



# Urine leak in minimally invasive partial nephrectomy: analysis of risk factors and role of intraoperative ureteral catheterization

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## ABSTRACT

**Purpose:** To investigate risk factors for urine leak in patients undergoing minimally invasive partial nephrectomy (MIPN) and to determine the role of intraoperative ureteral catheterization in preventing this postoperative complication.

**Materials and Methods:** MIPN procedures done from September 1999 to July 2012 at our Center were reviewed from our IRB-approved database. Patient and tumor characteristics, operative techniques and outcomes were analyzed. Patients with evidence of urine leak were identified. Outcomes were compared between patients with preoperative ureteral catheterization (C-group) and those without (NC-group). Univariable and multivariable analyses were performed to identify factors predicting postoperative urine leak.

**Results:** A total of 1,019 cases were included (452 robotic partial nephrectomy cases and 567 laparoscopic partial nephrectomy cases). Five hundred twenty eight patients (51.8%) were in the C-group, whereas 491 of them (48.2%) in the NC-group. Urine leak occurred in 31(3%) cases, 4.6% in the C-group and 1.4% in the NC-group ( $p < 0.001$ ). Tumors in NC-group had significantly higher RENAL score, shorter operative and warm ischemic times. On multivariable analysis, tumor proximity to collecting system (OR=9.2;  $p < 0.01$ ), surgeon's early operative experience (OR=7.8;  $p < 0.01$ ) and preoperative moderate to severe CKD (OR=3.1;  $p < 0.01$ ) significantly increased the odds of the occurrence of a postoperative urine leak.

**Conclusion:** Clinically significant urine leak after MIPN in a high volume institution setting is uncommon. This event is more likely to occur in cases of renal masses that are close to the collecting system, in patients with preoperative CKD and when operating surgeon is still in the learning curve for the procedure. Our findings suggest that routine intraoperative ureteral catheterization during MIPN does not reduce the probability of postoperative urine leak. In addition, it adds to the overall operative time.

## ARTICLE INFO

**Key words:** complications [Subheading]; Nephrectomy; Risk Factors; Urinary Incontinence; Ureter; Urinary Catheters

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## INTRODUCTION

Partial nephrectomy (PN) has widely replaced radical nephrectomy in the management

of renal neoplasms by offering renal functional preservation without compromising oncological outcomes (1). With widespread uptake of PN, complications unique to this surgery became more

recognized. Among them, postoperative urine leak is regarded as a clinically significant entity, which negatively impacts patient's recovery (2-5). Inadequate repair of a violated collecting system during renorrhaphy is the cause of postoperative urine leak. The management of urine leak is tailored depending on the case. The treatment options include observation, percutaneous drainage, ureteral drainage and surgical interventions (6-8).

Intraoperative ureteral catheterization during PN has been traditionally used as a measure to recognize and prevent the occurrence of urine leaks (9). The concept behind this practice was that intra-operative retrograde dilute methylene-blue instillation could confirm collecting system entry and water tightness of the repair. With accumulation of experience with the technique, routine ureteral cannulation was reserved for central, more complex renal tumors (10). Ureteral catheterization however adds to the total operative time and costs. With advancements in minimally invasive techniques for PN, the routine use of ureteral catheterization has been further questioned (11). Overall, the utility of routine ureteral catheterization during PN has not been well studied.

The aim of this study was to investigate risk factors for urine leak in patients undergoing minimally invasive partial nephrectomy (MIPN) and to determine the role of intraoperative ureteral catheterization in preventing this postoperative complication.

## MATERIALS AND METHODS

### Study population

Our IRB-approved prospectively maintained institutional database was queried to identify MIPN cases (laparoscopic and robotic) performed at our Center from September 1999 to July 2012.

Patients' demographic characteristics, including age, BMI, and ASA as well as tumor characteristics, including R.E.N.A.L nephrometry score (12) were assessed. Main intraoperative parameters, including technique modality (laparoscopic or robotic), use of ureteral catheterization, operative time (calculated from skin incision to skin closure, including ureteral catheterization time), warm ischemia time (WIT), and estimated blood loss (EBL) were recorded.

Cases with intraoperative ureteral injury were excluded. Patients with ureteral abnormality such as ureteropelvic junction obstruction or duplicated collecting were also excluded.

Surgical experience was taken into account in the analysis. Completion of the learning curve was considered to be 25 cases for RPN and 50 cases for LPN according to previous publications (13, 14).

Clinically significant urine leak was defined as persistent drain output >48 hours after PN with biochemical analysis consistent with urine or radiographic evidence of urine leak (15). Radiological imaging was only performed where patient's clinical status or symptoms were suggestive of urine leak (Figure-1).

### Surgical technique

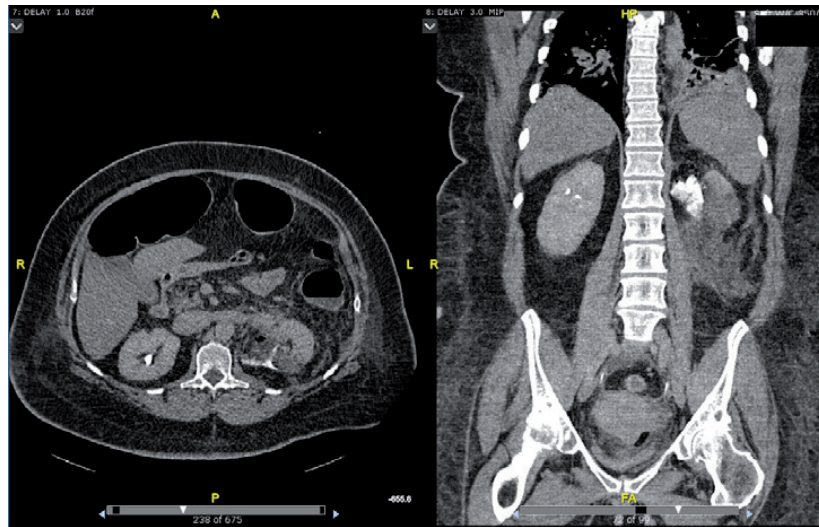
The decision for ureteral catheterization was at the discretion of surgeon on case by case basis. Ureteral catheterization was performed immediately after induction of general anesthesia with the patient in lithotomy position, using rigid cystoscopy. An open ended 6 French ureteral catheter was passed over the guide wire and catheter was secured to the Foley catheter. A syringe filled with dilute methylene blue was attached to the catheter for later instillation. The patient was then repositioned in the modified lateral decubitus position and PN commenced. Ureteric catheter was removed at the end of the procedure.

Our surgical techniques for both laparoscopic (LPN) and robot assisted PN (RPN) have been previously described (16, 17).

Essential steps of the laparoscopic technique include renal defatting, maintaining fat over the tumor, laparoscopic ultrasound to score the resection line, hilar clamping, tumor excision with cold scissors, suture repair of the collecting system and sutured renorrhaphy over a hemostatic bolster.

The robotic technique included tumor identification under ultrasound guidance and its demarcation, hilar clamping, tumor excision, closure of the kidney defect using two layers of horizontal mattress sutures, one to close entries to the collecting system and the other to approximate the renal capsule (17). Early in our robotic experience, standard interrupted bolstered renorrhaphy was used for capsule closure (18).

**Figure 1 - Axial and coronal CT images documenting left urine leak after surgery.**



For both laparoscopic and robotic cases, a Jackson-Pratt drain was left in the perinephric space.

### Analysis

Estimated glomerular filtration rate (eGFR) was calculated using modification of diet in renal disease (MDRD) formula. Moderate to severe chronic kidney disease (CKD) was defined as  $eGFR < 60 \text{ mL/min/1.73m}^2$ .

For continuous data with normal distribution variables are presented as mean  $\pm$  standard deviation (SD). The mean values were compared using student's t-test. For variables with non-normal distribution, data is presented as median (IQR) and the groups were compared using Mann-Whitney U test. Categorical variables were compared using chi-squared test.

A comparative analysis was performed between the group where a ureteral catheter was used (C group) and the one where this was not used (NC group).

Univariable and multivariable logistic regression analyses were performed to calculate odd ratios for factors affecting urinary leak. These included surgical technique (laparoscopic or robotic), learning curve (beyond or within), age (continuous), BMI (continuous), renal function (moderate to severe CKD vs. mild CKD to normal renal function), tumor size (continuous), growth

pattern ( $>$  or  $<$  50% endophytic), proximity to collecting system ( $>$  or  $<$  7mm), WIT (continuous), EBL (continuous) and use of intraoperative ureteral catheterization (yes or no).

Statistical significance was set at  $p < 0.05$ . Variables were entered into multivariable model if  $p < 0.2$  for univariable analysis. All analyses were performed using SPSS v21 software (IBM SPSS Statistics, Armonk, NY: IBM Corp).

### RESULTS

A total of 1019 MIPN cases were considered in this analysis, including 567 LPN cases (55.6%) and 452 RPN cases (44.4%) (Table-1).

Table-2 summarizes the main surgical outcomes for the entire series. In 528 cases (51.8%) intra-operative ureteral catheterization was used. A total of 31 (3.0%) urine leaks were detected postoperatively and managed using stenting, CT-guided drainage or observation.

There were no differences in the patients' age, gender, BMI, ASA, renal function, tumor laterality and solitary kidney status between C-group and NC-group (Table-3). Tumors in the C-group presented a lower overall R.E.N.A.L nephrometry score, longer distance from the collecting system, smaller size and more exophytic location compared to NC-group. The majority of cases in C-group

**Table 1 - Population Demographics (n=1019).**

Variable		Value
<b>Age, years</b>	Mean±SD	59.1±12.4
<b>ASA</b>	Median (IQR)	3 (1)
<b>BMI, kg/m<sup>2</sup></b>	Mean±SD	29.9±7
<b>Tumor Laterality, n (%)</b>	Right	552 (54.2)
	Left	467 (45.8)
<b>Tumor Size, cm</b>	Median (IQR)	2.5 (1.7)
<b>Technique, n (%)</b>	Laparoscopic	567 (55.6)
	Robotic	452 (44.4)
<b>Preoperative GFR, mL/min/1.73m<sup>2</sup></b>	Median (IQR)	81.1 (29.8)
<b>RENAL Nephrometry Score</b>	Median (IQR)	6 (3)
<b>Solitary Kidney, n (%)</b>		42 (4.1)

**ASA:** American Society of Anesthesiologists; **GFR:** Glomerular Filtration Rate; **BMI:** Body Mass Index; **SD:** Standard Deviation; **IQR:** Inter-Quartile Range.

**Table 2 - Surgical Outcomes (n=1019).**

Variable		Value
<b>Intra operative Ureteral Catheterization, n (%)</b>		528 (51.8)
<b>Operative Time, min</b>	Mean±SD	196.9±59.7
<b>Unclamped Renal Hilum, n (%)</b>		71 (7)
<b>Warm Ischemia Time, min</b>	Median (IQR)	26(15)
<b>Zero Ischemia, n (%)</b>		68 (6.7)
<b>Estimated Blood Loss, mL</b>	Median (IQR)	150 (200)
<b>Urine Leak, n (%)</b>		31 (3)
<b>Urine Leak Management, n (%)</b>	Ureteral Stenting	19 (61.3)
	CT-guided Drainage	3* (9.7)
	Observation	11 (35.5)
<b>Length of Stay, days</b>	Median (IQR)	3 (2)
<b>Follow up, months</b>	Median (IQR)	18 (34)

\*Two of those had also ureteral stents and counted also in that group  
**SD:** Standard Deviation, **IQR:** Inter-Quartile Range.

**Table 3 - Comparison between Populations under Study (n=1019).**

Variable		C-Group (n=528)	NC-Group (n=491)	p-Value
Technique, n (%)	Laparoscopic	468 (88.6)	99 (20.2)	0.001
	Robotic	60 (11.4)	392 (79.8)	
RENAL Nephrometry Score, median (IQR)		6 (2)	7 (4)	0.001
Cases performed by surgeons during learning curve, n (%)		124 (23.5)	64 (13)	0.001
Tumor size > 4cm, n (%)		67 (12.7)	102 (20.8)	0.001
Tumor growth pattern >50% endophytic, n (%)		190 (39.8)	201 (46.6)	0.03
Nearness to CS or Sinus < 7mm, n (%)		206 (42.4)	219 (50.8)	0.01
Operative Time, min, mean±SD		210.6±63.5	180.5±50.1	0.001
Warm Ischemia Time, min, median (IQR)		31 (13)	20 (12)	0.001
Urine Leak, n (%)		24 (4.6)	7 (1.4)	0.001

**C-Group:** Ureteral Catheterization used; **NC-Group:** Ureteral Catheterization not used; **CS:** Collecting System; **BMI:** Body Mass Index; **ASA:** American Society of Anesthesiologists

were done laparoscopically, whereas only 20% were done laparoscopically in NC-group (88.6% vs. 20.2%,  $p=0.001$ ). The operative time was longer for patients in C-group (211 vs. 180 min,  $p<0.01$ ). Once we control for ureteric catheterization, there is no difference in operating time between LPN and RPN ( $186\pm 51.2$  vs.  $178\pm 49.5$  min,  $p=0.17$ ). There were 24 (4.6%) cases of urine leak in C-group as compared to 7 (1.4%) cases in NC-group ( $p=0.001$ ). For LPN cases there was no difference in practice of ureteric catheter insertion with increasing experience. The rate of utility of ureteric catheter was 80.2% for surgeons within and 83% for surgeons beyond learning curve ( $p=0.49$ ). For RPN group, this proportions were 49.4% and 4.7 % respectively ( $p=0.001$ ) (Figure-2).

On univariable analysis, use of laparoscopy, presence of moderate to severe CKD, tumor nearness to collecting system or renal sinus, EBL and use of ureteral catheter had significantly higher odds of urine leak (Table-4).

On multivariable analysis, (Table-4), nearness of the tumor to collecting system (OR=9.2;  $p=0.003$ ), early surgeon's experience (OR=7.8;

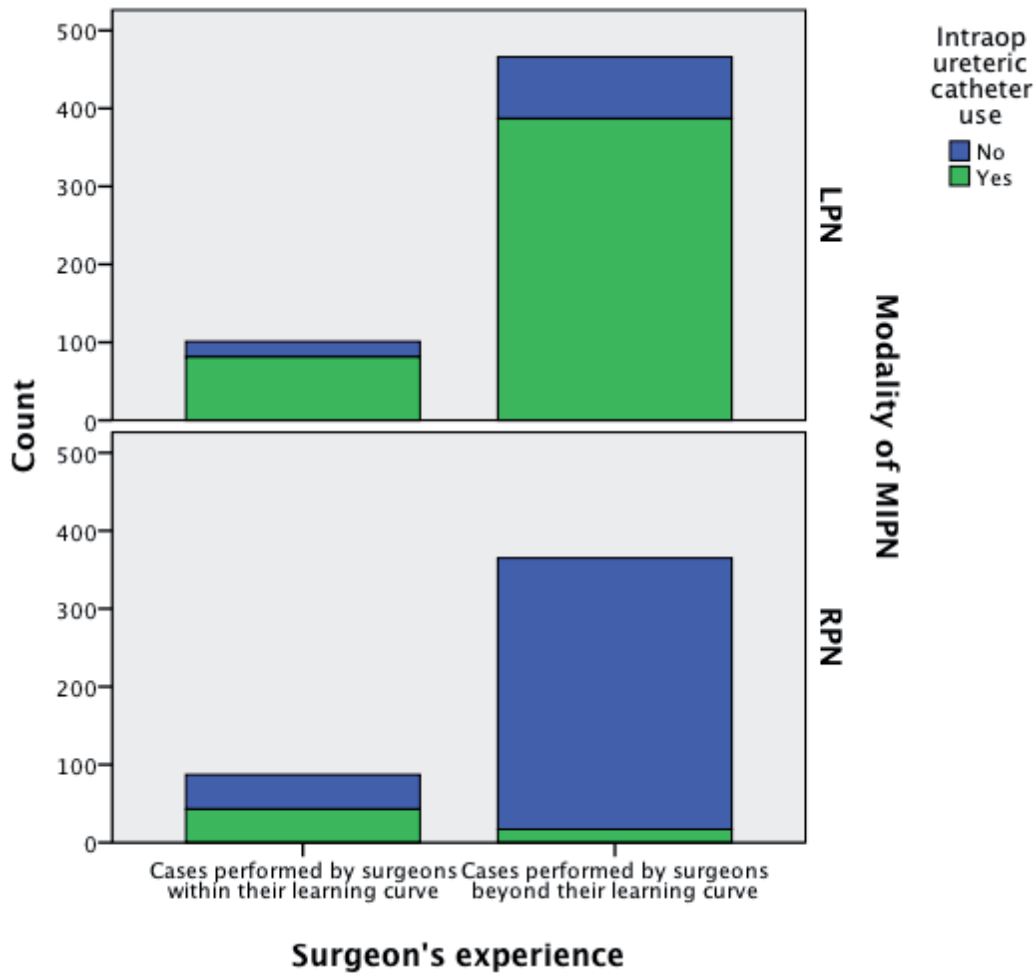
$p=0.001$ ), moderate to severe CKD (OR=3.1;  $p=0.04$ ) and EBL (OR 1.002;  $p=0.003$ ) were associated with higher urine leak occurrence. Intraoperative ureteral catheterization had no significant effect on urine leak occurrence (OR=1.3;  $p=0.67$ ).

## DISCUSSION

Urine leak is related to an incomplete repair of the collecting system at the time of renorrhaphy and it potentially represents a clinically significant complication of PN procedure (2-5). The reported incidence rate of urine leak post PN varies among institutions. Despite being low at high volume centers (3), as confirmed in the present analysis, it may result in considerable morbidity and financial cost.

Management of urine leak after PN is varied according to the clinical scenarios (8). Observation is the most conservative approach with serial cross sectional imaging at given time intervals. In other situations, selective placement of a ureteral stent facilitates drainage of urine from the collecting system and creates a low-pressure system that promotes healing of the defect. Complicated urine leaks may

**Figure 2 - Bar graphs demonstrating the rate of employment of intraoperative ureteric catheter according to surgeon's experience for both LPN and RPN.**



require invasive procedures, such as percutaneous drainage or surgical re-intervention. Investigational less invasive avenues are being explored, such as retrograde injection of sealant through the ureteral stent (6).

Routine intraoperative ureteral catheterization during PN has been used as an intra-operative measure to minimize the risk of urine leak. This practice has been carried from early open PN to LPN and even early RPN experience (9, 18, 19). Ureteral catheterization is time consuming, incurs additional cost and is not without risk of complications.

The decision for pre-operative ureteral catheterization in our series was based on surgeon's preference on case-by-case basis. This was also

influenced by the minimally invasive modality and surgeon's own experience with that modality. For LPN cases, the use of ureteral catheter was not influenced by surgeon's experience or tumor complexity. For RPN cases ureteral catheter was inserted in 49.4% of cases performed within the surgeons' learning curve and only in 4.7% of cases beyond that. This was the case despite an increase in overall tumor complexity.

Compared to RPN, tumors treated with LPN were less complex and had lower R.E.N.A.L nephrometry scores. This trend has been observed by other series (20). Surgeons experience with the modality of MIPN treatment affected the rate of urinary leak regardless of tumor complexity score (apart from the degree of endophytic growth) and

**Table 4 - Univariable and Multivariable Analysis of factors predicting postoperative urine leak.**

Variable	Univariable Analysis				Multivariate Analysis			
	OR	95% CI	p-value	OR	95% CI	p-value		
Laparoscopic vs. Robotic	2.3	1	5.3	0.04	1.29	0.3	5.6	0.73
Age	1	0.97	1.02	0.95				
Learning Curve (within vs. beyond)	1.84	0.8	4	0.13	7.8	2.5	24.3	<b>0.001</b>
BMI	1.03	0.99	1.07	0.13	1.06	0.99	1.13	0.07
Charlson Comorbidity Index	1.09	0.9	1.3	0.38				
Preop GFR (<60 vs. ≥60mL/min/1.73m <sup>2</sup> )	2.2	1.0	4.7	<b>0.049</b>	3.13	1.06	9.3	<b>0.04</b>
RENAL score	1.19	0.95	1.5	<b>0.13</b>				
REAL score (N removed)	1.19	0.95	1.5	<b>0.13</b>	0.91	0.62	1.3	0.62
Tumor Size (> 4 vs. ≤4cm)	1.2	0.5	3.0	0.67				
Tumor Growth (>50% vs. ≤50% endophytic)	1.0	0.4	2.4	0.99				
Nearness to CS or Sinus (<7mm vs. ≥7mm)	2.6	1.2	5.5	<b>0.01</b>	9.2	2.1	40.2	<b>0.003</b>
Ureteral Catheterization (presence vs. absence)	3.3	1.4	7.7	<b>0.006</b>	1.3	0.32	5.6	0.67
WIT	1	0.97	103	0.96				
Zero ischemia (Yes vs. No)	1.6	0.47	5.4	0.45				
EBL	1.001	1	1.002	<b>0.001</b>	1.002	1	1.003	<b>0.003</b>

CS: Collecting System; OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; Preop: Preoperative,

use of intraoperative ureteral catheter. Kidneys operated during the surgeons' learning curve, had 7.8 fold higher probability of developing urine leak (p=0.001).

Proximity of the tumor to the collecting system also increased the odds of urine leak (OR=9.2; p=0.003). This is not surprising as a complete excision of these tumors, without entering the collecting system is not possible. This in turn, increases the likelihood of subsequent urine leak. This has been previously reported in large multi-institutional series (3, 21). Bruner et al. identified tumor's R.E.N.A.L nephrometry score was associated with risk of urine leak after PN (10). The authors reported that for each unit increase

in R.E.N.A.L nephrometry the odds of urine leak increased by 35% (OR 1.35; 95% CI 1.08-1.69; P=0.009).

Presence of moderate to severe CKD was also found to be associated with increased likelihood of urine leak (OR=3.1; p=0.04). CKD has long been associated with poor wound healing (22) and this is a possible explanation for our finding.

On multivariable regression, the use of intraoperative ureteral catheterization was not a significant factor toward developing (or preventing) collecting system leak (p=0.19). EBL increased the odds of urinary leak, and this is likely a surrogate for complexity of surgery.

The rate of urine leak in contemporary PN series is around 1-5% (3, 23, 24). Kundu et al. reported that larger tumor sizes, higher estimated blood loss and longer ischemia time were associated with fistula formation. Apart from EBL, we did not identify any associated of urine leak with these factors in our cohort.

The operative time was longer for patients in C-group (211 vs. 180 min,  $p < 0.01$ ). Given smaller and less complex tumors in C-group, the ureteric catheterization is the likely reason for increase in operating time observed in this group.

On univariable analysis, RPN had significantly lower rate of urine leak compared to LPN group, but on multivariable analysis the groups were comparable despite more complex tumors in the RPN group. Given the small number of events (31 leaks) and differences in complexity of the tumors between the RPN and LPN groups, it is difficult to reach a definite conclusion on this. However, it can be speculated that the better vision offered by robotic console and the articulation ability of robotic instruments facilitate better identification and repair of the breached collecting systems (25, 26). This could be another explanation with regards to decrease utility of intraoperative ureteral catheter in the robotic cohort.

Bove et al. concluded that in selected group of patients ( $n=103$ ) with small (mean size  $< 3\text{cm}$ ) renal mass undergoing LPN, routine use of ureteral catheter is not indicated (11). We have confirmed this finding in a large ( $n=1019$ ) series of LPN and RPN cases, with 425 of patients having tumors in close proximity to collecting system and 169 patients having tumor sizes  $> 4\text{cm}$ .

Lack of randomization, heterogeneous nature of the series and retrospective aspect of data are the main limitation of our series. Moreover, the small number of events further limits the analysis. In addition, the large volume nature of our center's experience with PN might limit the applicability of our findings to other settings. Despite these, we believe that our results provide the answer to the question of routine ureteral catheter use in PN. Lastly, it was outside the scope of the present study to perform a formal cost-analysis, so it remains to be demonstrated whether additional cost and time for ureteral catheterization

outweighs the cost involved in the management of urine leaks eventually occurring postoperatively.

## CONCLUSIONS

Clinically significant urine leak after MIPN in a high volume institution setting is uncommon. This event is more likely to occur in cases of renal masses that are close to the collecting system, in patients with preoperative CKD and when operating surgeon is still in the learning curve for the procedure. Our findings suggest that routine intraoperative ureteral catheterization during MIPN does not reduce the probability of postoperative urine leak. In addition, it adds to the overall operative time.

## CONFLICT OF INTEREST

None declared.

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