The impact of non–hilar clamping open partial technique performed for the treatment of patients with small renal masses with lower R.E.N.A.L. nephrometry scores on renal functions during the early postoperative period

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ABSTRACT

Objective: Herein, the impact of off-clamp open partial nephrectomy on early postoperative period renal functions were evaluated in patients with low RENAL nephrometry scoring small renal masses.

Material and methods: Twenty-three patients (12 women, and 11 men) who had undergone non-hilar clamping open partial nephrectomy in our clinic between the years 2010, and 2013 were retrospectively evaluated. Mean age, body mass index (BMI), operative time, blood loss, renal nephrometry score, mean hospital stay, pre-, and postoperative serum creatinine (Cr), and glomerular filtration rate (GFR) of the patients were assessed.

Results: Mean age, BMI, tumor size, and preoperative renal nephrometry scores were 56.09±10.49 years (36–70 yrs), 24.81±2.44 kg/m², 3.68±1.125 cm, and 6.41±1.77 pts, respectively. Mean operative time, intra-operative blood loss, and hospital stay were detected as 139.14±33.60 min, 274.9±77.02 mL, and 4.27±1.12 days, respectively. Preoperative mean serum Cr, and GFR levels were 0.804±0.216 mg/dL, and 93.97±25.83 mL/min/1.73 m², respectively. Postoperative 1. day mean serum Cr, and GFR levels were 0.896±0.25 mg/dL, and 85.94±28.85 mL/min/1.73 m², while corresponding 3. month-values were 0.81±0.205 mg/dL, and 93.59±21.00 mL/dk/1.73 m², respectively. A statistically significant difference was not found between pre-operative, and postoperative 3. month- serum Cr, and GFR levels. However, postoperative 3.month-serum Cr, and GFR levels were lower than corresponding values estimated on postoperative 1. day (p<0.016).

Conclusion: One of the important considerations in partial nephrectomy is to preserve renal functions. Therefore, non-hilar clamping open partial nephrectomy should be taken into consideration for surgeons inexperienced especially in laparoscopic surgery with its lower morbidity, and complication rates.

Key words: Open partial nephrectomy; non-clamping; small renal masses; renal function.

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Introduction

Renal cell carcinoma (RCC) constitutes 2–3% of all cancers seen in adults, and ranks third in frequency among genito-urinary cancers.^[1,2] Nowadays, thanks to the development, and widespread use of radiological imaging modalities, small renal masses (SRMs) are more frequently diagnosed day by day.^[3] These masses are defined as low-grade, and low-stage lesions of ≤4 cm in diameter with relatively slow biological behaviour, and growth pattern.^[4] Open partial nephrectomy (OPN) has been described as an alternative to radical nephrectomy (RN) in the surgical treatment

of small renal masses with the intention to preserve renal functions, and ensure long-term beneficial effects.^[5] When compared with RN, it has been introduced into clinical practice as a gold standard in the surgical treatment of SRMs in that it better preserves renal functions with comparable oncological outcomes.^[6,7]

The most important factors in the preservation of renal functions after partial nephrectomy (PN), is to keep functional renal parenchyma at a maximal level, and decrease duration of warm ischemia as far as possible.^[8] It is acknowledged that warm ischemia lasting more than 30 minutes significantly decreases

renal functions.^[9] Therefore, nowadays, various methods have been tried to keep intraoperative ischemia times in PN at its lowest level.^[10-14] Herein, we evaluated the impact of non-hilar clamping OPN we performed in our clinic, on postoperative renal functions of patients with SRMs with low R.E.N.A.L nephrometry scores.

Material and methods

We retrospectively evaluated 22 patients (12 women, and 10 men) treated with non-hilar clamping retroperitoneal OPN performed by the same surgeon in our clinic between the years 2010, and 2013. Mean age, body mass index (BMI), operative time, blood loss, R.E.N.A.L nephrometry score, serum creatinine (Cr), glomerular filtration rate (GFR) values before, and 1 day, and 3 months after the operation and mean hospital stays were evaluated. Preoperatively, all patients underwent computed tomographic and/or magnetic resonance examinations, and their R.E.N.A.L nephrometry scores were estimated as described in the literature based on the size, exophytic or endophytic nature of the tumor, and its location (nearness to collecting system, and renal polar lines, anterior or posterior location). Four of these 5 components were scored between 1, and 3 points (Table 1).^[15]

Preoperatively, required consent forms were obtained from all patients, then they were operated using retroperitoneal approach while they were laid in the flank position. For safety, firstly renal pedicle was exposed with hilar dissection. Renal capsule was incised circumferentially around the mass. Then with the handle of the scalpel, the mass was enucleated. To achieve hemostasis, renal parenchyma on the periphery of the resected area was squeezed, and compressed between the thumb, and the index finger of the surgeon's dominant hand. After specimen was harvested, and sent for frozen section examination, renal parenchymal defect was closed over hemostatic material with widely spaced parenchymal sutures. Glomerular filtration rates

were calculated using Chronic Kidney Disease Epidemiology Collaboration formula.^[16]

Statistical analysis

For statistical analysis IBM SPSS (Statistical Package for the Social Sciences) v. 20 was used. For the evaluation of changes in the patients within the same group Friedman test, and for post-hoc analysis, Wilcoxon test with Bonferroni correction were used. For intergroup, and intragroup comparisons, $p < 0.05$, and $(0.05/3) p < 0.016$ were considered to be statistically significant, respectively.

Results

Mean values for the age of the patients (56.09 ± 10.49 years; range 36-70), BMI (24.81 ± 2.44 kg/m²), tumor size (3.68 ± 1.125 cm), preoperative R.E.N.A.L nephrometry score (6.41 ± 1.77 pts), operative time (139.14 ± 33.60 min), intraoperative blood loss (274.9 ± 77.02 mL) were also calculated as shown in parentheses. During the operation two patients required transfusions of one unit erythrocyte suspension because of excessive bleeding. Mean postoperative drainage was estimated as 222.04 ± 169.23 mL, and one patient required prolonged monitorization of the drainage for 6 days. Mean hospital stay was 4.27 ± 1.12 days. On histopathological examination RCC (n=17; 77.2%), and oncocytoma (n=5; 22.8%) were detected. As subtypes of RCC, clear-cell (n=13; 76.4%), chromophobe (n=3; 17.6%), and cystic RCC (n=1; 5.8%) were detected. Surgical margins were negative in all patients (Table 2). Preoperative mean serum Cr, GFR levels were 0.804 ± 0.216 mg/dL, and 93.97 ± 25.83 mL/min/1.73 m², respectively. Postoperative 1. day mean serum Cr, and GFR levels were 0.896 ± 0.25 mg/dL, and 85.94 ± 28.85 mL/min/1.73 m², respectively, while postoperative 3. month serum Cr, and GFR levels were 0.810 ± 0.205 mg/dL, and 93.59 ± 21.00 mL/min/1.73 m², respectively (Table 3). A statistically significant difference was not found between preoperative serum Cr, GFR,

Table 1. R.E.N.A.L Nephrometry scoring system

	1 point	2 points	3 points
(R) adius (maximum tumor size) (cm)	≤ 4	4.1-6.9	≥ 7
(E) xophytic/ endophytic properties	≤ 50 % endophytic	$\geq 50\%$ endophytic	Totally endophytic
(N) earness (distance from the collecting system) (cm)	≥ 7	4.1-6.9	≤ 4
(A) nterior/posterior location	No scoring		
(L)ocation (relative to the polar line)	Tumor is totally above or below the polar line	Tümör extends beyond the polar line	$\geq 50\%$ of the tumor extends beyond the polar line or it invades the middle part of the polar line completely
Evaluation:			
Total 4-6 points: nephrometry score indicating low risk			
Total 7-9 points: nephrometry score indicating moderate risk			
Total 10-12 points: nephrometry score indicating high risk			

and postoperative 3. month serum Cr, and GFR levels. Post-hoc analysis revealed that postoperative 1. day serum Cr, and GFR levels were significantly lower than postoperative 3. month serum Cr, and GFR levels ($p=0.002$, and $p=0.010$, respectively).

Discussion

In the treatment of small renal masses, partial nephrectomy yields 5-year cancer-specific survival rates of >95% similar to those of RN.^[17] A series of studies which compared PN, laparoscopic RN, and open RN in the treatment of SRMs, RN has been associated with increased mortality rates independently from comorbidities.^[18-20] Dash et al.^[21] could not detect any difference in the cancer-specific survival rates in the treatment of RCC for renal masses measuring between 4, and 7 cm. In a separate study which compared complications, and surgical safety, any intergroup difference was not observed between open partial, and open RN as for mean blood loss, hospital stay, and blood transfusion rates. However, mean operative time was significantly longer in the OPN group.^[22]

Table 2. Characteristic features of the patients

Total number of patients (n)	23
Gender (M/F)	10/12
Mean age (years)	56.09±10.49 (36-70)
Mean BMI (kg/m ²)	24.81±2.44 (20.5-30.86)
Mean tumor size (cm)	3.68±1.125 (1.2-6)
Mean R.E.N.A.L. nephrometry score	6.41±1.77 (4-10)
Mean operative time (min)	139.14±33.60 (90-223)
Ortalama kan kaybı (mL)	274.9±77.02 (180-470)
Postoperative drainage (mean ± SD) mL	222.04±169.23 (35-700)
Mean hospital stay (days)	4.27±1.12 (3-7)
Histopathological diagnosis (%)	
Benign (n)	5 (22.8)
RCC	17 (77.2)
Clear cell	13 (76.4)
Chromophobe	3 (17.6)
Cystic	1 (5.8)
Positive surgical margin (n)	0
BMI: body mass index; RCC: renal cell carcinoma	

As a general approach, tumors in solitary kidneys, and concurrent bilateral tumors constitute absolute PN indications, while increased risk of chronic renal failure secondary to hypertension, diabetes mellitus, and nephrolithiasis, and higher risk of metachronous renal carcinoma in hereditary kidney tumors including Von-Hippel Lindau disease, hereditary papillary kidney tumors, and tuberous sclerosis comprise relative indications. Nowadays, in 2013 guidelines of European Association of Urology, treatment of T1 renal carcinomas using nephron-sparing surgery was recommended as level “B” suggestion.^[23]

R.E.N.A.L nephrometry score was firstly described by Kutikov and Uzzo in 2009. First letters of five components of the scoring system were abbreviated to form an acronym of R.E.N.A.L (R, radius-the longest diameter of the tumor; (E) exophytic-endo-phytic properties of the tumor; (N) nearness of the tumor relative to the collecting system; (A) anterior or posterior location; (L) location of the tumor in relation with the polar line. Based on total R.E.N.A.L nephrometry scores, cases were classified as low (4-6 pts), moderate (7-9 pts), and high-risk (10-12 pts) patients.^[24] Primary reasons for the introduction of nephrometry systems are methodological analysis of tumor location, and standardization of the reporting of tumor data. Secondary reasons are related to the prediction of success of the partial nephrectomy, intra-, and postoperative potential complications, and oncological outcomes.^[25] In a retrospective study where among factors affecting preoperative approach in renal tumors, R.E.N.A.L nephrometry score was evaluated, R.E.N.A.L nephrometry scores were found to be significantly increased in patients who had undergone radical surgery.^[26] In another study where predictive value of R.E.N.A.L nephrometry score was analyzed, a strong correlation was observed between R.E.N.A.L nephrometry score, and duration of warm ischemia.^[27]

Limited warm ischemia time is very well known to be associated with reversible impairment of renal functions. Priorly warm ischemia time below 30 minutes was thought to be compatible with complete recovery of renal functions.^[28,29] However according to recently asserted recommendations its maximum duration has been restricted to 20 minutes.^[30,31] However Thompson et al.^[32] suggested that even every minute below 20 minutes has a crucial importance as for the recovery of renal functions.

Renal ischemia-reperfusion damage developed because of hilar vascular clamping so as to ensure warm ischemia is the primary

Table 3. Pre-, and postoperative serum creatinine, and GFR values as indicators of renal function of the patients

	Preoperative	Postoperative 1. day	Postoperative 3. month	p
Serum Cr (mg/dL)	0.804±0.216	0.896±0.25	0.810±0.205	0.005*
GFR(mL/min/1.73m ²)	93.97±25.83	85.94±28.85	93.59±21.00	0.005*
Cr: creatinine; GFR: glomerular filtration rate; *p<0.05 (Friedman test)				

etiological factor of acute renal injury.^[33] Free oxygen radicals released during reperfusion phase cause cellular damage via a series of complex events including derangement in cytoskeleton, alteration of ionic equilibrium in the cell, induction of proteolytic, and phospholytic pathways, acidosis, production of reactive oxygen/nitrogen species, and inflammatory mediators, leukocytic infiltration, microvascular reactivity, and cell death through apoptosis or necrosis.^[34] In a rat model, Liu et al.^[35] demonstrated that warm ischemia lasting for 4 hours caused ischemia-reperfusion injury mediated acute tubular necrosis, and renal dysfunction during the subsequent 24 hours. Whereas, Godwin et al.^[36] exposed rats to 30 min-warm ischemia, and reported progressive tubular loss, significant levels of interstitial fibrosis, dilation, and cystic formations together with tubular impairment, significant glomerular loss, and cortical contraction. In the same study, small clusters of tubuli was detected at 30. days, and all along the 30 days, infiltration of T cells, and macrophages were observed. Simmons et al.^[37] performed partial nephrectomies on 187 patients using open, laparoscopic, and robotic methods, and reported marked postoperative parenchymal atrophy in patients who were exposed to warm ischemia lasting more than 40 minutes.

The most important consideration in partial nephrectomy performed using various techniques -open surgery, laparoscopic, and robot-assisted techniques-, is preservation of renal functions.^[38,39] In a study by Marszalek et al.^[40], the authors reported relatively decreased warm ischemia times, but comparable amounts of blood loss in laparoscopic technique when compared with OPN. Lucas et al.^[41] performed a study on 96 patients with SRMs with similar size (2.3 cm), and a nephrometry score of 6, and reported comparable levels of preservability of renal functions, complication rates, and surgical margin positivity for all three methods. In the OPN group, mean operative time (147 min), and duration of warm ischemia (12 min) were reportedly decreased, while authors noted relatively increased blood loss (250 mL), and median hospital stay (3 days). Still in the same study, in a total of 44 patients statistically significant decrease ($\geq 10\%$) was observed in GFR. Intraoperative US guidance has been recommended during partial nephrectomy performed for totally endophytic tumors in order to facilitate excision of the tumor, and achieve negative surgical margins.^[42] Kaczmarek et al.^[43] performed robot-assisted PN on 22 patients with 21 (95%) endophytic tumors, and a median R.E.N.A.L nephrometry score of 6.9, and achieved surgical margin negativity in all patients. However adequate number of clinical trials have not been performed under intraoperative ultrasonographic guidance during OPN. In a different study targeting analysis of factors influential on postoperative renal functions, patients operated using hilar clamping (n=164), and non-hilar clamping techniques (n=64) were evaluated, and median R.E.N.A.L nephrometry scores were estimated as 6.9, and 6.4 points,

respectively. In the abovementioned study which revealed R.E.N.A.L nephrometry scores comparable to ours, as a diverse approach focal radiofrequency coagulation was applied in order to facilitate hemostatic control before resection Besides in this study non-ischemic dissection/resection was performed using hydrodissection technique or sharp resection following local compression. BMI, and R.E.N.A.L nephrometry scores following hilar clamping, and non-hilar clamping PN, and while warm ischemia times after hilar clamping PN were evaluated as predictive factors for the drop of GFR under 60 percent. In a study consisting of patient groups with similar demographic features, and tumor characteristics, complications of laparoscopic hilar clamping, and non-hilar clamping PN were evaluated, average intraoperative blood loss was relatively increased in non-hilar clamping group. However median operative time, rates of surgical margin positivity, and need for blood transfusion were found to be comparable in both groups. Still increase in serum Cr, and decrease in GFR at postoperative 6. months were found to be significantly higher in the hilar clamping group.^[45] Whereas in our study mean operative time was 139.14 ± 33.60 min, and mean intraoperative blood loss was 27.9 ± 77.02 mL. In all patients, surgical margins were tumor-free. A statistically significant difference was not detected between preoperative, and postoperative 3. month- serum Cr, GFR values, and renal functions were preserved more effectively relative to the hilar clamping group in compliance with the rationale of PN. Even though average blood loss, and operative time were comparable to those detected in standard OPN, the most important advantage of non-hilar clamping OPN is that preoperative GF remains the same during the postoperative period.

Scarce number of patients, and lack of a control group are limitations of the present study. Larger scale studies comparing non-hilar clamping laparoscopic PN, robot-assisted PN, and open PN are needed.

Although non-hilar clamping PN with its lower complication rates, and successful oncological outcomes has been performed using robotic, and laparoscopic methods, requirement of advanced level experience, and higher cost rates are disadvantages of these methods.^[46-48] In conclusion, we think that non-hilar clamping OPN which preserves renal functions at a high level in addition to its lower morbidity, and complication rates is an important alternative in the surgical treatment of SRMs performed by surgeons unexperienced in laparoscopic, and robotic surgery.

Ethics Committee Approval: This study was conducted retrospectively therefore Ethical committee approval was not received.

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

Peer-review: Externally peer-reviewed.

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