

Running Head: Hydronephrosis as a risk factor for bleeding in PCNL

Is Absence of Hydronephrosis a Risk Factor for Bleeding in Conventional Percutaneous Nephrolithotomy?

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ABSTRACT

Purpose: There is conflict of evidence regarding whether absence of hydronephrosis is a risk factor for bleeding in percutaneous nephrolithotomy (PNL). Moreover, among the stone complexity scoring system used for PNL (Guy's stone score, the S.T.O.N.E. nephrometry and the CROES nomogram), only the S.T.O.N.E. nephrometry score incorporates hydronephrosis as a risk factor. Therefore, this study aimed to compare perioperative outcomes according to the presence or absence of hydronephrosis in percutaneous nephrolithotomy (PCNL) patients and to investigate whether absence of hydronephrosis is a risk factor for blood transfusion rate.

Materials and Methods: 281 patients who had undergone PCNL between December 2009 and April 2017 were divided according to the absence or presence of hydronephrosis (group I and group II, respectively). Perioperative outcomes were compared between the two groups. A multivariable regression analysis was performed to investigate whether hydronephrosis was a risk factor for blood transfusion rate.

Results: Patients without hydronephrosis showed significantly longer operation time and admission period, lower stone-free rate and higher blood transfusion rate compared to patients with hydronephrosis ($p < 0.05$, $p = 0.002$, $p = 0.011$, and $p < 0.05$, respectively). Multivariate logistic regression analysis showed that hydronephrosis was a significant risk factor for blood transfusion (OR, 95% CI and p value was 0.353, 0.163-0.761 and 0.008, respectively).

Conclusion: Based on the results of the current study, we found that absence of hydronephrosis was a significant risk factor for blood transfusion in conventional PCNL.

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) remains an integral part of treatment for large complex renal stones. In studies where practice patterns of urolithiasis were surveyed, more than 80% of urologic practitioners responded that they performed PCNL ^(6,7). Despite its wide use, complication rates are still relatively high. A large prospective study using the modified Clavien-Dindo classification system reported an overall complication rate of 20.5% ^(8,9). Bleeding is the most significant complication of PCNL, with reported rates of bleeding requiring blood transfusion ranging between 0 and 20% ⁽¹⁰⁾. Numerous studies have attempted to elucidate the risk factors for bleeding ⁽¹¹⁻¹⁴⁾.

Among those factors, we focused on hydronephrosis. The presence or absence of hydronephrosis is associated with various steps in the PCNL procedure, especially during the initial renal access. In the absence of hydronephrosis, iatrogenic hydronephrosis is usually made via ureteral catheter, which can assist in successful renal access and theoretically, bleeding should not be a problem. Nevertheless, there is conflicting evidence in the literature whether the presence or absence of hydronephrosis affects bleeding during PCNL ^(11,13-15). Some claim that hydronephrosis did not have any effect on blood loss, while others claim that absence of hydronephrosis was a significant risk factor for severe bleeding. Moreover, among the stone complexity scoring system used for PNL (Guy's stone score ⁽¹⁶⁾, the S.T.O.N.E. nephrometry ⁽¹⁷⁾ and the CROES nomogram ⁽¹⁸⁾), only the S.T.O.N.E. nephrometry score incorporates hydronephrosis as a risk factor.

Therefore, the aim of this study was to compare perioperative outcomes according to the presence or absence of hydronephrosis in PCNL patients and to investigate whether absence of hydronephrosis is a risk factor for blood transfusion.

PATIENTS AND METHODS

Study Population and Design

The Institutional Review Board of St. Vincent's Hospital, the Catholic University of Korea, approved the study protocol. This was a retrospectively case-control study. Chart review of all patients who underwent PCNL with a follow up period of at least 3 months between December 2009 and April 2017 was conducted. The following patients were excluded: patients who underwent bilateral PCNL, patients with kidney anomalies (including horseshoe kidney), patients who underwent another operation simultaneously, patients who had multiple tracts, and patients with a preexisting percutaneous nephrostomy tract through which renal access was achieved. A total of 281 patients were eligible for the current study. The following information was recorded as patient characteristics: age, sex, body mass index (BMI), history of diabetes mellitus (DM), history of hypertension, and history of chronic kidney disease (CKD). The following information was recorded as stone characteristics: laterality, absence or presence of hydronephrosis, Guy's stone score ⁽¹⁶⁾, stone volume ⁽¹⁹⁾ and staghorn stone. Staghorn stones were excluded for stone volume calculation. Finally, the following information was recorded as perioperative outcomes: operation time (minutes), admission period (days), stone-free rate (%), blood transfusion rate (%) and infectious complication rate (%). Operation was considered successful when the follow up image showed no residual stones or clinically insignificant residual fragments (CIRFs). In the current study, CIRFs were considered to be $\leq 4\text{mm}$, nonobstructing, noninfectious, and asymptomatic residual fragments⁽²⁰⁾. Additionally, only microbiologically or radiographically confirmed febrile urinary tract infection was recorded as an infectious complication; simple postoperative fever was not included. The study population was divided into two groups: group I was defined as patients without hydronephrosis and group II as patients with hydronephrosis.

Surgical Technique

Urine culture with an antibiotic susceptibility test was done in every patient planned for PCNL.

If the urine culture result was positive, then susceptible oral antibiotics were administered for one week before admission. Otherwise, a prophylactic antibiotic was administered just before surgery. After general endotracheal anaesthesia, a ureteral occlusion balloon catheter was inserted via cystoscope with the patient in lithotomy position. The patient was then turned to the prone position. Percutaneous renal access was achieved with fluoscopic assistance. The access tract was dilated with a balloon dilator and a 30F Amplatz sheath was inserted. A rigid 26F nephroscope was inserted and the stone was fragmented with an ultrasonic lithotripter and removed with forceps. At the end of the operation, an antegrade ureteral catheter was inserted and a 20F nephrostomy tube was placed.

Data Analysis

SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was used for the statistical analysis. Descriptive statistics were used to describe the results. The comparison of continuous variables was performed using the unpaired t-test or the Mann-Whitney test based on the result of the Shapiro-Wilk test for normality. The comparison of categorical variables was performed using the chi-square test or Fisher's exact test. A multivariate logistic regression analysis was conducted to investigate whether hydronephrosis was a risk factor for blood transfusion. p values < 0.05 were considered significant.

RESULTS

Baseline patient and stone characteristics are described in **Table 1**. Of the 281 patients, the number of patients without hydronephrosis (group I) was 95 (33.8%) and the number of patients with hydronephrosis (group II) was 186 (66.2%). There were no significant differences in age, sex, BMI, history of DM, history of hypertension, history of chronic kidney disease or stone laterality. A significant difference was noted in Guy's stone score, as the percentage of

grade 2 stones was higher in group II ($p < 0.05$) and the percentage of grade 3 and grade 4 stones was higher in group I ($p = 0.001$ and $p < 0.05$, respectively), implying that the group without hydronephrosis contained patients with more complex stones. The stone volume was significantly higher in group II ($p = 0.01$), but this was because staghorn stones were not included for stone burden calculation. The proportion of staghorn stones was significantly higher in group I ($p = 0.001$).

The comparison of perioperative outcomes between group I and group II is described in **Table 2**. Significant differences were found in operation time, admission period, stone-free rate, and the blood transfusion rate between group I and group II ($p < 0.05$, $p = 0.002$, $p = 0.011$, and $p < 0.05$, respectively). In short, patients without hydronephrosis showed longer operation time and admission period, lower stone-free rates, and higher blood transfusion rate compared to patients with hydronephrosis.

To determine whether hydronephrosis was a risk factor for transfusion, a univariate and multivariate logistic regression analysis was performed (**Table 3**). Absence of hydronephrosis was a significant risk factor for blood transfusion, with an odds ratio of 0.353, a confidence interval of 0.163-0.761, and a p value of 0.008.

DISCUSSION

The current study sought to investigate whether hydronephrosis was a significant risk factor for blood transfusion rate. The implication of hydronephrosis on surgical outcomes, especially bleeding, in PCNL is not well established. Previous studies showed conflicting results. Kukreja et al reported in their prospective study in 2004 that hydronephrosis did not have any effect on blood loss⁽¹³⁾. However, in their study, the PCNL procedure was staged for a large stone burden, prolonged operation time and the occurrence of significant complications such as perforation or bleeding, which could have affected their results. In a study by Akman et al in which factors

affecting bleeding during PCNL were studied ⁽¹¹⁾, hydronephrosis was not a significant factor, although the *p* value nearly showed significance (*p* = 0.06). In contrast, Lee et al and Senocak et al found out that the absence of hydronephrosis was a significant risk factor for bleeding during PCNL ^(14,15). Moreover, among the stone complexity scoring system used for PCNL (Guy's stone score ⁽¹⁶⁾, the S.T.O.N.E. nephrometry ⁽¹⁷⁾ and the CROES nomogram ⁽¹⁸⁾), only the S.T.O.N.E. nephrometry score incorporates hydronephrosis as a risk factor, again showing that hydronephrosis is not thought of as an important factor during PCNL.

In the current study, the absence of hydronephrosis was found to be a significant risk factor for blood transfusion after PCNL. Several hypotheses can be proposed for the current result. First, the difference in Guy's stone score between the two groups may be the main reason. Patients without hydronephrosis tended to have higher Guy's stone scores, indicating more complex stones, which is thought to be due to diverticular and staghorn stones in the group without hydronephrosis. The higher proportion of higher complexity stones may have caused the higher transfusion rate in the group without hydronephrosis. This result is validated by other studies as increased Guy's stone scores were associated with increased complication rates ⁽²¹⁾. One interesting finding from the result of the current study is that even with the same Guy's stone score, blood transfusion rate can vary depending on the presence or absence of hydronephrosis, suggesting that Guy's stone score alone may be insufficient to predict the complication rate of PCNL. This may imply that hydronephrosis should be included in scoring systems to predict outcomes for PCNL. The only scoring system used for PCNL that includes hydronephrosis is, as previously mentioned, the S.T.O.N.E. nephrometry score ⁽¹⁷⁾. However, although this system has been validated for its predictive ability of the stone-free rate, the utility of this scoring system for stratifying complication rates has not been asserted ⁽²²⁾. Further study is needed in this aspect.

The second possible reason for the result of the current study is that the absence of

hydronephrosis may have led to increased bleeding due to vascular injury during initial renal access. The ideal location for initial renal access is through the calyceal fornix because this will avoid the interlobar (infundibular) arteries adjacent to the calyceal infundibula and the arcuate arteries along the renal pyramid⁽²³⁾. In the presence of hydronephrosis, this process is relatively straightforward because of the dilated calyces. However, in the absence of hydronephrosis, the calyceal fornix may be missed and puncture through the infundibulum or directly into the renal pelvis may occur, leading to massive bleeding. In addition, with little hydronephrosis, repeated attempts may be necessary to puncture the desired calyx, which can be a significant risk factor for bleeding in PCNL⁽²⁴⁾. The third possible reason is that the absence of hydronephrosis affords less space for manipulation within the kidney, leading to traumatic injury of the renal vasculature and parenchyma⁽¹⁵⁾.

Several suggestions can be made to reduce bleeding complications during PCNL in patients without hydronephrosis. First, the utilization of ultrasound guidance for initial renal access may help reduce bleeding during PCNL. In a meta-analysis that compared fluoroscopy and ultrasound guidance during initial renal access, ultrasound was found to be superior in terms of puncture time, the success rate of first puncture, blood loss, and transfusion requirements^(25,26). However, utilizing ultrasound alone for renal access can be difficult because of poor imaging of the renal anatomy in patients with a nondilated collecting system⁽²⁷⁾. Combining ultrasound and fluoroscopy can overcome this problem and help decrease bleeding by reducing puncture attempts and access time⁽²⁸⁾. Second, the utilization of smaller caliber access sheaths may reduce bleeding. Compared to conventional PCNL that uses a 30F Amplatz sheath, mini-PCNL utilizes smaller-sized sheaths, ranging between 11-20F. Several studies have reported the advantage of mini-PCNL over conventional procedure in terms of a reduced hemoglobin drop and the need for blood transfusion⁽²⁹⁾. Third, staging the procedure for patients with a large stone burden may reduce blood loss⁽¹³⁾. Lastly, utilizing RIRS in well-selected patients

with large renal stones may be helpful. Several studies have found that RIRS was a good alternative treatment to PCNL in patients with 2-4cm renal stones ^(30,31).

The current study also showed significant results for other outcomes. The operation time and admission period were significantly longer and the stone-free rate was significantly lower in the group without hydronephrosis. Again, a higher proportion of more complex stones in the group without hydronephrosis may have caused this result as Guy's stone score is known to be associated with surgical outcomes in PCNL. Infectious complications did not show significant difference between the two groups. Several studies have implicated hydronephrosis as one of the risk factors for infectious complications after PCNL ⁽³²⁻³⁴⁾. One possible reason for our result is the strict definition of infectious complication in the current study. Unlike other studies that included a simple febrile episode as an infectious complication, only microbiologically or radiographically confirmed febrile urinary tract infections were included in the current study. Lastly, urine leakage was not investigated in this study because both the nephrostomy tube and the ureteral catheter were routinely inserted at the end of the operation.

There were several limitations in the current study. Because of the retrospective nature of the study, there could have been selection bias. Another potential bias is misclassification bias, where patients may have been included into a wrong group especially when hydronephrosis is not distinct. Also, some data that could have been valuable for the purpose of the study were not available, such as the time taken for initial renal access and the number of puncture attempts. In addition, surgical experience was not taken into account in the analysis, which may have caused higher a transfusion rate in our early cases. A relatively small number of study population is another limitation.

CONCLUSION

Based on the results of the current study, we found that absence of hydronephrosis was a

significant risk factor for blood transfusion in conventional PCNL.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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Table 1. Comparison of baseline patient and stone characteristics between group I (patients without hydronephrosis) and group II (patients with hydronephrosis)

	Group I	Group II	<i>p</i> value
<i>n</i> (%)	95/281 (33.8%)	186/281 (66.2%)	
Age (years, mean ± SD)	54.9 ± 10.6	53.8 ± 12.3	0.453 ¹
Sex (%)			0.123 ²
Male	51/95 (53.7%)	118/186 (63.4%)	
Female	44/95 (46.3%)	68/186 (36.6%)	
BMI (kg/m ² , mean ± SD)	25.2 ± 3.1	25.4 ± 3.6	0.744 ³
DM (%)	27/95 (28.4%)	42/186 (22.6%)	0.307 ²
Hypertension (%)	36/95 (37.9%)	59/186 (31.7%)	0.351 ²
CKD (%)	4/95 (4.2%)	7/186 (3.8%)	1.000 ⁴
Laterality (%)			0.703 ²
Left	57/95 (60.0%)	107/186 (57.5%)	
Right	38/95 (40.0%)	79/186 (66.2%)	
Guy's stone score (%)			<0.05 ³
Grade 1	19/95 (20.0%)	54/186 (29.0%)	
Grade 2	18/95 (18.9%)	88/186 (47.3%)	
Grade 3	40/95 (42.1%)	43/186 (23.1%)	
Grade 4	18/95 (18.9%)	1/186 (0.5%)	
Stone burden (mm ³ , mean ± SD)	153.7 ± 123.0	207.0 ± 146.2	0.010 ³
Staghorn stone (%)	50/95 (52.6%)	22/186 (11.8%)	0.001 ²

¹ Unpaired t-test

² Chi-square test

³ Mann-Whitney test

⁴ Fisher's exact test

SD = standard deviation, BMI = body mass index, DM = diabetes mellitus, CKD = chronic kidney disease

Table 2. Comparison of perioperative outcomes between group I (patients without hydronephrosis) and group II (patients with hydronephrosis)

	Group I	Group II	<i>p</i> -value
Operation time (minutes, mean ± SD)	103.4 ± 47.4	82.7 ± 36.1	<0.05 ¹
Admission period (days, mean ± SD)	3.9 ± 1.9	3.5 ± 1.6	0.022 ¹
Stone-free rate (%)	60/95 (63.2%)	145/186 (78.0%)	0.011 ²
Transfusion rate (%)	27/95 (28.4%)	21/186 (11.3%)	<0.05 ²
Infectious complication rate (%)	3/95 (3.2%)	4/186 (2.2%)	0.692 ³

¹ Mann-Whitney test

² Chi-square test

³ Fisher's exact test

SD = standard deviation

Table 3. Univariate and multivariate logistic regression analysis to determine independent predictor of transfusion with regard to percutaneous nephrolithotomy

Variables	Univariate		Multivariate	
	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Sex	2.483 (1.319-4.677)	0.005	2.315 (1.152-4.649)	0.018
BMI	0.832 (0.750-0.924)	0.001	0.823 (0.733-0.925)	0.001
Guy score				
Grade 1(reference)		0.302		0.036
Grade 2	1.699 (0.621-4.651)	0.005	3.212 (1.034-9.975)	0.044
Grade 3	4.027 (1.531-10.592)	0.012	5.050 (1.696-15.035)	0.004
Grade 4	5.154 (1.436 (18.500)	0.000	3.925 (0.923-16.685)	0.064
Hydronephrosis	0.321 (0.170-0.606)	0.000	0.353 (0.163-0.761)	0.008

OR = odds ratio, CI = confidence interval, BMI = body mass index

Supplementary table 1. Comparison of baseline patient and stone characteristics between patients who did not receive transfusion and patients who received transfusion.

	No transfusion	Transfused	<i>p</i> value
<i>n</i> (%)	233/281 (82.9%)	48/281 (17.1%)	
Age (years, mean ± SD)	54.2 ± 12.0	54.0 ± 10.4	0.930 ¹
Sex (%)			0.004 ²
Male	149/233 (63.9%)	20/48 (41.7%)	
Female	84/233 (36.1%)	28/48 (58.3%)	
BMI (kg/m ² , mean ± SD)	25.7 ± 3.3	23.8 ± 3.5	0.001 ³
DM (%)	59/233 (25.3%)	10/48 (20.8%)	0.511 ²
Hypertension (%)	80/233 (34.3%)	15/48 (31.3%)	0.681 ²
CKD (%)	7/233 (3.0%)	4/48 (8.3%)	0.099 ⁴
Laterality (%)			0.744 ²
Left	137/233 (58.8%)	27/48 (56.3%)	
Right	96/233 (41.2%)	21/48 (43.8%)	
Guy's stone score (%)			<0.05 ³
Grade 1	19/95 (20.0%)	54/186 (29.0%)	
Grade 2	18/95 (18.9%)	88/186 (47.3%)	
Grade 3	40/95 (42.1%)	43/186 (23.1%)	
Grade 4	18/95 (18.9%)	1/186 (0.5%)	
Stone burden (mm ³ , mean ± SD)	192.1 ± 139.7	213.2 ± 169.2	0.782 ³
Staghorn stone (%)	48/233 (20.6%)	24/48 (50.0%)	<0.05 ²

¹ Unpaired t-test

² Chi-square test

³ Mann-Whitney test

⁴ Fisher's exact test

SD = standard deviation, BMI = body mass index, DM = diabetes mellitus, CKD = chronic kidney disease