DOI: 10.4081/aiua.2023.12130

ORIGINAL PAPER

Oncological and functional outcomes of patients who underwent open partial nephrectomy for kidney tumor

Efe Bosnali [1], Enes Abdullah Baynal [2], Naci Burak Cinar [2], Enes Malik Akdas [2], Engin Telli [2], Büsra Yaprak Bayrak [3], Kerem Teke [2], Hasan Yilmaz [2], Ozdal Dillioglugil [2], Onder Kara [2]

[1] University of Health Sciences, Derince Training and Research Hospital, Department of Urology, Kocaeli, Turkey;
[2] Kocaeli University, School of Medicine, Department of Urology, Kocaeli, Turkey;
[3] Kocaeli University, School of Medicine, Department of Pathology, Kocaeli, Turkey.

Summary ***Objective:** To report long-term functional and oncological outcomes of OPN*
***Methods:** We enrolled 182 patients who underwent consecutive OPN with a diagnosis of kidney tumor in our clinic between April 2002 and February 2020 and were selected from our prospective OPN database. Preoperative demographic and clinical characteristics, intraoperative and pathological results, and patients' postoperative functional and oncological follow-up data were retrospectively analyzed. Overall survival (OS) and disease-free survival (DFS) were evaluated using Kaplan-Meier survival analysis. The time-dependent variation between preoperative and postoperative functional results was statistically analyzed and presented in a graph.*
***Results and limitations:** The mean age was 54.4 ± 10.8 yr, and the median age-adjusted Charlson comorbidity index (ACCI) was 1 (interquartile range [IQR] 0-1). The mean tumor size was 3.1 ± 1.2 cm, and the median RENAL score was 6 (IQR 5-8). The most common malign histopathological subtype was clear cell carcinoma with 76.6%, and five cases (3.4%) had positive surgical margins (PSMs). The most common surgical techniques were the retroperitoneal approach (98.9%) and cold ischemia (88.5%). Estimated glomerular filtration rate (eGFR) preservation was 92% (80.8-99.3, IQR), which translates to 32% chronic kidney disease (CKD) upstaging. Acute kidney injury (AKI) was detected in 27 (14.8%) patients according to RIFLE criteria. The intraoperative complication rate was 5.5%, and the postoperative overall complication rate (Clavien-Dindo 1-5) was 30.2%. Major complications (Clavien-Dindo 3-5) were observed in 13 (7.1%) patients. The median oncological follow-up was 42 mo (21.3-84.6, IQR), and the 5- and 10-yr OS were 90.1% and 78.6%, 5 and 10-yr DFS were 99.4% and 92.1%, respectively. No local recurrence was observed in 5 (3.4%) patients with PSMs; only one had distant metastasis in the 8th postoperative month. The retrospective design, the small number of patients who underwent PN based on mandatory indication, and one type of surgical approach may limit the generalizability of our findings.*
***Conclusions:** This study confirms excellent long-term oncologic and functional outcomes after OPN in a cohort of patients selected from a single institution. In light of the information provided by the literature and our study, our recommendation is to push the limits of PN under every technically feasible condition in the treatment of kidney tumors to protect the kidney reserve and achieve near-perfect oncological results.*

KEY WORDS: Kidney tumor; Open Partial Nephrectomy; Functional outcomes; Oncological outcomes.

Submitted 25 November 2023; Accepted 30 November 2023

INTRODUCTION

Renal cell cancer (RCC) incidence is rising in Western countries and accounts for approximately 3% of adult cancers (1). During the last two decades, *nephron-sparing surgery* (NSS) has become the standard for managing localized renal tumors, achieving excellent oncological outcomes and functional preservation (2). Long-term oncological results of OPN in masses smaller than 4 cm have been well-defined, and it has been reported that similar results are obtained with *radical nephrectomy* (RN) in local recurrence, *disease free survival* (DFS), and metastasis-free survival (3, 4). The purpose of PN is to protect the maximum kidney tissue without compromising oncological principles, thereby reducing kidney failure and related cardiac problems that may develop at various levels and extending the OS times compared to RN (5). With the increase in the diagnosis of incidental masses, interest in NSS has increased. In the *National Comprehensive Cancer Network* (NCCN) and EAU guidelines, PN is recommended to treat early-stage renal tumors under any technically feasible condition (6). We presented our experience of single-center OPN, including long-term functional and oncological outcomes, in describing the complications and rates that developed during and after surgery.

MATERIALS AND METHODS

Patient selection

A retrospective analysis of the prospective OPN database approved by our institutional review board was performed in May 2020. All consecutive patients undergoing surgery between April 2002 and February 2020 were selected. Five surgeons experienced in OPN performed the surgeries. Due to limited access to the previous hospital patient record system, patients who underwent open PN between 1996 and 2001 were excluded. Overall, 182 patients were included in this study.

Variables

Preoperative demographic and clinical data of the patients included age, gender, race, *body mass index* (BMI), *age-adjusted Charlson comorbidity index* (ACCI), *American society of anesthesiologists* (ASA) score, history of diabetes and hypertension, previous abdominal surgery and smoking status, presence of a solitary kidney, and preoperative eGFR.

Tumor complexity was graded as low (RENAL score 4-6, PADUA score 6-7), moderate (RENAL score 6-9, PADUA score 8-9), or high (RENAL score 10-12, PADUA score 10-14). Clinical UICC-TNM stage and nephrometry scores could not be determined in 51 patients whose preoperative cross-sectional imaging could not be accessed.

Intraoperative variables included surgical approach and technique (ureteral stenting), operative time, *estimated blood loss* (EBL), ischemia type, *cold ischemia time* (CIT), *warm ischemia time* (WIT), use of a hemostatic agent, transfusion rate, and intraoperative complications.

Postoperative variables included *length of hospital stay* (LoS), 30-day readmission rate, and types of postoperative complications and their incidence. Postoperative complications were graded using the Clavien-Dindo classification, with grade 3a or higher considered major complications. Patients with *acute kidney ınjury* (AKI) were determined based on the RIFLE criteria for creatinine and eGFR values in the first week postoperatively. Urine leakage was defined as a creatinine value ≥ 2 mg /dl in the drain fluid in addition to postoperative follow-up for at least 4 days or a significant collection around the kidney in postoperative radiological examinations.

Tumor histology was performed according to the 2004 World Health Organization criteria, and grade classification followed the Fuhrman/*International Society of Urological Pathology* (ISUP) scheme. The 2017 yr *Union for International Cancer Control* (UICC)-TNM classification system was used for pathological staging. PSM was defined as an extension of tumor to the inked surface of the resected specimen on final pathology.

Follow up

Renal function assessment was based on serum eGFR measurements postoperative days 1 and 3 at regular intervals of 1, 3, 6, and 12 months. The time difference between the preoperative and final eGFR dates of the patients constituted the functional follow-up period.

eGFR was estimated using the *Chronic Kidney Disease Epidemiology Collaboration* (CKD-EPI) equation and CKD staging were assigned according to the eGFR value based on the NKF-KDOQI guideline. eGFR preservation was calculated as the proportion of postoperative eGFR was measured at the last follow-up to preoperative eGFR, and rates of CKD upstaging were evaluated (upstaging from class I-II to III-V, class III to IV-V, or class IV to V).

Oncological outcomes were evaluated through routine postoperative follow-up cross-sectional imaging studies, e.g., CT of the chest, abdominal CT and/or MRI. Imaging was carried out at 6, 12 months, then yearly and when clinically indicated. Postoperative cross-sectional imaging and medical records of the patients were examined, and the presence of local recurrence or distant metastasis and the causes of death were included in oncological follow-up data. *Overall survival* (OS) was defined as the time between the date of surgery and the date of death (all causes). *Disease-free survival* (DFS) was defined as the period between the date of surgery and the date of local recurrence or distant metastasis diagnosed by cross-sectional imaging in postoperative follow-up. Local recurrence was defined as detecting a new enhancing lesion in the surgical bed or the same renal space. Distant metastasis was defined as disease recurrence in the contralateral kidney or other body organs.

Surgical technique

We used the previously described standard OPN surgical method in all patients. The most common surgical technique in the study was the retroperitoneal flank approach (98.9%) and cold ischemia (88.5%). Depending on the tumor's location, a subcostal incision was made parallel to the 11^{th} or 12^{th} rib. The kidney was mobilized entirely with the surrounding Gerota fascia, and the renal pedicle was exposed.

In order to prevent ischemic kidney damage and reduce intracellular edema, 16 grams of 20% mannitol solution was given intravenously to all patients who underwent cold ischemia a few minutes before arterial clamping. Then, by placing a bulldog clamp on the renal artery, renal hypothermia was induced by intracorporeal ice melting for 15 minutes. Three different (cold, hot, zero) ischemia types were preferred. While mannitol and ice slush application were not applied in the warm ischemia group, a clamp was not placed on the renal artery in the zero ischemia group. Tumor tissue was excised in a wedge shape with a scalpel and cold scissors, leaving approximately 3-5 mm of normal renal parenchyma around it, preserving the overlying fat tissue. 3/0 absorbable polyglactin sutures were used to close the defect that may develop in the collecting system after excision and to provide hemostasis due to bleeding. After achieving hemostasis, the bulldog clamp was removed, and the duration of cold or warm ischemia was recorded. The preserved fatty tissue was wrapped and sutured (with absorbable suture material) in oxidized regenerated cellulose (Surgicel) or polyglactin (Vicryl) mesh and placed into the bed of the defect.

The fatty tissue was wrapped in order to provide the appropriate shape for the defect after excision and to help hemostasis with the effect of foreign materials around it. Blunt-tipped non-traumatic 1/0 absorbable polyglactin sutures were passed through the renal parenchyma along the edges of the defect and tied separately, and the wrapped fat tissue was fixed to the resection bed, and renorrhaphy was completed.

Statistical analysis

The normal distribution of variables was evaluated with the Kolmogorov-Smirnov test.

Mean ± *standard deviation* (SD) was used for parametric variables, and median and *interquartile range* (IQR) values were used for nonparametric variables. The median eGFR values in the preoperative and postoperative follow-ups were compared in pairs using the nonparametric Friedman test. The time-dependent change of postoperative eGFR was shown with a Box and whisker plot graph. OS and DFS analyses for 5 and 10 years were performed using the Kaplan-Meier method. All statistical analyses were performed using SPSS v24 software (*IBM SPSS Statistics, Armonk, NY: IBM Corporation, USA*). $P < 0.05$ was considered statistically significant.

Table 1.
Patient's Demographics and Preoperative Data.

Variables	Total OPN (n = 182)
Age years, mean (± SD)	54.4 (± 10.8)
Male, n (%)	79 (43.4)
White race, n (%)	182 (100)
BMI, mean (± SD)	28.3 (± 5.3)
CCI, med (IQR)	1 (0-1)
ASA, med (IQR)	2 (2-2)
Diabetes, n (%)	51 (28)
Hypertension, n (%)	
No	92 (50.5)
Yes	90 (49.5)
Controlled	81 (44.5)
Non controlled	9 (5)
Smoker, n (%)	
No	115 (63.2)
Yes	55 (30.2)
Former	12 (6.6)
Prior Abdominal Surgery, n (%)	48 (26.4)
Pre-op Hb g/dl, mean (± SD)	13.7 (± 1.5)
Solitary Kidney, n (%)	6 (3.3)
Pre-op eGFR, med (IQR)	96 (82.4-105.9)
Pre-op CKD stages, n (%)	
I. (eGFR ≥ 90 ml/min/1.73 m^2)	113 (62.1)
II. (eGFR 60-89 ml/min/1.73 m^2)	53(29.1)
IIIa. (eGFR 45-59 ml/min/1.73 m^2)	7 (3.8)
IIIb. (eGFR 30-44 ml/min/1.73 m^2)	5 (2.7)
IV. (eGFR 15-29 ml/min/1.73 m^2)	2 (1.1)

ASA, American Society of Anesthesiologists; BMI, Body mass index; CCI, Charlson comorbidity index; CKD, Chronic kidney disease; eGFR, Estimated glomerular filtration rate; Hb, Hemoglobin; IQR, Interquartile range; OPN, Open partial nephrectomy; SD, Standard deviation.

Table 2.
Preoperative tumor characteristics and R.E.N.A.L. Score Details.

Tumor size, cm, mean (±SD)	3.1 (± 1.2)
Side, right, n (%)	110 (60.4)
Clinical UICC-TNM stage, n (%)	
T1a	108 (82.4)
T1b	18 (13.7)
T2	0
T3a	5 (3.8)
Cystic Lesion, n (%)	46 (33.1)
Hilar Location, n (%)	4 (3)
Total Number of Arteries, n (%)	
1	155 (88.1)
> 1	21 (11.9)
N/A, n	6
CSA, cm^2, med (IQR)	11 (6.7-19.7)
R.E.N.A.L score, med (IQR)	6 (5-8)
R.E.N.A.L Complexity, n (%)	
Simple (4-6)	81 (61.8)
Intermediate (7-9)	48 (36.6)
Complex (10-12)	2 (1.5)
®adius (max diameter in cm), n (%)	
≤ 4	146 (81.6)
> 4 but < 7	31 (17.3)
≥ 7	2 (1.1)
(E)xophytic/Exophytic Properties, n (%)	
≥ 50%	67 (51.2)
< 50%	57 (43.5)
Entirely endophytic	7 (5.3)
(N)earness of The Tumor to the Collecting System or Renal Sinus (mm), n (%)	
≥ 7	59 (45)
> 4 but < 7	41 (31.3)
≤ 4	31 (23.7)
(L)ocation Relative to the Polar Lines (points), n (%)	
1	71 (54.2)
2	35 (26.7)
3	25 (19.1)

CSA, Contact surface area; IQR, Interquartile range; SD, Standard deviation.

RESULTS

Patients' characteristics

In total, 182 OPNs were performed during this initial time frame for our OPN experience.

The mean age at surgery was 54.4 ± 10.8 yr, and 56.6% of patients were women. Six (3.3%) patients underwent PN for a solitary kidney tumor, and 4 (2.1%) patients presented with bilateral renal neoplasms requiring PN. Median preoperative eGFR was 96 ml/min/1.73 m^2 CKD-EPI (7.6% of patients had preoperative CKD stage ≥ 3). The demographic and preoperative data are presented in Table 1.

The mean tumor size on preoperative imaging (CT or MRI) was 3.1±1.2 cm, and 82.4% of neoplasms were classified as clinical stage T1a. Median RENAL and PADUA scores were 6 (IQR 5-8) and 7 (IQR 7-9), respectively. According to the RENAL and PADUA nephrometry scoring systems, 38.1% and 49.6% of tumors were classified as moderately to highly complex, respectively. Seven (5.3%) patients had completely endophytic tumors. The preoperative characteristics of the tumors are presented in Table 2 and Table 3.

Intraoperative outcomes

The retroperitoneal approach (98.9%) and cold ischemia (88.5%) were the most common surgical techniques. Six cases had zero ischemia; the mean WIT for the remaining patients was 26.1 ± 7.7 minutes. The median operative time was 240 min (IQR 180-240), and the median EBL was 400 ml (IQR 300-600). The intraoperative complication rate was 5.5%, and renal vein injury was the most common (1.7%). The intraoperative transfusion rate was 28.6%.

The intraoperative data are summarized in Table 4.

Postoperative and pathological outcomes

The median postoperative LoS was 5 days (IQR 4-7). The postoperative overall complication rate was 30.2%, and pulmonary complications were the most common (9.3%). Major complications (Clavien-Dindo grade ≥ 3) were observed in 13 (7.1%) patients (Table 5). Urinary leakage occurred in 3.2% of cases and pseudo-aneurysm in 1.1% of the patients. According to the RIFLE criteria, AKI was detected in 27 (14.8%) patients. No patients required postoperative hemodialysis during follow-up. Postoperative complications are detailed in Table 6.

Final histopathologic analysis revealed clear cell RCC in 81% of cases. Most tumors (78%) were classified as pT1a and 16.2% were of high Fuhrman/ISUP grade (3 or 4).

Table 3.
Preoperative Tumor Characteristics and PADUA Score Details.

PADUA score, med (IQR)	7 (7-9)
PADUA Complexity, n (%)	
Simple (6-7)	66 (50.4)
Intermediate (8-9)	42 (32.1)
Complex (10-14)	23 (17.5)
Tumor Size (max diameter in cm), n (%)	
≤ 4	146 (81.6)
> 4 but < 7	31 (17.3)
≥ 7	2 (1.1)
Exophytic Rate, n (%)	
≥ 50%	67 (51.2)
< 50%	57 (43.5)
Entirely endophytic	7 (5.3)
Tumor Relationship with Renal Sinus, n (%)	
Absent relationship	114 (87)
With renal sinus location	17 (13)
Tumor Relationship with Urinary Collecting System, n (%)	
Absent relationship	76 (58)
Dislocated/Infiltrated	55 (42)
Renal Rim Location, n (%)	
Not involved	101 (77.1)
Involved	30 (22.9)
Location Relative to the Sinus Lines (points), n (%)	
1	79 (60.3)
2	52 (39.7)

IQR, Interquartile range; PADUA, (P)reoperative (A)spects and (D)imensions used for an (A)natomical.

Table 4.
Intraoperative Data of The Patients.

Variables	Total OPN (n = 182)
Surgical Approach, n (%)	
Retroperitoneal	180 (98.9)
Transperitoneal	2 (1.1)
Operation Time, min, med (IQR)	240 (180-240)
Double J Stent, n (%)	
Routinely	95 (52.2)
As required (intra-operative)	14 (7.7)
No	73 (40.1)
EBL, ml., med (IQR)	400 (300-600)
Management of Renal Pedicle, n (%)	
Off clamp	6 (3.3)
Global clamp	176 (96.7)
Technique of Ischemia, n (%)	
Warm	15 (8.2)
Cold	161 (88.5)
Zero	6 (3.3)
Ischemia Time, min, mean (±SD)	26.1 (± 7.7)
Warm	19.4 (± 3.5)
Cold	32.1 (± 4.9)
Use of Haemostatic Agents, n (%)	17 (9.3)
Tissel	3 (1.6)
Floseal	12 (6.6)
Arista	2 (1.1)
Intraoperative Complications, n (%)	10 (5.5)
1 cm size injury to the proximal ureter	1 (0.5)
Serosal injury to the colon	1 (0.5)
Injury to the renal vein	3 (1.6)
Pleural injury	1 (0.5)
Laceration of the spleen	1 (0.5)
Vascular injury in the vena cava	2 (1.1)
Injury of the aberrant artery supplying the lower pole	1 (0.5)
Intraoperative Transfusion, n (%)	52 (28.6)
ES Units, med (IQR)	1 (1-2)

EBL, Estimated blood loss; ES, Erythrocyte suspension; IQR, Interquartile range; SD, Standard deviation; OPN, Open partial nephrectomy.

Table 5.
Postoperative Data of The Patients.

Variables	Total OPN (n = 182)
Length of Stay (LoS), days, med (IQR)	5 (4-7)
Postoperative Transfusion, n (%)	14 (7.7)
ES Units, med (IQR)	2 (1-2.2)
Overall Postop Complications, n (%)	55 (30.2)
Major (Clavien-Dindo 3-5) Postop Complications	13 (7.1)
Minor (Clavien-Dindo 1-2) Postop Complications	41 (23.1)
Readmission for Urologic Reasons, n (%)	11 (6)
< 30 days	7 (3.8)
≥ 30 days	4 (2.2)

ES, Erythrocyte suspension; IQR, Interquartile range; OPN, Open partial nephrectomy.

Table 6.
Postoperative Complication Type of The Patients.

Postoperative Complication Type	Total OPN (n = 182)
Cardiac Complications, n (%)	3 (1.6)
1 Hypertension	2 (1.1)
2 Cyanosis	1 (0.5)
Pulmonary Complications, n (%)	17 (9.3)
1 Atelectasis (Need for Antibiotics)	14 (7.6)
2 Pleural Effusion	3 (1.6)
Genitourinary Complications, n (%)	16 (8.7)
1 Urine Leakage	14 (7.6)
2 Perirenal/Psoas Abscess	2 (1.1)
Bleeding Complications, n (%)	16 (8.7)
1 Postoperative Transfusion	14 (7.6)
2 Need for Angioembolization	2 (1.1)
Other Infections (Use of Antibiotics), n (%)	4 (2.2)
Ileus/ Small Bowel Obstruction, n (%)	2 (1.1)
Hernia, n (%)	4 (2.2)
Acute Kidney Injury (RIFLE Criteria), n (%)	27 (14.8)
R Risk (Increased Cre x 1,5 or eGFR decrease > %25)	23 (12.6)
I Injury (Increased Cre x 2 or eGFR decrease > %50)	4 (2.2)
F Failure (Increased Cre x 3 or eGFR decrease ≥ %75)	0
L Loss (Complete loss of renal function ≥ 4 weeks)	0
E End stage renal disease	0

Five (3.4%) patients had PSMs. Among the benign pathologies, oncocytoma was reported most frequently (70.6%). The pathological data of the patients are presented in Table 7.

Oncological and functional outcomes

The median oncological follow-up of the patients was 42 (IQR 21.3-84.6) mo. Local recurrence was observed in three (1.6%) patients at the postoperative 63rd, 73rd and 89th mo. respectively. Distant metastasis developed in 4 (2.2%) patients at 8th, 63rd, 64th, and 96th mo. after surgery secondary to RCC. Seventeen patients died (9.3%), including one from renal cancer (0.5%). No local recurrence was observed in 5 (3.4%) patients with PSMs.
Only one (0.5%) patient with PSMs had distant metastasis in the 8th postoperative mo. The 5-and 10-yr OS were determined as 90.1% and 78.6%, 5 and 10-yr DFS rates with the Kaplan-Meier method, respectively, were 99.4% and 92.1% (Figure 1). Oncological data are summarized in Table 8.

Table 7.
Pathological Data of The Patients.

Variables	Total OPN (n = 182)
Malignant Disease, n (%)	145 (81)
Benign Disease, n (%)	34 (19)
N/A, n	3
Pathological UICC-TNM stage, n (%)	
T1a	120 (83.3)
T1b	21 (14.5)
T2a	0
T3a	3 (2.1)
N/A, n	1
Histological Subtype, n (%)	
Clear Cell	111 (76.6)
Papillary	25 (17.2)
Chromophobe	7 (4.8)
Malignant mezenchymal	1 (0.7)
Tubulocystic carcinoma	1 (0.7)
Benign Disease, n (%)	34 (19)
Histological Subtype, n (%)	
Oncocytoma	24 (70.6)
Angiomyolipoma	5 (14.7)
Other benign types	5 (14.7)
Positive Surgical Margin, n (%)	5 (3.4)
Fuhrman/ ISUP Grade, n (%)	
Low FG (1-2)	113 (83.7)
High FG (3-4)	24 (16.2)
N/A, n	10

FG, Fuhrman grade; ISUP, International Society of Urological Pathology; OPN, Open partial nephrectomy.

Table 8.
Oncological Outcomes and Follow-up Data of The Patients.

Follow-up Times (oncological), mo., med (IQR)	42 (21.3-84.6)
Local Recurrence, n (%)	3 (1.6)
Time to Local Recurrence, mo., med (IQR)	73 (63-89)
Distant Metastasis, n (%)	4 (2.2)
Time to Distant Metastasis, mo., med (IQR)	63.5 (21.7-88)
Death, n (%)	5 (3.5)
RCC-Related Death, n (%)	1 (0.5)

Table 9.
Functional Outcomes and Follow-up Data of The Patients.

Follow-up Times (functional), mo., med (IQR)	32.8 (12.3-71)
Preop eGFR, med (IQR)	96 (82.4-105.9)
Postop 1st day eGFR, med (IQR)	88.1 (70.3-100.3)
Postop 1st day % eGFR preservation, med (IQR)	94.2 (81.9-100)
Postop 3rd day eGFR, med (IQR)	91.4 (73.8-101.4)
Postop 3rd day % eGFR preservation, med (IQR)	95 (87.4-100.9)
Postop 1st mo. eGFR, med (IQR)	91.1 (77.3-102)
Postop 1st mo. % eGFR preservation, med (IQR)	95.2 (86.3-100.6)
Postop 3rd mo. eGFR, med (IQR)	87.2 (70.4-100.2)
Postop 3rd mo. % eGFR preservation, med (IQR)	92.6 (82-99.2)
Postop 6th mo. eGFR, med (IQR)	87 (70.4-97)
Postop 6th mo. % eGFR preservation, med (IQR)	92.2 (83.2-99.2)
Postop 1st yr. eGFR, med (IQR)	87.3 (70.9-99.8)
Postop 1st yr. % eGFR preservation, med (IQR)	92.4 (82.2-99.3)
Latest eGFR, med (IQR)	86.8 (70.4-99.1)
Latest Follow up % eGFR preservation (IQR)	92.9 (80.8-99.3)
Latest CKD Upstaging, n (%)	58 (32.2)

The median eGFR preservation after OPN was 92.9% (IQR 80.8-99.3%), which translates to a CKD upstaging rate of 32.2%. The median postoperative eGFR was 86.8 ml/min/1.73 m2; data for all patients were available with a median interval of 32.8 mo (IQR 12.3-71) after surgery (Table 9). Time-dependent change between eGFR values in preoperative and postoperative follow-up was statistically analyzed using the Friedman test and demonstrated using a Box and whisker plot graph (Figure 2).

Discussion

With an increased diagnosis of incidental masses, the interest in NSS has increased and as a result, PN has been suggested to be performed according to the NCCN and EAU guidelines, irrespective of the surgery method, for the treatment of early-stage kidney tumors.

In order to obtain good oncological and functional results in PN, all uro-oncologists are required to know the indications, technical details, and complications of PN as well as its management by using the advantages of minimally invasive techniques. Currently, at least 50% of new RCCs are diagnosed incidentally and smaller than 4 cm. This is further supported by previous studies focused on high number OPN series, which show mean tumor sizes of 2.7-3.4 cm (7, 8). Despite this regression, concerning previous years, the more extensive lesions, centrally located and related to the collecting system, were chosen to perform OPN (9). In our study, the mean preoperative tumor size was 3,1 ± 1.2 cm) and RENAL and PADUA scores showed that over half of the tumors are low-complexity lesions. On the other hand, RN was chosen for high-complexity preoperative cases. It is known that long ischemia times in PN harm kidney function. It was well reported that irrespective of the surgical method, hot and cold ischemia should not take longer than 20 and 30-35 minutes, respectively (10). Thus, cold ischemia was advised to be performed in the literature for cases requiring longer clamping times. In order to benefit from the advantages of cold ischemia, researchers from Cleveland Clinic defined icing techniques that can be utilized during *laparoscopic PN* (LPN) and *robotic-assisted PN* (RAPN) for complex cases (11). *Yossepowitch et al.* (12) demonstrate that while CIT correlated with eGFR decrease immediately after surgery, this correlation was no longer present 1 year after the procedure, highlighting the impact of cold ischemia on preserving long-term kidney function in a study that included 592 cases of cold PN series with a median CIT of 35 minutes. In our study, cold and hot ischemia was performed in 88.5% and 8.2% of our patients, respectively, whereas zero ischemia was performed in 3.3%. The mean cold and hot ischemia times were 32.1 and 19.4 minutes, respectively, within the previously suggested range; therefore, we envision comparable and normal long-term kidney function for both cohorts.

A 2020 meta-analysis study, comparing OPN and LPN from 26 different studies with 8095 cases, did not show any differences in intraoperative complication rate and

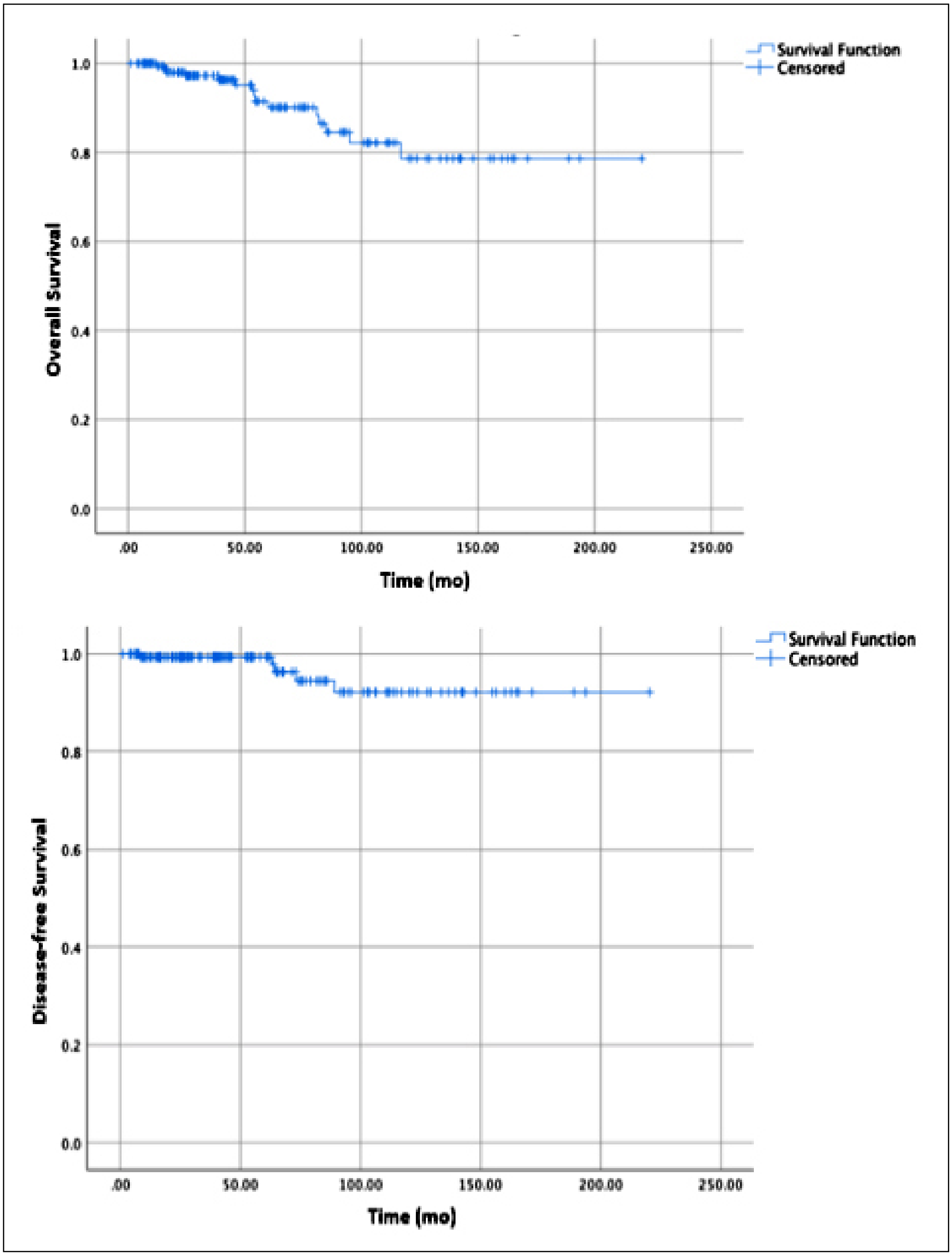
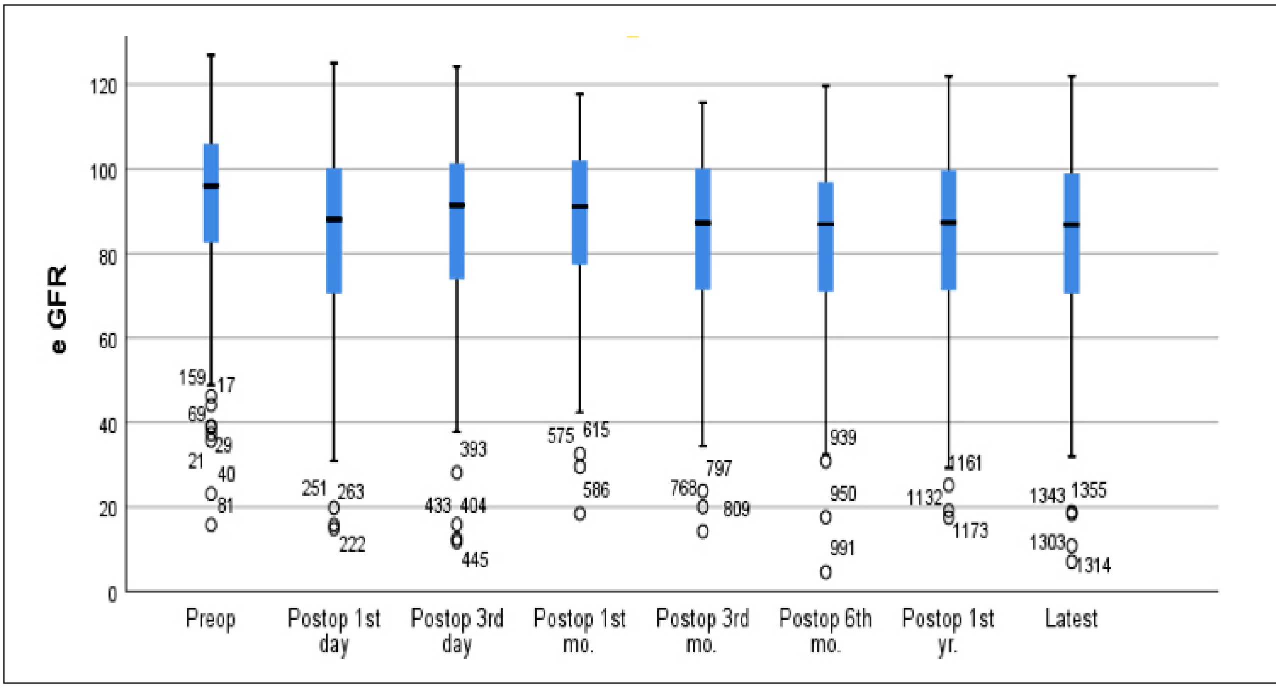


Figure 1.
Kaplan-Meier curves of the survival of patients undergoing open partial nephrectomy.
(A) Overall survival.
(B) Disease-free survival.

operation time between these two methods. However, it was reported that LPN decreased the EBL, LoS, and blood transfusion requirements (13). In another study comparing OPN, LPN, and RAPN performed for tumors less than 4 cm, it was found that OPN led to increased surgery time (199 ± 56 min) and bleeding (168 ± 266 ml) compared to RAPN (174 ± 64 min, 84 ± 165 ml) (14). In our series, the median operative time of 240 min and bleeding of 400 ml is greater than in previous reports. The routine ureteral stenting (52.2%), 15 minutes application of intracorporal ice slush treatment (88.5%), and additional application of lipocorticoplasty could have contributed to the elongation of the operation time.

The rate of general complications in various PN series varies between 4.1-38.6% in previous studies (4, 7, 15), with urine leakage and bleeding as the most frequent postoperative complications (7, 8). We found a general (major and minor) complication rate of 30.2 %, with pulmonary complications (9.2%), bleeding (8.7%), and urine leakage (7.6%) being the most common. *Chang et al.* (16) reported a major complication rate of 7.3% in 122 patients that resemble those in our study in terms of tumor characteristics and demographics. Thus, our postoperative major complication rate of 7.1% is in accordance with previous studies. An intraoperative complication rate of 3-5% was detected in the OPN series with a

Figure 2.
Time-dependent change between eGFR values in preoperative and postoperative follow-up (Box and whisker plot graph).



high number of patients, with pleural injuries being the major case (17, 18). In our study, the rate of intraoperative complications was 5.5%, in accordance with the literature.

AKI is observed in approximately 20% of all PN, negatively affecting long-term kidney function (19). Our study defined AKI for RIFLE criteria for up to 3 days post-operation (20). In a recent study, 25% of AKI was observed in a cohort of 944 pT1 stage patients operated with three different PN techniques by RIFLE criteria (21). We found an AKI of 14.8% in our study. This lower AKI rate could be attributed to good preoperative kidney function and a small number of solitary kidneys in our cohort.

Time-dependent decrease in renal function has been extensively studied, primarily in bilateral kidneys. Kidney function was found to decrease post-PN immediately but reached stable levels 3 weeks to 3 months after surgery upon partial recovery (22). *Porpiglia et al.* (23) followed the kidney function of patients with bilateral kidneys following LPN via scintigraphy. They found a significant recovery of kidney function 3 months post-operation. In our study, when the postoperative eGFR was compared with the preoperative eGFR in the time-dependent graph, a statistically significant loss of kidney function was found on the postoperative 1st day. The postoperative 3th day, we observed partial recovery of eGFR levels followed by stabilization of kidney function after 1 month, which was in accordance with the results obtained by *Porpiglia et al.*

CKD is defined as a heterogeneous distortion affecting the structure and function of kidneys. NKF-KDOQ1 developed this term in 2002, and the guides demonstrate that these distortions can elevate to life-threatening levels (24). In our cohort, primarily composed of cold ischemia patients, we found 92.9% median preservation of final eGFR levels during 32 months of functional follow-up; thus, temporary dialysis was deemed unnecessary. When compared with the literature, we think that the normal preoperative renal function of most patients, the low number of patients with high complexity lesions and solitary kidneys, utmost care on the maximum ischemia time, and experience of open surgery in our clinic have contributed to the low incidence of short-term kidney damage post-PN and improved functional recovery in the long-term.

A negative surgical margin is required to be left out following tumor excision according to standard surgical principles. PSMs can be observed between 1.3-18% in OPN cohorts. When PN was carried out in large tumors (> 4 cm) or complex tumors with mandatory indications, a higher rate of PSM was observed (23, 25). Even if, minimally invasive strategies involving optical magnification and pedicule clamping with ischemia and tumor's cold scission, are advantageous with increased surgical experience, PSM was higher in large cohorts than in open surgeries (7). PSM rates were found to be 4.9, 8.1 and 8.7% in OPN, LPN, and RAPN, respectively, in a study including more than 11500 cases with comparable numbers for each PN (26). In minimally invasive techniques, the lack of tactile sensations in determining the extension of the masses to the renal parenchyma at different axis angles and difficulty in determining the plan between the renal parenchyma and the tumor border due to the use of energy devices may cause higher rates of PSM compared to open surgery. In our clinic, where all patients were subjected to OPN, PSM rate was 3.4%. In OPN, three-dimensional masses extending into the renal parenchyma at different axis angles can be clearly excised from the kidney and tumor border can be identified by means of tactile senses and use of cold scissors, contributing to the lower detection of PSM observed in our clinic.

No local recurrence was observed in the close follow-up of 5 (3.4%) patients with PSM. A distant metastasis was detected in one (0.5%) at the postoperative 8^{th} mo. PSM was previously correlated with increased local recurrence risk and distant metastasis progression (27). In another study with a median follow-up of 62 months, PSM was reported as an independent predictor of OS, RFS, and DFS (28). Studies indicate that PSM does not influence survival; however, shorter follow-up and smaller cohort sizes may not had the statistical power to determine PSM's effect (29, 30).

The objective of PN is to preserve the kidney tissue while adhering to oncological principles maximally, in order to decrease the prevalence of different levels of kidney failure and related cardiac problems, and ultimately to increase longevity compared to RN (5). Local recurrence rates have been reported in the 1.4-3.3% range in large OPN cohorts with at least 5 yrs of follow-up (3, 31). *Lane et al.* (32) reported a 10-yr minimum OS of 72 and 78% in 299 patients with OPN and LPN, respectively. Marszalek et al. (33) reported the oncological outcomes of 100 age-, sex-, and tumor size-matched patients treated with OPN and LPN. In this study, the 5-yr OS were 85% and 96%, and 5-yr DFS were 94% and 96.3%, respectively.

In our study, local recurrence was observed in 3 (1.6%) patients and a distant metastasis was observed in 4 (2.1%) patients during a median of 42 (21.3-84.6, IQR) months of oncological follow-up. RCC-related death occurred in one (0.5%) patient with distant metastasis. 5 and 10-yr DFS were 99.4 and 99.2%. 5 and 10-yr OS were 90.1 and 78.6%, respectively. Most of the tumors belonging to the pT1a stage (83.3%) and with low Fuhrman/ISUP grade (83.7%) combined with low PSM rates obtained with our open surgical technique play critical roles in this high long-term oncological survival. Our results are consistent with previous studies, and we anticipate that our study will add to the successful oncological outcome of OPN studies.

The limitations of our study are retrospective design, a small number of patients subjected to PN upon mandatory indications, and inclusion of a single type of surgical method. In addition, more recent studies demonstrate that the amount of remaining kidney tissue post-operation is the most significant indicator of long-term kidney function. The absence of this parameter is the most significant limitation of our work and will be our field of study in the future.

Conclusions

This study confirms excellent long-term oncologic and functional outcomes after OPN in a cohort of patients selected from a single institution. We contributed to the literature by reporting that our patients who underwent open PN had high oncologic survival, and their kidney functions were well preserved in the long-term follow-up.

References

1. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer. 2018; 103:356-87.

2. Fergany AF, Hafez KS, Novick AC. Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year follow-up. J Urol. 2000; 163:442-5.

3. Pahernik S, Roos F, Hampel C, et al. Nephron sparing surgery for renal cell carcinoma with normal contralateral kidney: 25 years of experience. J Urol. 2006; 175:2027-31.

4. Patard J-J, Shvarts O, Lam JS, et al. Safety and efficacy of partial nephrectomy for all T1 tumors based on an international multicenter experience. J Urolo. 2004; 171:2181-5.

5. Thompson RH, Boorjian SA, Lohse CM, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. J Urol. 2008; 179:468-73.

6. Kaouk JH, Autorino R. Laparoendoscopic single-site surgery (LESS) and nephrectomy: current evidence and future perspectives. Eur Urol. 2012; 62:613-5

7. Gill IS, Kavoussi LR, Lane BR, et al. Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. J Urol. 2007; 178:41-6.

8. Patard J-J, Pantuck AJ, Crepel M, et al. Morbidity and clinical outcome of nephron-sparing surgery in relation to tumour size and indication. Eur Urol. 2007; 52:148-54.

9. Weight CJ, Fergany AF, Gunn PW, et al. The impact of minimally invasive techniques on open partial nephrectomy: a 10-year single institutional experience. J Urol. 2008; 180:84-8.

10. Becker F, Van Poppel H, Hakenberg OW, et al. Assessing the impact of ischaemia time during partial nephrectomy. Eur Urol. 2009; 56:625-35.

11. Ramirez D, Caputo PA, Krishnan J, et al. Robot-assisted partial nephrectomy with intracorporeal renal hypothermia using ice slush: step-by-step technique and matched comparison with warm ischaemia. BJU Int. 2016; 117:531-6.

12. Yossepowitch O, Eggener SE, Serio A, et al. Temporary renal ischemia during nephron sparing surgery is associated with short-term but not long-term impairment in renal function. J Urol. 2006; 176:1339-43.

13. You C, Du Y, Wang H, et al. Laparoscopic Versus Open Partial Nephrectomy: A Systemic Review and Meta-Analysis of Surgical, Oncological, and Functional Outcomes. Front Oncol. 2020; 10:2261.

14. Tachibana H, Kondo T, Yoshida K, et al. Lower incidence of postoperative acute kidney injury in robot-assisted partial nephrectomy than in open partial nephrectomy: A propensity score-matched study. J Endourol. 2020; 2020; 34:754-762

15. Lerner SE, Hawkins CA, Blute ML, et al. Disease outcome in patients with low stage renal cell carcinoma treated with nephron sparing or radical surgery. J Urol. 1996; 155:1868-73.

16. 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.

17. Minervini A, Mari A, Borghesi M, et al. The occurrence of intraoperative complications during partial nephrectomy and their impact on postoperative outcome: results from the RECORd1 project. Minerva Urol Nefrol 2018; 71:47-54

18. Caraballo ER, Palacios DA, Suk-Ouichai C, et al. Open partial nephrectomy when a non-flank approach is required: indications and outcomes. World J Urol. 2019; 37:515-22.

19. Capitanio U, Bensalah K, Bex A, et al. Epidemiology of renal cell carcinoma. European urology. 2019; 75:74-84.

20. Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004; 8:R204.

21. Bravi CA, Mari A, Larcher A, et al. Toward Individualized Approaches to Partial Nephrectomy: Assessing the Correlation Between Ischemia Time and Patient Health Status (RECORD2 Project). Eur Urol Oncol. 2021; 4:645-650.

22. Porpiglia F, Fiori C, Bertolo R, et al. The effects of warm ischaemia time on renal function after laparoscopic partial nephrectomy in patients with normal contralateral kidney. World J Urol. 2012; 30:257-63.

23. Porpiglia F, Fiori C, Bertolo R, et al. Long-term functional evaluation of the treated kidney in a prospective series of patients who underwent laparoscopic partial nephrectomy for small renal tumors. Eur Urol. 2012; 62:130-5.

24. Valente MA, Hillege HL, Navis G, et al. The Chronic Kidney Disease Epidemiology Collaboration equation outperforms the Modification of Diet in Renal Disease equation for estimating glomerular filtration rate in chronic systolic heart failure. Eur J Heart Fail. 2014; 16:86-94..

25. Peycelon M, Hupertan V, Comperat E, et al. Long-term outcomes after nephron sparing surgery for renal cell carcinoma larger than 4 cm. J Urol. 2009; 181:35-41.

26. Tabayoyong W, Abouassaly R, Kiechle JE, et al. Variation in surgical margin status by surgical approach among patients undergoing partial nephrectomy for small renal masses. J Urol. 2015; 194:1548-53.

27. Yossepowitch O, Thompson RH, Leibovich BC, et al. Positive surgical margins at partial nephrectomy: predictors and oncological outcomes. J Urol. 2008; 179:2158-63.

28. Petros FG, Metcalfe MJ, Yu K-J, et al. Oncologic outcomes of patients with positive surgical margin after partial nephrectomy: a 25-year single institution experience. World J Urol. 2018; 36:1093-101.

29. Bensalah K, Pantuck AJ, Rioux-Leclercq N, et al. Positive surgical margin appears to have negligible impact on survival of renal cell carcinomas treated by nephron-sparing surgery. Eur Urol. 2010; 57:466-73.

30. Ani I, Finelli A, Alibhai SM, et al. Prevalence and impact on survival of positive surgical margins in partial nephrectomy for renal cell carcinoma: a population-based study. BJU Int. 2013; 111:E300-E5.

31. Becker F, Siemer S, Humke U, et al. Elective nephron sparing surgery should become standard treatment for small unilateral renal cell carcinoma: long-term survival data of 216 patients. Eur Urol. 2006; 49:308-13.

32. Lane BR, Campbell SC, Gill IS. 10-year oncologic outcomes after laparoscopic and open partial nephrectomy. J Urol. 2013; 190:44-9.

33. Marszalek M, Meixl H, Polajnar M, et al. Laparoscopic and open partial nephrectomy: a matched-pair comparison of 200 patients. Eur Urol. 2009; 55:1171-8.

Correspondence

Efe Bosnali, MD Corresponding Author)
efebosnali415@gmail.com
Department of Urology, University of Health Sciences, Derince Training and Research Hospital, Turkey, 41380

Enes Abdullah Baynal, MD
abdullahbaynal@gmail.com
Naci Burak Çınar, MD
n.burak.cinar@gmail.com
Enes Malik Akdas, MD
enesmalikakdas@gmail.com
Engin Telli, MD
engintelli@gmail.com
Kerem Teke, MD
drtekekerem@gmail.com
Hasan Yılmaz, MD
hasanyilmazm.d@gmail.com
Özdal Dillioğlugil, MD
odillioglugil@gmail.com
Önder Kara, MD
onerkara@yahoo.com
Kocaeli University, School of Medicine, Department of Urology, Kocaeli, Turkey

Büşra Yaprak Bayrak, MD
busra.yaprakbayrak@kocaeli.edu.tr
Kocaeli University, School of Medicine, Department of Pathology, Kocaeli, Turkey

Conflict of interest: The authors declare no potential conflict of interest.