

Estimated blood loss to urine output ratio during partial nephrectomy as a predictor of postoperative acute kidney injury in a hereditary renal cancer-enriched population

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ABSTRACT

INTRODUCTION: We aimed to assess whether the intraoperative estimated blood loss (EBL) to urine output (UOP) ratio is a predictor of postoperative acute kidney injury (AKI) in a cohort of patients enriched with hereditary renal cancer syndromes undergoing partial nephrectomy (PN).

METHODS: We performed a retrospective chart review of patients who underwent PN at our institution from January 2006 to October 2024. We recorded and analyzed the clinical, demographic, and intraoperative characteristics of all patients.

RESULTS: A total of 1166 PNs (761 patients and 5903 renal tumors) were analyzed, of which 484 (41.5%) developed postoperative AKI. The average EBL/UOP was 1.06 (0.46–2.35) for patients without AKI and increased as AKI worsened, with a ratio of 5.00 (2.34–9.43) in patients with KDIGO AKI grade 3 ($p < 0.001$). EBL/UOP was associated with AKI in all patients (odds ratio [OR] 1.079, $p = 0.002$) and those with bilateral native kidneys (OR 1.083, $p = 0.003$). After adjustment in patients with a solitary kidney, no AKI association with EBL/UOP (OR 1.039, $p = 0.447$) was found.

CONCLUSIONS: EBL/UOP is a novel tool associated with the increased risk of developing post-PN AKI in select patients. In multiplex and repeat PNs, a higher ratio can assist the surgical team in identifying patients at risk of developing AKI. Prospective evaluation involving management strategies based on the EBL/UOP is needed to determine its true utility in clinical practice and generalization in the broader PN population.

INTRODUCTION

Partial nephrectomy (PN) has become the standard treatment for localized renal masses, as it incurs favorable renal function and oncologic outcomes. Acute kidney injury (AKI) commonly develops after PN, occurring in approximately 27% of patients, and is associated with longer postoperative stays, as well as predisposition for developing chronic kidney disease (CKD) later in life.¹⁻³ A stepwise decrease in renal function with each multiple reoperative PN (rePN) has been shown in patients with hereditary renal cancer syndromes who are at high risk of metachronous renal masses.^{4,5} Therefore, early identification of patients at increased risk for postoperative AKI is critical to guide perioperative decision-making and mitigate long-term renal complications.

Previous research has shown that the likelihood of postoperative AKI increases with intraoperative estimated blood loss (EBL) during PN, a relationship attributed to high blood loss resulting in intraoperative hypotension and decreased renal perfusion.^{6,7} No association has been found between post-PN AKI and intraoperative urine output (UOP), although past literature has found that low intraoperative UOP may be a risk factor for AKI after radical nephrectomy and in broad surgical populations.^{8,9}

Intraoperative UOP is an easily accessible and universally recorded indicator of both renal perfusion and hemodynamic status during surgery,

KEY MESSAGES

- Our objective was to assess a novel, variable estimated blood loss (EBL)/urine output (UOP) ratio as a potential intraoperative predictor of post-partial nephrectomy (PN) acute kidney injury (AKI) and short-term renal functional outcomes.
- In a cohort of predominantly hereditary renal cancer patients undergoing PN, EBL/UOP ratio was associated with postoperative AKI in our whole cohort and a subgroup analysis of patients with complex surgeries and bilateral kidneys.
- An increase in EBL/UOP ratio is associated with an increase in KDIGO AKI stage.

so the urology community maintains high interest in determining what role, if any, intraoperative UOP plays in predicting post-PN AKI. Additionally, its calculation is simple and does not require complex nomograms with multiple data points.

While both EBL and UOP have been shown to be associated with post-PN AKI, to our knowledge, no prior research has combined these variables into one predictive instrument. Because EBL and UOP are both linked to hemodynamics and renal perfusion, our objective was to assess a novel variable EBL-to-UOP ratio (EBL/UOP), as a potential intraoperative predictor of post-PN AKI and short-term renal functional outcomes.

METHODS

Patient selection and variable collection

Patients were selected retrospectively from an institutional review board-approved, prospectively maintained database of patients who underwent PN between January 2006 and October 2024 (No. NCI-97-C-0147). There were 42 PN cases excluded from the analysis: 16 due to no available ischemia time, 15 due to no available preoperative and/or postoperative serum creatinine values in their charts, six due to no operative time recorded, four with no intraoperative UOP recorded, and one patient who underwent a complete radical nephrectomy during the same hospital admission (Supplementary Figure 1; available at cuaj.ca). There

were no patients with prior renal transplants in this cohort. A total of 1166 PNs from 761 individuals were analyzed, with each PN analyzed as an individual case/patient, as each surgical intervention was performed at a different time.

Demographic and clinical data were collected, including surgical and pathologic data such as operative time, ischemia time, number of tumors removed, tumor size, number of previous PNs, hereditary renal cancer syndrome (if applicable), surgical approach, EBL, and intraoperative UOP. All patients with underlying germline pathogenic variations were confirmed using clinical laboratory improvement.

Tumor size was defined as the largest tumor removed during each surgery, and the number of previous PNs was determined by the number of ipsilateral PNs on that renal unit. To accurately denote the number of prior PNs, each patient's surgical history was retrospectively constructed by reviewing surgical records.

Intraoperative EBL and total UOP at the end of the case were obtained from operative and anesthesia reports, respectively, and EBL/UOP was calculated for each surgery. Intraoperative EBL is routinely recorded and documented at the end of the case; as per standard practice, it is obtained by evaluating the volume in the suction canister (excluding irrigation volume) and the amount of blood on laparotomy pads used during the procedure. Intraoperative fluid management and the decision to administer blood products are individualized based on each patient's clinical characteristics and intraoperative circumstances. Overall, intraoperative management is a series of joint decisions made by the anesthesia and surgical teams.

Postoperative serum creatinine (Cr) values were obtained from patient lab records. Collected values included peak Cr during the postoperative stay, Cr at three-month followup, and Cr at 12-month followup. From these values, estimated glomerular filtration rate (eGFR) was calculated using the 2021 CKD-EPI equation such that for the baseline, nadir, three-month, and 12-month Cr values, we had corresponding eGFRs.^{10,11} Based on the change in Cr from baseline to peak value, the postoperative AKI stage for each surgery was determined via staging guidelines put forward in the Kidney Disease: Improving Global Outcomes (KDIGO) 2016 recommendations.¹²

Of note, KDIGO AKI stage was based solely on comparing postoperative peak Cr to baseline, with stage 1 defined as postoperative Cr 1.5–1.9 times baseline or ≥ 0.3 mg/dL absolute increase in Cr, stage 2 defined as postoperative Cr 2.0–2.9 times baseline,

and stage 3 defined as postoperative Cr \geq 3.0 times baseline or initiation of renal replacement therapy or, for patients under the age of 18, decrease in eGFR to $<$ 35 mL/min/1.73 m². Patients with no AKI, per KDIGO guidelines, were recorded as stage 0.

Statistical analysis

The statistical analysis was performed using SPSS v.30. In patients who underwent multiple PNs during the study period, each PN was analyzed as an independent event with independently recorded perioperative variables and outcomes. Medians and interquartile ranges (IQR: 25th–75th percentile) were calculated according to the data distribution on a normality test. Numerical variables were compared using the Kruskal-Wallis test, while categorical variables were compared using the Chi-squared test.

Correlational analysis was performed with Spearman’s correlation test (ρ). Receiver operating characteristic (ROC) curves were constructed to assess

AKI (KDIGO 0 vs. 1, 2, or 3) against the EBL/UOP ratio, and the area under the curve (AUC) of ROC curves was reported for the overall population, patients with bilateral native kidneys, and solitary kidneys. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy for different EBL/UOP ratio cutoff points were assessed. Univariable and multivariable-adjusted logistic regression analyses were performed to evaluate the association of clinical variables and AKI (KDIGO 0 vs. 1, 2, or 3) in the overall population and subgroups. A p-value $<$ 0.05 was considered statistically significant.

RESULTS

After selection, a total of 1166 PNs were analyzed. The most common hereditary kidney cancer syndrome was von Hippel-Lindau disease in 550 (47.2%) cases, while 69 (5.9%) cases had a sporadic renal mass. The median age at surgery was 50 (IQR 38–59) years. A total of 718 (61.6%) and 879 (75.4%) surgeries were

Table 1. Clinical and demographic characteristics of the analyzed patients and comparison between groups

Clinical variable	AKI KDIGO classification					
	Overall	0	1	2	3	p
n	1166 (100%)	682 (58.5%)	365 (31.3%)	78 (6.7%)	41 (3.5%)	
Age at surgery (years)	50 (38–59)	49 (38–59)	49 (38–59)	53.5 (44–60)	40 (52–62)	0.094
Male (%)	718 (61.6%)	381 (55.9%)	258 (70.7%)	49 (62.8%)	30 (73.2%)	$<$ 0.001
Laterality						
Left (%)	600 (51.5%)	350 (51.3%)	193 (52.9%)	37 (47.4%)	20 (48.8%)	
Right (%)	564 (48.4%)	332 (48.7%)	171 (46.8%)	40 (51.3%)	21 (51.2%)	
Bilateral (%)	2 (0.2%)	0	1 (0.3%)	1 (1.3%)	0	0.245
Race						
White (%)	879 (75.4%)	537 (78.7%)	254 (69.6%)	65 (83.3%)	23 (56.1%)	
Black/African American (%)	149 (12.8%)	76 (11.1%)	58 (15.9%)	5 (6.4%)	10 (24.4%)	
Asian (%)	32 (2.7%)	15 (2.2%)	8 (2.2%)	5 (6.4%)	4 (9.8%)	
Other, multiracial, not reported (%)	106 (9.1%)	54 (7.9%)	45 (12.3%)	3 (3.8%)	4 (9.8%)	$<$ 0.001
Ethnicity						
Not Hispanic (%)	1034 (88.7%)	607 (89.0%)	317 (86.8%)	74 (94.9%)	36 (87.8%)	
Hispanic (%)	106 (9.1%)	61 (8.9%)	39 (10.7%)	2 (2.6%)	4 (9.8%)	
Not reported (%)	26 (2.2%)	14 (2.1%)	9 (2.5%)	2 (2.6%)	1 (2.4%)	0.490
Diabetes mellitus (%)	192 (16.5%)	100 (14.7%)	68 (18.6%)	15 (19.2%)	9 (22%)	0.242
Hypertension (%)	577 (49.5%)	316 (46.3%)	191 (52.3%)	46 (59%)	24 (58.5%)	0.045

KDIGO AKI: Kidney Disease Improving Global Outcomes criteria for acute kidney injury. Median (interquartile range 25th–75th).

Table 2. Clinical, surgical, and renal outcomes characteristics of the analyzed patients and comparison between groups

Clinical variable	AKI KDIGO classification					p
	Overall	0	1	2	3	
Solitary kidney (%)	129 (11.1%)	41 (6%)	42 (11.5%)	29 (37.2%)	17 (41.5%)	<0.001
Approach						
Open (%)	394 (33.8%)	179 (26.2%)	143 (39.2%)	45 (57.7%)	27 (65.9%)	
Robotic (%)	735 (63%)	485 (71.1%)	204 (55.9%)	32 (41%)	14 (34.1%)	
Laparoscopic (%)	37 (3.2%)	18 (2.6%)	18 (4.9%)	1 (1.3%)	0	<0.001
Partial nephrectomy count						
1 (%)	793 (68%)	498 (73%)	232 (63.6%)	42 (53.8%)	21 (51.2%)	
2 (%)	239 (20.5%)	131 (19.2%)	79 (21.6%)	20 (25.6%)	9 (22%)	
3 (%)	101 (8.7%)	42 (6.2%)	40 (11%)	12 (15.4%)	7 (17.1%)	
≥4 (%)	33 (2.8%)	11 (1.6%)	14 (3.8%)	4 (5.1%)	4 (9.8%)	<0.001
Tumors removed	3 (1–6)	2 (1–5)	4 (1.5–8.5)	6 (2–10)	9 (5–17)	<0.001
Largest tumor removed (cm)*	3.5 (3–4.5)	2.7 (3.2–4.3)	4 (3–5)	4 (3.1–4.5)	4 (3.4–4.9)	<0.001
Overall ischemia time (minutes)**	1.3 (0–27)	0 (0–22)	19 (0–34)	3.8 (0–26.3)	0 (0–29.5)	<0.001
Ischemia time (minutes)***	27 (19 - 36)	23 (17 - 31)	32 (24 - 42)	26 (21.3 - 34.8)	30 (20 - 43)	<0.001
PN tumor removal technique						
Without hilar clamping (%)	583 (50.0%)	361 (52.9%)	160 (43.8%)	38 (48.7%)	24 (58.5%)	
With hilar clamping (%)	583 (50.0%)	321 (47.1%)	205 (56.2%)	40 (51.3%)	17 (41.5%)	0.027
Operative time (minutes)	356 (280–440)	315 (252–390)	404 (340.5–500.5)	417 (371.5–492)	453 (400–538.5)	0.001
EBL (mL)	750 (300–1800)	500 (200–1300)	1100 (500–2200)	1550 (745–2350)	3000 (1050– 4825)	<0.001
UOP (mL)	500 (350–750)	500 (350–700)	550 (400–800)	500 (395–650)	500 (312.5–760)	0.005
Baseline Cr (ng/dL)	1.0 (0.84–1.2)	0.96 (0.80–1.14)	1.05 (0.90–1.27)	1 (0.82–1.20)	1.33 (0.96–1.72)	<0.001
Baseline eGFR (mL/min/1.73 m ²)	86.3 (70.6–102.4)	87.3 (70.7–103.1)	80.1 (64.2–99.4)	81.8 (60.9–99.2)	60.1 (46.3–86.6)	<0.001
Peak Cr (ng/dL)	1.30 (1.0–1.72)	1.07 (0.9–1.3)	1.61 (1.36–1.99)	2.46 (1.92–2.98)	4.57 (3.99–5.75)	<0.001
Nadir eGFR (mL/min/1.73 m ²)	66.1 (48.2–87)	79.4 (63–97.1)	49.4 (37.8–61.9)	30.6 (23.9–41.5)	13.8 (11–16.7)	<0.001
Change in peak Cr (ng/dL)	0.27 (0.10–0.58)	0.13 (0.03–0.22)	0.53 (0.39 - 0.75)	1.45 (1.02 - 1.69)	3.11 (2.79 - 4.19)	<0.001
Change in nadir eGFR (mL/min/1.73 m ²)	-17.6 (-31.2–-4.8)	-7.5 (-15.7–0)	-29.7 (-38.5–-20.8)	-50.9 (-57.6–-35.9)	-49.1 (-72.2–-34)	<0.001
Need for hemodialysis inpatient (%)	4 (0.3%)	0	0	0	4 (9.8%)	<0.001
EBL/UOP ratio (per cutoff point)						
Ratio ≥0.5 (%)	1.48 (0.67–3.14)	1.06 (0.46– 2.35)	1.86 (0.87–3.67)	3.33 (1.66– 5.66)	5.00 (2.34–9.43)	<0.001
Ratio ≥1 (%)	945 (81%)	505 (74%)	329 (90.1%)	72 (92.3%)	39 (95.1%)	<0.001
Ratio ≥1 (%)	747 (64.1%)	375 (55%)	266 (72.9%)	68 (87.2%)	38 (92.7%)	<0.001
Ratio ≥2 (%)	470 (40.3%)	205 (30.1%)	176 (48.2%)	54 (69.2%)	35 (85.4%)	<0.001
Ratio ≥3 (%)	312 (26.8%)	126 (18.5%)	116 (31.8%)	41 (52.6%)	29 (70.7%)	<0.001
Ratio ≥4 (%)	208 (17.8%)	79 (11.6%)	80 (21.9%)	26 (33.3%)	23 (56.1%)	<0.001

*1162 patients analyzed. Ischemia time was calculated. **In the overall population, with those without hilar clamping considered 0 minutes and ***only for those who underwent tumor removal with hilar clamping. Median (interquartile range 25th–75th). Cr: serum creatinine; EBL: estimated blood loss; eGFR: glomerular filtration rate; KDIGO AKI: Kidney Disease Improving Global Outcomes criteria for acute kidney injury; UOP: urine output.

performed on male and white patients, respectively; 192 (16.5%) surgeries were on patients with diabetes mellitus. The robotic approach was the most common and performed in 735 (63%) surgeries. One hundred ninety-one (16.4%) patients had a baseline, while 129 (11.1%) were performed on a solitary kidney. Throughout the study, 5903 tumors were removed, with a median of 3 (IQR 1–6) tumors per procedure (Table 1, Supplementary Table 1; available on [cuaj.ca](#)).

In the overall cohort, postoperative AKI occurred in 484 (41.5%) patients. In the subgroup analysis of the 311 (26.7%) index patients with bilateral kidneys undergoing first-time PN for a single tumor, the rate of postoperative AKI was 79 (25.4%). As expected, the incidence of postoperative AKI was highest in surgeries performed on patients with a solitary kidney (88/129, 68.2%), followed by those with baseline eGFR <60 mL/min/1.73 m² (109/191, 57.1%). The median operative time was 356 (IQR 280–440) minutes; the median intraoperative EBL was 750 (IQR 300–1800) mL; the median total intraoperative UOP was 500 (350–750) mL; and four (0.3%) patients needed hemodialysis during hospitalization after PN (Table 2).

The median EBL/UOP of the total cohort was 1.48 (IQR 0.67–3.14). Surgeries with worse postoperative AKI tended to have higher EBL/UOP. For patients without AKI, the EBL/UOP was 1.06 (0.46–2.35), whereas in patients with KDIGO AKI grade 3, the median EBL/UOP was 5.00 (2.34–9.43) ($p < 0.001$) (Figure 1, Table 2). At the three- and 12-month followups, the renal function parameters generally remain diminished for patients with postoperative AKI, where the change in Cr and eGFR from baseline to 12 months post-surgery was significantly greater for those who experienced a higher KDIGO stage AKI (Supplementary Table 2; available at [cuaj.ca](#)).

Upon further evaluation of EBL/UOP, a significant negative correlation between EBL/UOP and change in nadir eGFR was found in the total cohort and subgroup analyses (patients with a solitary or bilateral native kidneys), while a positive correlation between change in peak Cr and EBL/UOP was also observed ($p < 0.05$). The association between EBL/UOP using a ROC analysis showed fair association in the overall PN cohort and in the subgroups characterized by bilateral kidney status, solitary kidney status, first-time PN, and baseline eGFR <60 mL/min/1.73 m² (overall AUC 0.671, bilateral kidneys AUC 0.654, solitary kidney AUC 0.663, bilateral kidneys undergoing first PN of single tumor AUC 0.596, baseline eGFR <60 AUC 0.628; $p < 0.05$) (Figure 1, Supplementary Figure 2; available at [cuaj.ca](#)). When there was an increase in the ratio, the specificity and

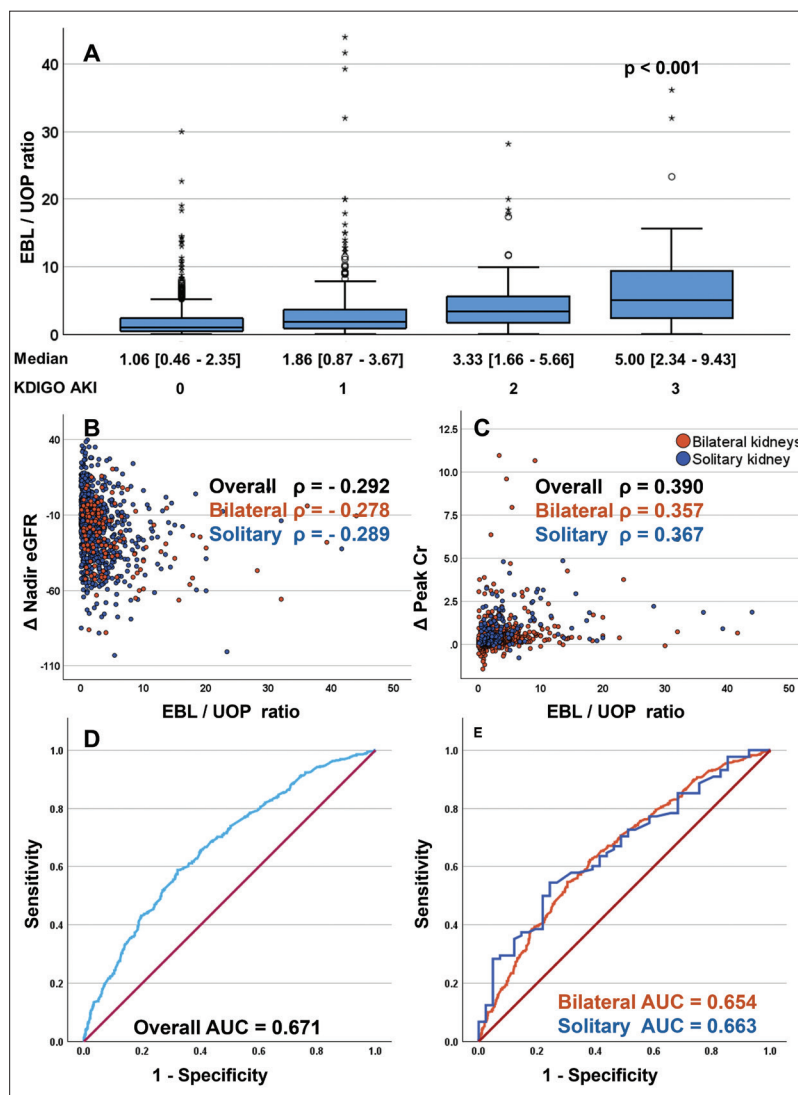


Figure 1. (A) Boxplot figure reporting median and interquartile range (25th–75th) of the estimated blood loss (EBL) to urine output (UOP) ratio under the Kidney Disease Improving Global Outcomes (KDIGO) guidelines for acute kidney injury (AKI) classification after partial nephrectomy. Scatterplot figures and correlational analysis showing of cohort variables; (B) change in nadir estimated glomerular filtration rate (eGFR) in mL/min/1.73 m² (overall $\rho = -0.292$, $p < 0.001$; bilateral native kidneys $\rho = -0.278$, $p < 0.001$; solitary kidney $\rho = -0.289$, $p < 0.001$); and (C) change in peak serum creatinine (Cr) in ng/dL (overall $\rho = 0.390$, $p < 0.001$; bilateral native kidneys $\rho = 0.357$, $p < 0.001$; solitary kidney $\rho = 0.367$, $p < 0.001$) during inpatient hospitalization after partial nephrectomy in correlation with EBL/UOP ratio in patients with bilateral native and solitary kidneys. Receiver operating characteristic (ROC) curves for AKI based on KDIGO (0 vs. 1, 2, or 3) on the (D) overall population (area under the curve (AUC) 0.671, 95% confidence interval (CI) 0.640–0.702, $p < 0.001$); and (E) patient with bilateral native kidneys (AUC 0.654, 95% CI 0.620–0.688, $p < 0.001$) and solitary kidneys (AUC 0.663, 95% CI 0.566–0.761, $p < 0.001$).

PPV increased, and the sensitivity and NPV decreased (Supplementary Table 3; available at [cuaj.ca](#)).

On univariable analysis, a significant association between EBL/UOP and postoperative AKI was observed in the overall population (odds ratio [OR] 1.178, $p < 0.001$) and patients with bilateral (OR 1.102, $p < 0.001$) and solitary kidneys (OR 1.138, $p = 0.020$) (Supplementary Table 4; available at [cuaj.ca](#)). Multivariable analysis showed

Table 3. Multivariable adjusted logistic regression analysis to determine the association between clinical and demographic variables and AKI (KDIGO 0 vs. 1, 2, or 3), in the overall population (N=1166), patients with bilateral kidneys (n=1037), and solitary kidney (n=129)

	Overall			Bilateral kidneys			Solitary kidney		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age at surgery (per 1 year)	1.016	1.003–1.029	0.013	1.011	0.997–1.024	0.115	1.060	1.008–1.116	0.024
Female	0.586	0.426–0.764	<0.001	0.523	0.383–0.716	<0.001	1.119	0.66–3.325	0.879
Race									
White	1			1			1		
Black/African American	1.553	1.002–2.408	0.049	1.634	1.034–2.582	0.035	0.442	0.079–2.351	0.330
Asian	1.276	0.546–2.982	0.573	1.211	0.504–2.910	0.669	–		
Other, multiracial, not reported	1.207	0.740–1.968	0.450	1.274	0.753–2.157	0.367	1.265	0.294–5.263	0.766
Diabetes mellitus	1.357	0.926–1.998	0.117	1.610	1.068–2.427	0.023	0.542	0.167–1.783	0.315
Hypertension	0.939	0.699–1.260	0.673	0.882	0.644–1.208	0.434	1.451	0.491–4.367	0.494
Baseline eGFR (per 10 mL/min/1.73 m ²)	1.037	0.961–1.119	0.348	1.015	0.936–1.102	0.716	1.180	0.880–1.474	0.324
Approach									
Open	1			1			1		
Robotic	0.561	0.408–0.770	<0.001	0.516	0.368–0.724	<0.001	0.927	0.327–2.930	0.969
Laparoscopic	1.459	0.668–3.184	0.343	1.573	0.682–3.629	0.288	0.527	0.032–9.726	0.989
Solitary kidney	2.998	1.862–4.826	<0.001	–	–	–	–	–	–
Partial nephrectomy count									
1	1			1			1		
2	0.986	0.686–1.425	0.941	1.019	0.687–1.511	0.926	0.662	0.196–2.089	0.460
3	1.248	0.740–2.107	0.406	1.161	0.650–2.074	0.613	1.644	0.345–7.475	0.547
≥ 4	2.057	0.848–4.988	0.110	1.681	0.650–4.328	0.284	–		
Tumors removed (per 1 tumor)	1.050	1.019–1.082	0.001	1.041	1.009–1.074	0.011	1.116	1.001–1.256	0.049
Largest tumor removed (per 1 cm)	1.093	1.006–1.187	0.036	1.086	0.998–1.181	0.057	1.178	0.756–1.824	0.476
Overall ischemia time (per 1 minute)	1.028	1.018–1.037	<0.001	1.028	1.018–1.037	<0.001	1.023	0.986–1.064	0.219
Operative time (per 10 minutes)	1.064	1.048–1.080	<0.001	1.064	1.048–1.081	<0.001	1.080	1.006–1.151	0.034
EBL/UOP ratio (per 1 unit)	1.079	1.029–1.131	0.002	1.083	1.028–1.142	0.003	1.039	0.935–1.165	0.447

AKI: acute kidney injury; CI: confidence interval; EBL: estimated blood loss; eGFR: estimated glomerular filtration rate; KDIGO: Kidney Disease Improving Global Outcomes; OR: odds ratio; UOP: urine output.

that in the overall population and patients with bilateral native kidneys, postoperative AKI was associated with increased age at surgery, African American race, number of tumors removed, overall ischemia time, and operative time (p<0.05).

In patients with a solitary kidney, increased age at surgery and operative time were associated with AKI (p<0.05). In the overall population, the robotic surgical

approach and being a female were associated with a lower risk of AKI (p<0.05). Furthermore, EBL/UOP had a significant association with AKI in all patients (OR 1.079, p=0.002) and those with bilateral kidneys (OR 1.083, p=0.003); however, after adjustment in patients with a solitary kidney, no association with EBL/UOP (OR 1.039, p=0.447) was identified (Table 3). EBL/UOP was not significantly associated with AKI in patients with bilateral

kidneys undergoing their first-time single-tumor PN (OR 1.023, $p=0.743$) or patients with baseline eGFR <60 mL/min/1.73 m² (OR 1.065, $p=0.266$) (Supplementary Table 5; available at cuaj.ca).

DISCUSSION

Despite significant advances in urologic surgery, post-PN AKI remains a prevalent complication and must be considered in the management of patients with renal tumors. This hypothesis-generating study aimed to evaluate the utility of EBL/UOP as a potential predictor of AKI following PN and to better identify the populations and clinical contexts in which this novel metric is most informative.

We observed that a higher EBL/UOP was associated with postoperative AKI, worsening KDIGO AKI grade, and lower postoperative eGFR compared to baseline across our entire PN cohort. EBL/UOP appears to be helpful in the immediate postoperative setting to identify patients at increased risk of developing AKI. As the EBL/UOP increased, the risk of developing a higher KDIGO AKI increased, and an EBL/UOP ratio >1 or >2 was found to be associated with increased AKI risk. The ratio was associated with AKI in a subgroup analysis of patients undergoing complex PN (multiple tumors, rePN) and in patients with bilateral kidneys.

Postoperative AKI results from a combination of preoperative risk factors, intraoperative factors (e.g., medications, renal perfusion, ischemia time, parenchymal tissue preserved), and postoperative events, all of which contribute to shared injury pathways involving renal microcirculation, oxygen demand, and inflammation and can have transitional and permanent renal function implications.^{13,14}

We observed an AKI rate of 41.5% in our cohort, with 31.3%, 6.7%, and 3.5% of the total patient cohort experiencing KDIGO stages 1, 2, and 3, respectively. We believe that our cohort's overall AKI rate, which is higher than the previously reported populations, is driven primarily by the relative surgical complexity inherent to hereditary renal cancer patients that are not always present in the broad PN population. Hereditary renal cancer patients are more likely to have a solitary kidney, multiple tumors, and rePN compared to patients with sporadic renal cancer.¹⁵ Therefore, the high prevalence of patients with hereditary kidney cancer syndromes in the analyzed cohort may limit the generalizability of the EBL/UOP to patients with bilateral kidneys undergoing first-time, single-tumor PN.

Given the unique nature of our cohort, we analyzed different subgroups to identify which patients the EBL/UOP can best apply to. We found that EBL/UOP was

a better predictor for AKI in rePN, where more than one tumor was removed, and in patients with bilateral kidneys.

For patients with bilateral kidneys, each unit increase in the ratio was associated with an 8.3% (OR 1.083, $p=0.003$) increased risk of postoperative AKI. For patients with a solitary kidney or baseline eGFR <60 mL/min/1.73 m², no significant association was found between EBL/UOP and postoperative AKI. Patients with solitary kidneys and baseline renal dysfunction are at higher risk of developing post-PN AKI, which may reduce the utility of a predictive measure such as the EBL/UOP.¹⁶

In a small cohort of patients undergoing first-time, single-tumor PN, EBL/UOP appears to be a poor predictor of AKI, possibly due to the preserved renal function of the contralateral kidney, which allows for dynamic autoregulation and maintenance of UOP.¹⁷

Our analysis also supports previous findings that surgical approach, tumor size, and overall operative time are predictors of AKI.¹⁸⁻²¹ We found that a higher EBL/UOP is associated with postoperative AKI for complex PN patients, providing surgeons with an opportunity to modify postoperative management and allowing surgeons a better understanding of the role of hemodynamics in post-PN recovery.²² Urologists may use this ratio in the broader context of the patient's clinical status, intraoperative surgical events, and other medical factors to determine the patient's risk of developing post-PN AKI.

We consider that an EBL/UOP >1 or >2 can be a risk predictor of AKI, thus assisting the surgical team in detecting individuals at risk of AKI before the patient leaves the operating room and facilitating expedited postoperative AKI management;¹³ however, the surgical team should consider the progressive nature of worsening post-PN AKI with higher EBL/UOP, as implementing a strict cutoff value may risk excluding patients who could still benefit from early postoperative AKI diagnosis and tailored management.

Limitations

The limitations of this study include its retrospective design and single-center setting, spanning nearly two decades during which perioperative care for patients undergoing PN has evolved. Those changes in perioperative management protocols might have influenced the EBL and UOP, potentially confounding the EBL/UOP. Additionally, changes over time in PN technical approach might influence the incidence of postoperative AKI.

Our study does not report intraoperative intravenous fluid volume, a critical variable that can directly influence UOP and potentially the ratio. Furthermore, our whole cohort is significantly enriched with hereditary renal cancer syndromes compared to typical urology practice, thus limiting the applicability of our findings to first-time single-tumor PNs, which was observed in our results.

Our sample sizes for subanalysis groups (solitary kidney, baseline eGFR <60, etc.) were small and underpowered, and thus may not be reliable. Moreover, intraoperative confounders such as hypotension, fluid resuscitation protocol, vasopressor use, mannitol use, intraoperative pneumoperitoneum pressure, and transfusion were not addressed due to limitations of retrospective data collection.

There is an inherent patient selection bias, as individuals with certain clinical or surgical characteristics may have been selected for radical nephrectomy and are therefore not represented in this study. Additionally, the present analysis does not account for the experience level of the surgical or anesthesia teams, which may also influence perioperative outcomes.

This study introduces EBL/UOP as a novel tool to assess for post-PN AKI risk in a large PN cohort with a wide range of surgical and clinical complexity. We report that the EBL/UOP is moderately associated with the development of post-PN AKI for patients undergoing multiplex PN or with a history of ipsilateral PN.

In the present analysis, intraoperative fluid management strategies and tumor complexity were not accounted for. Future prospective studies may benefit from incorporating intraoperative fluid management protocols and a standardized tumor complexity grading system, such as the RENAL or PADUA nephrometry scoring system in solitary tumors, the multiplex score system in patients with multiple tumors, or preoperative renal parenchyma volume.²³⁻²⁵ Additionally, in the current era of minimally invasive procedures, where robotic PN is widely adopted for managing sporadic renal tumors, future studies should focus on assessing the utility of EBL/UOP in cohorts consisting solely of patients undergoing a robotic approach, as this more accurately reflects current practice patterns in the management of sporadic renal tumors.²⁶

CONCLUSIONS

In a cohort of predominantly hereditary renal cancer patients undergoing PN, EBL/UOP was associated with postoperative AKI in our whole cohort and a subgroup of patients with complex surgeries and bilateral kidneys.

An increase in the ratio is associated with an increase in KDIGO AKI stage. The ratio can be applied alongside other AKI predictors, including operative time, baseline renal function, hypertension, intraoperative events, and tumor size, to better assess patients' risk of developing post-PN AKI. Prospective evaluation involving management strategies based on the EBL/UOP is needed to determine its true utility in clinical practice and generalization in the broader PN population.

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REFERENCES

- Antonelli A, Allinovi M, Cocci A, et al. The predictive role of biomarkers for the detection of acute kidney injury after partial or radical nephrectomy: A systematic review of the literature. *Eur Urol Focus* 2020;6:344-53. <https://doi.org/10.1016/j.euf.2018.09.020>
- Xu L, Li C, Zhao L, et al. Acute kidney injury after nephrectomy: A new nomogram to predict postoperative renal function. *BMC Nephrol* 2020;21:181. <https://doi.org/10.1186/s12882-020-01839-0>
- Chawla LS, Kimmel PL. Acute kidney injury and chronic kidney disease: An integrated clinical syndrome. *Kidney Int* 2012;82:516-24. <https://doi.org/10.1038/ki.2012.208>
- Speed JM, Trinh QD, Choueiri TK, et al. Recurrence in localized renal cell carcinoma: A systematic review of contemporary data. *Curr Urol Rep* 2017;18:15. <https://doi.org/10.1007/s11934-017-0661-3>
- Antony MB, Kozel Z, Gopal N, et al. Cumulative impact of serial partial nephrectomy for the treatment of recurrent renal masses. *J Urol* 2024;212:431-40. <https://doi.org/10.1097/JU.0000000000004099>
- Zhang S, Jin D, Zhang Y, et al. Risk factors and predictive model for acute kidney injury transition to acute kidney disease in patients following partial nephrectomy. *BMC Urol* 2023;23:156. <https://doi.org/10.1186/s12894-023-01325-3>
- Makevičius J, Čekauskas A, Želvyš A, et al. Evaluation of renal function after partial nephrectomy and detection of clinically significant acute kidney injury. *Medicina (Kaunas)* 2022;58:667. <https://doi.org/10.3390/medicina58050667>
- Hur M, Park SK, Yoo S, et al. The association between intraoperative urine output and postoperative acute kidney injury differs between partial and radical nephrectomy. *Sci Rep* 2019;9:760. <https://doi.org/10.1038/s41598-018-37432-7>
- Shiba A, Uchino S, Fujii T, et al. Association between intraoperative oliguria and acute kidney injury after major noncardiac surgery. *Anesth Analg* 2018;127:1229-35. <https://doi.org/10.1213/ANE.0000000000003576>
- Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med* 2021;385:1737-49. <https://doi.org/10.1056/NEJMoa2102953>
- Antony MB, Gopal N, Kozel Z, et al. Comparison of race-based and non-race-based glomerular filtration rate equations for the assessment of renal functional risk before nephrectomy. *Urology* 2023;172:144-8. <https://doi.org/10.1016/j.urology.2022.11.032>
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int* 2024;105(4S):S117-314. <https://doi.org/10.1016/j.kint.2023.10.018>
- Boyer N, Eldridge J, Prowle JR, Forni LG. Postoperative acute kidney injury. *Clin J Am Soc Nephrol* 2022;17:1535-45. <https://doi.org/10.2215/CJN.16541221>
- Rosiello G, Capitanio U, Larcher A. Acute kidney injury after partial nephrectomy: Transient or permanent kidney damage? impact on long-term renal function. *Ann Transl Med* 2019;7(Suppl 8):S317. <https://doi.org/10.21037/atm.2019.09.156>
- Yanus GA, Kuligina ES, Imyanitov EN. Hereditary renal cancer syndromes. *Med Sci (Basel)* 2024;12:12. <https://doi.org/10.3390/medsci12010012>
- Zhu K, Song H, Zhang Z, et al. Acute kidney injury in solitary kidney patients after partial nephrectomy: Incidence, risk factors and prediction. *Transl Androl Urol* 2020;9:1232-43. <https://doi.org/10.21037/tau.2020.03.45>
- Carlström M, Wilcox CS, Arendshorst WJ. Renal autoregulation in health and disease. *Physiol Rev* 2015;95:405-511. <https://doi.org/10.1152/physrev.00042.2012>

18. Pyrgidis N, Schulz GB, Stief C, et al. Surgical trends and complications in partial and radical nephrectomy: Results from the GRAND study. *Cancers (Basel)* 2023;16:97. <https://doi.org/10.3390/cancers16010097>
19. Rajan S, Babazade R, Govindarajan SR, et al. Perioperative factors associated with acute kidney injury after partial nephrectomy. *Br J Anaesth* 2016;116:70-6. <https://doi.org/10.1093/bja/aev416>
20. Lazebnik T, Bahouth Z, Bunimovich-Mendrazitsky S, et al. Predicting acute kidney injury following open partial nephrectomy treatment using SAT-pruned explainable machine learning model. *BMC Med Inform Decis Mak* 2022;22:133. <https://doi.org/10.1186/s12911-022-01877-8>
21. Wu Y, Chen J, Luo C, et al. Predicting the risk of postoperative acute kidney injury: Development and assessment of a novel predictive nomogram. *J Int Med Res* 2021;49:3000605211032838. <https://doi.org/10.1177/03000605211032838>
22. Cannesson M, Pestel G, Ricks C, et al. Hemodynamic monitoring and management in patients undergoing high risk surgery: A survey among North American and European anesthesiologists. *Crit Care* 2011;15:R197. <https://doi.org/10.1186/cc10364>
23. Xiao Y, Shan ZJ, Yang JF, et al. Nephrometric scoring system: Recent advances and outlooks. *Urol Oncol* 2023;41:15-26. <https://doi.org/10.1016/j.urolonc.2022.06.019>
24. Chalfin HJ, Yerram N, Owens-Walton J, et al. A novel multiplex score to predict outcomes of partial nephrectomy for multiple tumors. *Urol Oncol* 2023;41:257.e1-6. <https://doi.org/10.1016/j.urolonc.2023.03.007>
25. Antony MB, Anari PY, Gopal N, et al. Preoperative renal parenchyma volume as a predictor of kidney function following nephrectomy of complex renal masses. *Eur Urol Open Sci* 2023;57:66-73. <https://doi.org/10.1016/j.euros.2023.08.010>
26. Alameddine M, Koru-Sengul T, Moore KJ, et al. Trends in utilization of robotic and open partial nephrectomy for management of cT1 renal masses. *Eur Urol Focus* 2019;5:482-7. <https://doi.org/10.1016/j.euf.2017.12.006>

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