Ann Med Res 2020;27(7):1875-80

Annals of Medical Research
DOI: 10.5455/annalsmedres.2020.04.304

Original Article

Comparison of acute kidney injury after zero ischemia robot-assisted partial nephrectomy versus open and laparoscopic partial nephrectomy in patients with renal mass

Burak Kopru[1], Giray Ergin[1], Turgay Ebiloglu[2], Mustafa Kirac[1], Yusuf Kibar[1], Hasan Biri[1]

[1]Clinic of Urology, Koru Ankara Hospital, Ankara, Turkey
[2]Department of Urology, Gulhane Training and Research Hospital, Ankara, Turkey

Abstract

Aim: Robotic assisted laparoscopic partial nephrectomy (RALPN) is promising option for RCC treatment with favorable outcomes. In this present study we aimed to compare the incidence of (AKI) acute kidney injury measured by AKIN (Acute Kidney Injury Network) criteria between open partial nephrectomy (OPN), laparoscopic partial nephrectomy (LPN) and RALPN procedures with zero ischemia periods.

Material and Methods: The medical records of 88 patients with renal mass who underwent OPN, LPN and RALPN at our institution [24 female/64 male; median age of 55 (IQR: 46–65) years] were evaluated retrospectively. AKI was defined by AKIN criteria.

Results: Twenty-six patients underwent OPN, 32 LPN and 30 patients RALPN. Mean preoperative creatinine was 0.92 ±0.43 mg/dl, mean hemoglobin level was 14.0±1.9 g/dl. Total of 19 patients developed AKI according to the AKIN criteria, all of those had stage 1 AKI, 10 (53%) in OPN, 7 (3%) in LPN and 2 (11%) in RALPN group (p=0,004). Multivariate regression analysis adjusted by age and gender showed that operation time per minute [1.02 (CI 95%, 1.00, 1.04) p=0.04], fluid administered as ml/kg/hour [1.003 (CI 95%, 1.000, 1.006) p=0.04], red blood cell transfused as unit [1.27 (CI 95%, 1.07, 1.52) p=0.006] and operation type as RALPN surgery versus OPN and LPN [0.11 (CI 95%, 0.02, 0.58) p=0.01] were significantly associated with development ıf AKI.

Conclusion: Robot assisted partial nephrectomy is more favorable approach compared to OPN and LPN with lower operation time and lower hemoglobin loss.

Keywords: Acute kidney injury; nephron- sparing surgery; robotic surgery; zero ischemia

INTRODUCTION

Renal cell cancer (RCC) represents 2-3% of all adult cancers among all over the world (1, 2). The standard curative treatment for localized RCC was radical nephrectomy (RN) involving total tumor excision. However, partial nephrectomy (PN) with successful outcomes has become the standard treatment for T1-stage tumors (3).

Since 90s, laparoscopic partial nephrectomy (LPN) with minimally invasive and satisfactory oncologic outcomes has emerged as an alternative method compared to the traditional open approach (4). Laparoscopic partial nephrectomy has some limitations, including need for high technique to intracorporeal suturing and long-term learning curve. Hence, robotic assisted LPN (RALPN) has been started to use to alleviate these difficulties and facilitate the adoption of minimally invasive nephron-sparing surgery (5). The major advantages of RALPN were having high-quality three-dimensional images with shortened learning curve and the mobility of the expanded human hand (6).

Long warm ischemia times lead to acute kidney injury (AKI) after PN procedures (7). Minimally invasive PN approaches have favorable perioperative outcomes and lower morbidity rates compared to open PN (OPN). Recent studies suggest that RALPN might help promote early recovery of renal functions compared to OPN (8). Here in this study we aimed to compare the incidence of AKI measured by AKIN (Acute Kidney Injury Network) criteria (Table 1) between OPN, LPN and RALPN procedures with zero ischemia periods.

Received: 04.04.2020 **Accepted:** 08.05.2020 **Available online:** 03.07.2020
Corresponding Author: Burak Kopru, Clinic of Urology, Koru Ankara Hospital, Ankara, Turkey
E-mail: dr_burak83@yahoo.com

MATERIAL and METHODS

Study population

After obtaining the approval by the institutional review board of local ethic committee, a retrospective review of medical records of all patients who underwent OPN, LPN and RALPN at our institution between November 2015 and December 2019 was undertaken. A total of 177 patients were searched. Sixty eight patients were excluded due to had cold or warm ischemia partial nephrectomy and 21 patients were excluded due to the history of chronic kidney disease (Figure 1). Total of 88 patients were included in to the analysis. The following data were recorded: preoperative and postoperative creatinine (at 48th hours) and hemoglobin levels, intro-operative anesthesia time per minutes (defined as anesthesia induction to tracheal extubation), operation time per minutes, total administered fluid amount as ml/kg, total number of packed red blood cell transfusion and also baseline characteristics included age, weight, comorbidities (diabetes, hypertension or cardiovascular disease).

The aim of our study was the comparison of the incidence of AKI based on AKIN criteria (Table 1). Acute kidney injury was evaluated using only glomerular filtration rate criteria, as urine output could not be determined for all patients.

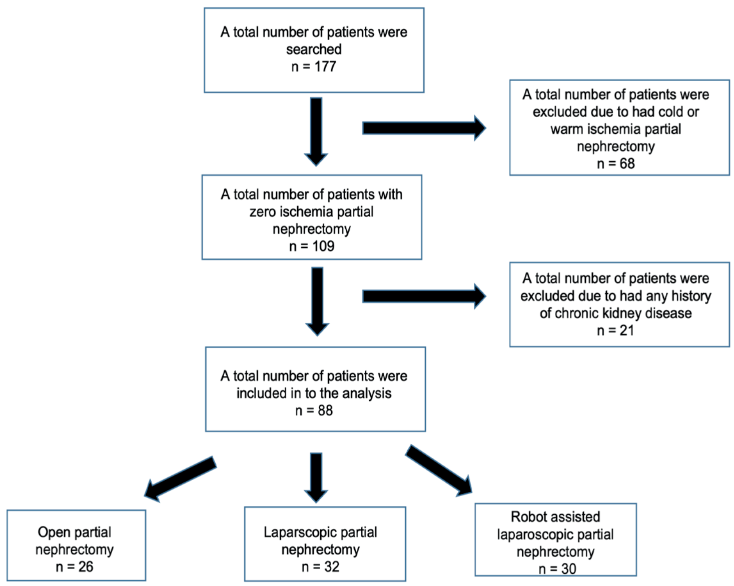

Figure 1. Patients Chart

Table 1. The AKIN classification system

Stage	Serum creatinine	Urine output
1	↑SCr ≥26.5 μmol/L (≥0.3 mg/dL) or ↑SCr ≥150 a 200% (1.5 a 2×)	<0.5 mL/kg/h (>6 h)
2	↑SCr >200 a 300% (>2 a 3×)	<0.5 mL/kg/h (>12 h)
3b	↑SCr >300% (>3×) or if baseline SCr ≥353.6 μmol/L (≥4 mg/dL) ↑SCr ≥44.2 μmol/L (≥0.5 mg/dL)	<0.3 mL/kg/h (24 h) oranuria (12 h)

a. SCr, serum creatinine; UO, urine output.
b. Stage 3 also includes patients requiring RRT independent of the stage (defined by SCr and/or UO) they are in at the moment they initiate RRT

Surgical technique

In all three surgical approaches with zero ischemia PN method were performed as defined first by Gill et al (9). The patients were placed flank position. In OPN surgery, transperitoneal approach performed by using Chevron incision. After incision of the skin, subcutaneous and muscle tissue, the gerato fascia was opened and the tumor was determined. The mean arterial pressure during tumor resection was adjusted to be 60-70 mmHg (for laparoscopic and robotic approach). During the resection of the tumor, the parenchymal clamp effect with the fingers of the surgeon reduced the parenchymal blood flow and then a cold knife resection was performed. After the resection, the resection area and pelvicalyceal system was repaired with 4.0 absorbable sutures.

In laparoscopic and robotic surgery, transperitoneal approach was performed for PN. Hasson open technique was performed for laparoscopic access (10). Primary access is obtained approximately half way between the anterior superior iliac spine and the umbilicus. After CO2 insufflation a second 12 mm trocar was placed lateral to the rectus muscle, in parallel to the primary access trocar but closer to the costal margin. A third 12mm trocar was placed in the midline, midway between the two working trocars for the camera. In robotic technique, Instead of the 2nd and 3rd trocars, 8 mm trocars were used. Extra 12 mm assistant trocar was placed to between camera port and second port in robotic surgery.

During surgery, intraabdominal pressure was between 12-15 mm Hg. After trocar placements, tumor tissue was found after opening the gerato fascia in both surgical approaches and cold ischemia was enucleated by PN. The parenchymal tissues and pelvicalyceal system were repaired with 4.0 absorbable sutures.

Statistical analysis

All values were expressed as means ± standard deviation or median with interquartile range (IQR) depending on their distribution. Non-parametric tests were performed to compare the levels of serum creatinine, hemoglobin, operation time, anesthesia time, fluid administration amount and hemoglobin loss for comparison analysis. The predictors of AKI were assessed in univariate and multivariate logistic regression analysis. Since we have 19 AKI events, we have restricted our multivariate logistic regression analysis with three variables. All multivariate logistic regression analysis adjusted by age and gender and other parameters were used as third parameter (preoperative creatinine, having diabetes mellitus, operation time, anesthesia time, fluid administration amount, red blood cell transfusion, hemoglobin loss and operation type). Statistical significance was assessed at the 95% confidence interval. Analysis was performed using SPSS version 23 for Windows (SPSS, Chicago, IL, USA).

RESULTS

Patient Characteristics

A total of 88 patients who underwent OPN, LPN or RALPN were included in to the analysis. Median age was 55 years (IQR: 46, 65 y), with overall male predominance. Twenty-six patients underwent OPN, 32 LPN and 30 patients RALPN. Mean preoperative creatinine was 0.92 ±0.43 mg/dl, mean hemoglobin level was 14.0±1.9 g/dl. Twenty one percent of study population was diabetic and 30% were hypertensive. Median operation time was 130 (IQR: 120,141) minutes, and anesthesia time 161 (150,175) minutes. Six patients were needed 4 packed red blood cell transfusion in open surgery and 1 packed in robot-assisted surgery group. The comparison of hemoglobin loss between groups showed lower blood loss in robot-assisted surgery group with marginal statistical significance (p=0,046) (Table 2).

Table 2. The comparison of demographic factors between surgery groups

Variables	OPN(N=26)	LPN (N=32)	RAPLN (N=30)	P VALUE
Age (years, median, IQR)	54±15	55±11	55±13	0.907
Gender (n, %)				
Female	8 (31%)	5 (16%)	11 (37%)	
Male	18 (69%)	27 (84%)	19 (63%)	0.56
Diabetes Mellitus (n, %)	6 (23%)	5 (16%)	7 (23%)	0.95
Hypertension (n, %)	7 (27%)	9 (28%)	10 (33%)	0.59
Preoperative creatinine (mg/dl, median±sd)	1.01±0.7	0.90±0.2	0.84±0.2	0.36
Postoperative creatinine (mg/dl, median±sd)	1.17±0.7	1.01±0.2	0.93±0.23	0.21
Preoperative hemoglobin (gr/dl, mean±sd)	14±2.1	14±1.2	14±2	0.58
Postoperative hemoglobin (gr/dl, mean±sd)	12±1.8	13±1.3	12±2.0	0.22
AKI by AKIN criteria (n, %)	10 (53%)	7 (37%)	2 (11%)	0.004

AKI; Acute Kidney Injury, AKIN; Acute Kidney Injury Network, Opn; Open Partial Nephrectomy, LPN; laparoscopic Partial Nephrectomy, RALPN; Robot-Assisted Laparoscopic Partial Nephrectomy

There were no significant differences between surgery groups in terms of, age, gender, preoperative creatinine levels, preoperative hemoglobin levels and diabetes mellitus or hypertension percentage (Table 2). The median operation time, median anesthesia time were significantly longer in OPN group compared to LPN and RALPN groups. Median hemoglobin loss was significantly higher in OPN group with more red blood cell transfusion need compared to LPN be RALPN groups (Table 3).

Total of 19 patients developed AKI according to the AKIN criteria, all of those had stage 1 AKI, 10 (53%) in OPN, 7 (3%) in LPN and 2 (11%) in RALPN group (p=0,004) (Figure 2, Table 2).

Table 3. The comparison of per-operative factors that affect AKI between surgery groups				
Variables	OPN(N=26)	LPN (N=32)	RAPLN (N=30)	P VALUE
Operation time (min)	142 (130, 154)	129 (120, 138)	120 (108, 130)	<0.001
Anesthesia time (min)	176 (169, 190)	154 (148, 169)	154 (150, 166)	<0.001
Fluids administered (ml/kg/hour)	24 (22, 28)	20 (18, 23)	21 (19, 24)	0.001
Red blood cell transfused (unit)	4	0	1	0.06
Hemoglobin loss (gr/dL)	-1.9 (-2.6, -1.5)	-1.6 (-1.9, -1.2)	-1.5 (-2.02, -1.1)	0.046

OPN; Open Partial Nephrectomy, LPN; Laparoscopic Partial Nephrectomy, RALPN; Robot-Assisted Laparoscopic Partial Nephrectomy

Table 4. The comparison of variables between AKI versus non-AKI group			
Variables	AKI (n=69)	non-AKI (n=19)	P value
Age (years, median, IQR)	54±12	55±13	0.83
Gender (n, %)			
Female	5 (26.3%)	19 (27.5 %)	
Male	14 (73.7%)	50 (72.5%)	0.58
Diabetes Mellitus (n, %)	5 (26.3%)	13 (18.8%)	0.33
Hypertension (n, %)	5 (26.3 %)	21 (30.4)	0.48
Preoperative creatinine (mg/dl, median±sd)	0.9±0.3	0.9±0.4	0.96
Operation Type (n, %)			
Open	10 (52.6%)	16 (23.2%)	
Laparoscopy	7 (36.8 %)	25 (36.2%)	
Robotic	2 (10.6%)	28 (40.6 %)	0.004
Preoperative hemoglobin (gr/dl, mean±sd)	13.6±1.7	14.1±1.9	0.29
Hemoglobin loss (gr/dL, median±sd)	-1.6 (-2.0, -0.9)	-1.7 (-2.1, -1.25)	0.29
Operation time (min, median±sd)	132 (124, 150)	129 (119, 140)	0.04
Anesthesia time (min, median±sd)	168 (150, 183)	160 (150, 174)	0.18
Fluids administered (ml/kg/hour, median±sd)	23 (21, 29)	21 (18, 25)	0.05
Red blood cell transfused (unit, median±sd)	2	3	0.29

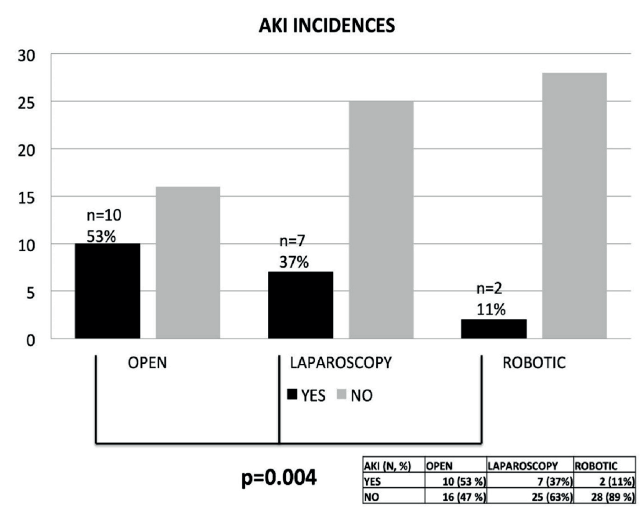

Figure 2. The comparison of the incidence of postoperative AKI by AKIN criteria between surgery types

Determinants of AKI in Study Population

When we divided the study population as AKI and non-AKI group, the comparison analysis showed only significant difference for surgery type and operation time. In AKI group, 52,6 % of patients had OPN, 36,8 % had LPN and 10,6 % had RALPN, however non-AKI group predominantly had RALPN (p=0,004). Also operation time was significantly longer in AKI group compared to non-AKI group (p=0,004) (Table 4).

Unadjusted univariate logistic regression analysis showed operation time [1.02 (CI 95%, 1.00, 1.057) p=0.04] suggesting longer operation time is associated with AKI and operation type [0.11 (CI 95%, 0.02, 0.58) p=0.009] suggesting RALPN seems like protective for development of AKI. In the adjusted analysis for age and gender factors that were statistically significantly associated with development of AKI included operation time per minute [1.02 (CI 95%, 1.00, 1.04) p=0.04], fluid administered as ml/kg/hour [1.003 (CI 95%, 1.000, 1.006) p=0.04], red blood cell transfused as unit [1.27 (CI 95%, 1.07, 1.52) p=0.006] and operation type as RALPN surgery versus OPN and LPN [0.11 (CI 95%, 0.02, 0.58) p=0.01] (Table 5).

Table 5. Determinants of AKI multivariate logistic regression analysis*		
	Multivariate Analysis*	
Variables	β(95% CI)	P value
Preoperative creatinine (mg/dl,)	0.99 (0.95, 1.03)	0.81
Diabetes Mellitus	1.64 (0.47, 5.61)	0.43
Operation time (min, median±sd)	1.02(1.00, 1.04)	0.04
Anesthesia time (min, median±sd)	1.02 (0.99, 1.04)	0.13
Fluids administered (ml/kg/hour, median±sd)	1.003 (1.000, 1.006)	0.04
Red blood cell transfused (unit, median±sd)	1.27 (1.07, 1.52)	0.006
Hemoglobin loss	1.63 (0.80, 3.32)	0.17
Operation type (RALPN)	0.11 (0.02, 0.58)	0.01

*Adjusted by age and gender
RALPN: Robot-Assited Laparoscopic Partial Nephrectomy

DISCUSSION

Nephron-sparing partial nephrectomy is accepted as the first-line treatment for T1a tumors smaller than 7 cm with the satisfactory oncological outcomes (11-13). Compared to open surgical technique, minimally invasive methods such as LPN or RALPN have both similar oncologic and better perioperative outcomes (14).

In this present study we showed that the incidence of AKI significantly lower in RALPN group compared to OPN and LPN. Also longer operation time, higher fluid administration need and also higher blood transfusion need were also significantly associated with AKI.

Traditionally, warm ischemia was applied by placing clamps on the renal artery to reduce bleeding and successful resection during partial nephrectomy (15). However, the warm ischemia technique causes increased AKI incidence, hence, nowadays, zero ischemia partial nephrectomy has been frequently preferred method with its advantages in minimally invasive methods (16). In partial nephrectomy, hemoglobin loss is an important parameter that negatively affects renal function, additional parenchymal loss due surgery, which decreases renal function. Loss of hemoglobin creates mitochondrial dysfunction and hypoxic damage in renal parenchyma, causing negative effects on renal function by apoptosis (17). In several studies have shown that RALPN causes lower blood loss than OPN and LPN. Increased intraabdominal pressure in laparoscopic and robotic methods and high instrument ability especially in robotic surgery are the most important factors for lower blood loss rates compared to open surgery (8, 18, 19).In our study, the lowest hemoglobin loss was seen in RALPN as compared to the OPN and LPN groups (-1.5 vs -1.9 vs -1.6 gr/dL, respectively).

Surgical stress due to the anesthesia and prolonged operation time can negatively affect kidney function and body fluid regulation with direct or indirect ways. Increased fluids administration rates which are a sign of defective fluid balance for patient creates adverse effects on eGFR (20). In our study post-operative AKI development rate was seen in open surgery group due to the highest anesthesia and operation times with higher fluid administration rates.

There is a limited data in the literature regarding the comparison of AKI incidence between RALPN versus open and laparoscopic PN with zero ischemia. The minimally invasive techniques with cold and warm ischemia procedures have lower risk of AKI than open surgery, however, it has been concluded that with the increasing use of zero ischemia technique AKI incidence is more or less even in minimally invasive surgeries (14). To the best of our knowledge our study is the first in kinds by using zero ischemia method in all procedures which allows us to eliminate the deterioration effect of ischemia on renal functions.

Due to the advantages of having three-dimensional image quality, fast learning curve and extended movement ability like human hand, robotic surgery became favorable approach for nephron-sparing partial nephrectomy field in whole around the world (21). Although, both perioperative and postoperative bleeding seems like more frequent in zero ischemia used RALPN compared to either cold or warm ischemia types, still zero ischemia is preservative for development of AKI with several factors predominantly shorter operation times (22). In appropriate cases such as with exophytic renal mas, low tumor size and proper location, hemoglobin loss and development of AKI might see lower rates in RALPN with zero ischemia (23,24).

CONCLUSION

The gold standard method for the treatment of < 7cm renal masses is PN. In order to minimize ischemic damage in PN, zero ischemia appears to be an applicable method with acceptable hemoglobin losses. Today, minimally invasive methods replace open PN and RALPN are becoming widespread among urologist due to important advantages compared to LPN. To the best of our knowledge, there is no study about evaluating the early postoperative results of OPN, LPN and RAPN with the zero ischemia method in the literature. We compared early results of the three PN technique with zero ischemia and found statistically significant differences between surgical methods including RALPN has lower hemoglobin loss, less operation time and protective for development of AKI than other PN techniques. Prospective randomized studies with higher patient numbers are needed which evaluates the best and safest surgical method with effective in zero ischemia partial nephrectomy.

****Some part of this manuscript has been presented as oral presentation at 21st National Hypertension and Renal Disease Congress, May 2019, Cyprus.*

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports.
Ethical approval: Approval was obtained from the Local Ethics Committee of Koru Ankara Hospital with the number 2019/004.

REFERENCES

1. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013;49:1374-403.
2. Shao IH, Kan HC, Liu CY, et al. Role Of Robot-Assisted Partial Nephrectomy For Renal Cell Carcinomas In The Purpose Of Nephron Sparing. Onco Targets Ther 2019;12:8189-96.
3. Van Poppel H, Becker F, Cadeddu JA, et al. Treatment of localised renal cell carcinoma. Eur Urol 2011;60:662-72.
4. Allaf ME, Bhayani SB, Rogers C, et al. Laparoscopic partial nephrectomy: evaluation of long-term oncological outcome. J Urol 2004;172:871-3.
5. Mullins JK, Feng T, Pierorazio PM, et al. Comparative analysis of minimally invasive partial nephrectomy techniques in the treatment of localized renal tumors. Urology 2012;80:316-21.
6. Benway BM, Bhayani SB, Rogers CG, et al. Robot assisted partial nephrectomy versus laparoscopic partial nephrectomy for renal tumors: a multi-institutional analysis of perioperative outcomes. J Urol 2009;182:866-72.
7. Lane BR, Babineau DC, Poggio ED, et al. Factors predicting renal functional outcome after partial nephrectomy. J Urol 2008;180:2363-8.
8. Choi SY, Jung H, You D, Jeong IG, et al. Robot-assisted partial nephrectomy is associated with early recovery of renal function: Comparison of open, laparoscopic, and robot-assisted partial nephrectomy using DTPA renal scintigraphy. J Surg Oncol 2019;119:1016-23.
9. Gill IS, Eisenberg MS, Aron M, et al. Zero ischemia' partial nephrectomy: novel laparoscopic and robotic technique. European Urology 2011;59:128-34.
10. Varma R, Gupta JK Laparoscopic entry techniques: clinical guideline, national survey, and medicolegal ramifications. Surg Endosc 2008;22:2686-97.
11. Bex A, Albiges L, Ljungberg B, et al. Updated European Association of Urology Guidelines for Cytoreductive Nephrectomy in Patients with Synchronous Metastatic Clear-cell Renal Cell Carcinoma. Eur Urol 2018;74:805-9.
12. Capitanio U, Montorsi F Renal cancer. Lancet 2016;387:894-906.
13. Capitanio U, Bensalah K, Bex A, et al. Epidemiology of Renal Cell Carcinoma. Eur Urol 2019;75:74-84.
14. Bravi CA, Larcher A, Capitanio U, et al. Perioperative Outcomes of Open, Laparoscopic, and Robotic Partial Nephrectomy: A Prospective Multicenter Observational Study (The RECORd 2 Project). Eur Urol 2019.
15. Greco F, Autorino R, Altieri V, et al. Ischemia Techniques in Nephron-sparing Surgery: A Systematic Review and Meta-Analysis of Surgical, Oncological, and Functional Outcomes. Eur Urol 2019;75:477-91.
16. Boga MS, Sonmez MG Long-term renal function following zero ischemia partial nephrectomy. Res Rep Urol 2019;11:43-52.
17. Sims CA, Yuxia G, Singh K, et al. Supplemental arginine vasopressin during the resuscitation of severe hemorrhagic shock preserves renal mitochondrial function. PloS one 2017.
18. Luciani LG, Chiodini S, Mattevi D, et al. Robotic-assisted partial nephrectomy provides better operative outcomes as compared to the laparoscopic and open approaches: results from a prospective cohort study. J Robot Surg 2017;11:333-9.
19. Chang KD, Abdel Raheem A, Kim KH, et al. Functional and oncological outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a multicentre comparative matched-pair analyses with a median of 5 years' follow-up. BJU Int 2018;122:618-26.
20. Burchardi H, Kaczmarczyk G The effect of anaesthesia on renal function. Eur J Anaesthesiol 1994;11:163-8.
21. Liu JJ, Leppert JT, Maxwell BG, et al. Trends and perioperative outcomes for laparoscopic and robotic nephrectomy using the National Surgical Quality Improvement Program (NSQIP) database. Urol Oncol 2014;32:473-9.
22. Kaczmarek BF, Tanagho YS, Hillyer SP, et al. Off-clamp robot-assisted partial nephrectomy preserves renal function: a multi-institutional propensity score analysis. Eur Urol 2013;64:988-93.
23. Simone G, Papalia R, Guaglianone S, et al. 'Zero ischaemia', sutureless laparoscopic partial nephrectomy for renal tumours with a low nephrometry score. BJU Int 2012;110:124-30.
24. Rizkala ER, Khalifeh A, Autorino R, et al. Zero ischemia robotic partial nephrectomy: sequential preplaced suture renorrhaphy technique. Urology 2013;82:100-4.