168 205	≤4 >4	L,R	6.4% 18.6%	Decreased 1.8% Decreased 4.1%
Gill et al. ^[27]	2012	57	264	206	3.2	L,R	Clavien grade 1 to 2) in 19.3%, and 3 - 5) in 3.5% of the patients	-11.4 mL/min/ 1.73 m(2), 13%
Abreu et al. ^[21]	2011	21	222	150	4.1	R	Clavien grade 1 and 2 in two patients	5 (-16 -29) mL/min per 1.73 m(2)
*On-clamp		22	131	85	3.2	R	No Clavien 2-5 complication	Better in the off-clamp group
Off-clamp		12	122	183	3.3			

*Current study. R: robotic; L: laparoscopic; OT: operation time; EBL: estimated blood loss; eGFR: estimated glomerular filtration rates

were significantly smaller than those in the on- clamp group. As a result, eGFR was preserved better in the off-clamp group. The authors stated that, laparoscopic PN without hilar clamping was associated with less renal injury in terms of postoperative GFR, without any differences in the transfusion rate or positive surgical margin. Another study evaluated the technical feasibility, safety and functional outcomes of zero- ischemia laparoscopic and robotic PN with controlled hypotension for renal tumours larger than 4 cm. Consequently, the authors indicated apparently excellent benefits of avoiding hilar clamping to preserve kidney function.^[26] Similarly, another study evaluated the feasibility of anatomical vascular microdissection technique in complex tumors without hilar clamping. The authors have called attention to unnecessary global surgical renal ischemia in majority of the patients undergoing robotic and laparoscopic PN.^[27]

Our experience supports that, zero- ischemia RPN is a safe and feasible minimally invasive surgical method with excellent surgical and short-term oncological outcomes in the treatment of small renal masses. Therefore, with the development of robotic technology, zero- ischemia RPN may be performed more frequently in cases with exophytic small renal masses.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki “Ethical Principles for Medical Research Involving Human Subjects”, (amended in October 2013).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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