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Original Article

Comprehensive analysis of factors associated with significant blood loss during percutaneous nephrolithotomy

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Abstract: Introduction: The objective of this study is to conduct a thorough investigation of the risk factors associated with blood loss during PCNL, within the setting of a US urban tertiary care center. Materials and methods: We conducted a retrospective analysis of our endourology database to identify adult patients who underwent PCNL for stone extraction at our tertiary stone center between October 2014 and December 2022. Patients were categorized into two groups based on the extent of blood loss: significant blood loss (SBL) and no significant blood loss (NSBL). The cut-off value for SBL was determined as the median change in hematocrit levels from preoperative to postoperative among patients who required postoperative transfusions. Several factors were evaluated, including stone dimensions, operative details, the presence of preoperative drains, patient position, type of access, access site, number of accesses, tract size, tract length, stone location, number of stones, operative time, and the S.T.O.N.E. Nephrolithometry Scoring System. Results: Our analysis included a total of 695 procedures performed on 674 distinct patients who met our inclusion criteria. Of these, 102 patients (14.7%) were included in the SBL group. Patients in the SBL group had a higher mean number of accesses (1.57 vs. 1.29, P<0.001), were positioned prone more often (96.0% vs. 88.6%, P = 0.025), and underwent fluoroscopic-guided access more frequently (89.9% vs. 64.8%, P<0.001). Additionally, significant differences were observed in stone morphology, with the SBL group having higher rates of complete staghorn stones (42.2% vs. 27.0%, P = 0.019) and lower rates of partial staghorn stones (27.7% vs. 36.8%, P = 0.019). A larger proportion of patients in the SBL group required a 16 French nephrostomy tube for postoperative drainage (13.3% vs. 10.4%, P = 0.041). Lastly, the SBL group had a longer mean operative time compared to the NSBL group (P<0.001). Multiple logistic regression analysis identified stone volume (P = 0.039), number of accesses (P = 0.047), and operative time (P = 0.006) as independent risk factors associated with SBL status. Conclusion: Surgical complexity factors such as stone volume, number of accesses, and operative time are linked to a higher risk of SBL during PCNL. Stone volume and the requirement for multiple accesses can usually be estimated with reasonable accuracy before surgery.

Keywords: Percutaneous nephrolithotomy, blood loss anemia, nephrolithiasis

Introduction

Kidney stones are a common and burdensome illness with an estimated prevalence of 8.8% in the United States (US) [1]. Kidney stones have a 50% recurrence rate in first time-stone formers and cost the US an estimated 5.2 billion dollars annually through direct and indirect expenditures [1, 2]. Multiple surgical treatment modalities exist for kidney stone disease depending on stone size and location. Percutaneous nephrolithotomy remains the standard procedure for renal calculi larger than 2 cm, providing considerably high stone free rate [3, 4].

The most common complications associated with PCNL include fever, transfusion due to bleeding, thoracic complications, sepsis, organ injury, embolisation, urinoma, and death [5]. However PCNL is considered a relatively safe procedure, with 88.1% of surgeries being graded 0 or I by the Dindo-modified Clavien system [5].

Among the previous mentioned complications, blood loss anemia is a common concern for surgeons, considering PCNL is stratified as a high-risk bleeding procedures [3]. Perioperative bleeding during PCNL is typically caused by rupture of parenchymal vessels during tract dilation, or tearing of the renal parenchyma secondary to nephrostomy sheath bending [6]. Blood loss during PCNL is usually self-limited and does not require additional management. However, aborting PCNL due to excessive bleeding occurs in 0.4% of cases, and a systematic review by Seitz et al. found the overall blood transfusion rate after PCNL to be 7% [5, 6]. Notably, there is great variance in the transfusion rates reported by previous studies, with transfusion rates ranging from 0-20% [7, 8].

Several studies have examined predictors of blood loss during PCNL and identified that factors often related to surgical complexity were associated with increased risk of blood loss including stone size or burden, staghorn stones, degree of preoperative hydronephrosis, multiple accesses, and operative time [9-14]. Studies have also identified several medical history risk factors associated with increased risk for blood loss during PCNL including high body mass index (BMI) and diabetes [9, 10, 12, 13, 15-17]. Furthermore, though supine PCNL has been associated with shorter operative times compared to prone PCNL, transfusion rates are similar [18]. Yet, many of the studies evaluating predictors of blood loss in PCNL have relatively small sample sizes.

Previous studies conducted abroad report a wide range of transfusion rates and often disagree on which factors increase risk for blood loss. It is unclear whether this variation is related to different patient populations or other factors. Data from a stone center within the US may provide more generalizable results for patients treated in the US. Accordingly, this study aims to comprehensively examine these previously identified risk factors for blood loss during PCNL in the context of an urban tertiary care center in the US with a high volume of PCNL cases.

Methods

Patient selection

After obtaining Institutional Review Board approval, we retrospectively queried our prospectively maintained endourology database of patients that have undergone PCNL for stone extraction between October 2014 and December 2022. Patients with recorded preoperative and postoperative complete blood count (CBC) tests were included in the study. Exclusion criteria were the following: medical conditions impairing coagulation, assumption of anti-coagulants and incomplete or undocumented CBC.

To analyze factors associated with significant blood loss during PCNL, patients were divided into two groups: significant blood loss (SBL) and no significant blood loss (NSBL). The cutoff value for significant blood loss was defined as the median change in preoperative to postoperative hematocrit among all patients who required postoperative transfusions. Of note, for standard PCNL in our practice, we perform tract dilation to 24 French.

Demographic data was inclusive of BMI, prescription medications, medical and surgical history, CBC, and preoperative computed tomography (CT) imaging was obtained from the electronic medical record (EMR). Stone dimensions were recorded from preoperative CT imaging and stone volume was calculated using the formula for ellipsoid volume (stone volume $= \pi/6 \times \text{length} \times \text{width} \times \text{height}$). Samples of surgically retrieved stones were analyzed using infrared spectroscopy (Labcorp, Burlington, NC, USA). Based on the infrared spectroscopy stone analysis results, stones were categorized into one of three groups: >50% calcium oxalate (CaOx), >50% uric acid (UA), or other/mixed. Operative data was queried from our prospectively maintained database wherein data is recorded by the surgeon following each case. Operative parameters incorporated into our analysis included presence of preoperative drains (i.e., percutaneous nephrostomy tube and/or ureteral stent), patient position, type of access, access site, number of accesses, tract size, tract length, stone location, number of stones, stone impaction, degree of hydronephrosis and inflammation, type of lithotripter, type of wound closure, and operative time. A post-hoc analysis to assess stone complexity using the S.T.O.N.E. Nephrolithometry Scoring System was performed. Patients' stones were categorized as low, moderate, or high complexity based on following criteria: S.T.O.N.E. score <5 = Low; S.T.O.N.E. score 5-8 = Moderate;

S.T.O.N.E. score >9 = High) [19]. Of note, several patients in our database underwent PCNL prior introduction of our institutions current EMR system, thus preventing the complete collection of all parameters required to accurately assign a S.T.O.N.E. Nephrolithometry score.

Statistical analysis

Univariate analyses were performed comparing preoperative and operative factors between the two groups, i.e., SBL and NSBL. In univariate testing, we performed an independent t-test to compare mean values of continuous variables between the SBL and NSBL group. Differences in categorical variables between the SBL and NSBL groups were compared using a chi-square test. A multivariate logistic regression was conducted to determine independent associations between SBL. Variables included in the multivariate analysis were chosen based on both clinical relevance and significance in univariate tests. All analyses were two tailed with a significance level of alpha = 0.05 of and performed using Stata/MP software version 14.1 (StataCorp, College Station, TX).

Results

Descriptive statistics

Of the 720 PCNL procedures performed during the study period, data from 695 procedures performed on 674 unique patients met the inclusion criteria and was included in our analysis. Mean age of the entire study cohort was 57.5 (95% confidence interval (CI): 56.3, 58.6) years. Among those patients included, 352 (52.2%) were male and 322 (47.8%) were female. Mean BMI was 28.54 kg/m^2 (95% CI: 28.0, 29.1). Postoperative blood transfusion was performed following nine PCNLs (1.3%) and the median preoperative to postoperative change in hematocrit among those patients was -4.7%.

Using the median preoperative to postoperative change in hematocrit among those patients requiring blood transfusions as a cutoff, the NSBL group included 593 patients (85.3%) with a mean age of 57.18 years, of which 297 (50.1%) were male. The SBL group included 102 patients (14.7%) with a mean age of 58.07, of which 55 (53.9%) were male. No significant demographic or clinical differences were appreciated between the two groups (**Table 1**).

Univariate analysis

In a univariate analysis evaluating the association of operative and postoperative factors with blood loss, several significant differences were noted (**Table 2**). Patients in the SBL group had a higher mean number of accesses (1.57 vs. 1.29, P<0.001), were positioned prone more often (96.0% vs. 88.6%, P = 0.025), underwent fluoroscopic guided access more frequently (89.9% vs. 64.8%, P<0.001). They also had a higher incidence of stones located in the ureteropelvic junction (29.8% vs. 19.8%, P = 0.041), an increased mean number of involved calyces (3.8 vs. 2.5, P = 0.007), and a larger mean stone volume (3,277.64 mm^3 vs. 1,445.6 mm^3, P = 0.001). Significant differences were also noted in stone morphology where the SBL group had higher rates of complete staghorn stones (42.2% vs. 27.0%, P = 0.019) and lower rates of partial staghorn stones (27.7% vs. 36.8%, P = 0.019). In respect to postoperative drainage, a larger proportion of patients in the SBL group required 16 French nephrostomy tube placement for postoperative drainage (13.3% vs. 10.4%, P = 0.041). Lastly, operative time was higher in the SBL group with a mean of 116.1 minutes compared to 91.09 in the NSBL group (P<0.001). No significant differences were noted in mean hospital length of stay (1.25 vs. 1.43, P = 0.231). Univariate analysis of stone complexity using the S.T.O.N.E. Nephrolithometry score revealed no significant differences between the two groups across Low-risk, Moderate-risk, and High-risk categories (Low: 10.7% vs. 16.0%, Moderate: 65.2% vs. 44.0%, High: 24.1% vs. 40.0%; P = 0.110), though notably only 249 patients had complete data for S.T.O.N.E Nephrolithometry score calculation.

Multivariate analysis

Multiple logistic regression revealed stone volume (P = 0.039), number of accesses (P = 0.047), and operative time (P = 0.006) to be independently associated with SBL status (**Table 3**).

Discussion

PCNL is a surgical modality often used for the treatment of large and complex renal stones.

Table 1. Univariate analysis evaluating the association of preoperative factors with significant blood loss

	No Significant Blood Loss N = 593	Significant Blood Loss N = 102	*p*
Mean (95% CI)			
Age	57.18 (55.9, 58.4)	58.07 (55.4, 60.7)	0.584
Body Mass Index, kg/m^2	28.53 (28.0, 29.1)	28.37 (26.9, 29.9)	0.819
N (%)			
Sex			0.547
Male	306 (51.5)	55 (53.9)	
Female	287 (48.5)	47 (46.1)	
African American	37 (7.63)	7 (7.61)	0.955
ASA Score			0.137
0	0 (0.0)	1 (1.0)	
1	39 (6.9)	6 (5.9)	
2	392 (69.5)	65 (64.4)	
3	120 (21.3)	26 (25.7)	
4	12 (2.3)	3 (3.0)	
Obesity	171 (32.1)	25 (24.5)	0.192
Diabetes Mellitus	123 (21.2)	24 (23.5)	0.605
Hypertension	262 (45.3)	48 (47.1)	0.735
Hyperlipidemia	140 (24.22)	29 (28.4)	0.364
Hypertriglyceridemia	94 (17.5)	14 (14.6)	0.483
Coronary Artery Disease	58 (10.1)	10 (9.8)	0.930
UTI Within One Year	165 (34.7)	29 (32.6)	0.695
Recurrent UTI	82 (34.2)	6 (35.3)	0.925
Recurrent Stone Former	155 (64.3)	13 (76.47)	0.309
Asthma	6 (5.2)	1 (14.3)	0.317
COPD	2 (1.7)	0 (0.0)	0.725
Other Respiratory Illness	12 (10.4)	1 (14.3)	0.749
Immunocompromised	39 (8.1)	8 (8.42)	0.914
Aspirin Use			0.628
No	487 (82.1)	80 (78.4)	
Stopped	59 (10.0)	11 (10.8)	
Continued	47 (7.9)	11 (10.9)	
Statin Use	123 (32.8)	20 (37.7)	0.476

Continuous variables reported as mean (95% C.I.) were analyzed with a student's t test. Categorical variables reported as n (%) were analyzed using Chi-square analysis. Significant ($P<0.05$) values denoted in bold font. ASA Score = American Society of Anesthesiologists Physical Status Score. UTI = urinary tract infection. COPD = chronic obstructive pulmonary disease.

Overall, the procedure is relatively safe, with only 11.9% of patients having Clavien Grade II or higher complications, and less than 5% of patients having Clavien Grade III and higher complications [5]. One of the more common complications is blood loss anemia requiring subsequent blood transfusion. Accordingly, understanding which patients are at higher risk for needing a blood transfusion may allow for better preoperative optimization and counseling of patients undergoing PCNL. To this end, we have retrospectively reviewed our prospectively maintained database of patients undergoing PCNL at a high volume, urban tertiary referral center to identify which factors predict risk of SBL. In our analysis of 695 PCNL procedures, only nine cases required blood transfusion. This 1.3% transfusion rate is at the low end of the 0-20% range reported in the literature, and lower than in the 7% transfusion rate

Table 2. Univariate analysis evaluating the association of operative factors and outcome with significant blood loss during PCNL

	No Significant Blood Loss N = 593	Significant Blood Loss N = 102	*p*
Preoperative Drain			0.051
None	368 (81.8)	70 (81.4)	
Stent	65 (14.4)	9 (10.5)	
Nephrostomy Tube	17 (3.8)	6 (7.0)	
Both	0 (0.0)	1 (1.6)	
Calcified Stent	24 (6.4)	8 (9.5)	0.306
Preoperative Drain Duration, days	166.8 (36.6, 297.0)	74.36 (27.2, 121.5)	0.568
Patient Position			**0.025**
Prone	497 (88.6)	96 (96.0)	
Supine	64 (11.4)	4 (4.0)	
Mini PCNL	52 (14.1)	4 (6.8)	0.12
Number of Accesses	1.29 (1.2, 1.3)	1.57 (1.4, 1.8)	**<0.001**
Access Type			**<0.001**
Fluoroscopy	219 (64.8)	62 (89.9)	
Ultrasound	81 (24.0)	4 (5.8)	
Combined	38 (11.2)	3 (4.4)	
Access Site			0.306
Upper Pole	46 (21.3)	7 (26.9)	
Interpolar	43 (19.9)	2 (7.7)	
Lower Pole	127 (58.8)	17 (65.4)	
Dilator			0.251
Balloon	146 (76.0)	21 (80.8)	
Amplatz	11 (5.7)	3 (11.5)	
Metallic (Mini)	35 (18.2)	2 (7.7)	
Tract Length, cm	8.94 (8.5, 9.3)	9.29 (7.6, 10.9)	0.607
Stone Location			
Upper Pole	102 (22.6)	19 (22.6)	0.992
Interpolar	91 (20.1)	20 (23.5)	0.472
Lower Pole	304 (65.7)	54 (63.5)	0.705
Renal Pelvis	181 (39.7)	29 (34.5)	0.372
Ureteropelvic Junction	89 (19.8)	25 (29.8)	**0.041**
Ureter	38 (6.4)	4 (3.9)	0.33
Number of Calyces	2.51 (2.2, 2.8)	3.8 (2.5, 5.2)	**0.007**
Stone Burden, cm	31.01 (29.1, 32.9)	33.50 (28.0, 39.0)	0.316
Stone Volume, mm^3	1,446.62 (1,151.6, 1,741.6)	3,277.64 (1,196.7, 5,358.5)	**0.001**
Staghorn			**0.019**
Partial	177 (36.8)	23 (27.7)	
Complete	130 (27.0)	35 (42.2)	
Hydronephrosis			0.357
Mild	84 (26.8)	8 (22.2)	
Moderate	78 (24.8)	10 (27.8)	
Severe	34 (10.8)	1 (2.8)	
Inflammation			0.478
Mild	64 (47.1)	4 (40.0)	
Moderate	24 (17.7)	1 (10.0)	
Severe	9 (6.6)	0 (0.0)	

Lithotripter			0.768
Shockpulse	57 (9.6)	7 (6.9)	
Laser	42 (7.1)	7 (6.9)	
Mechanical Removal	36 (6.1)	6 (5.9)	
Other	106 (17.9)	17 (16.7)	
Stented	233 (70.0)	38 (69.1)	0.895
Wound Closure			**0.041**
Nothing	170 (47.8)	30 (66.7)	
Sealant	53 (14.9)	6 (13.3)	
Sealant and Bupivicaine	93 (26.1)	3 (6.7)	
16 Fr. Nephrostomy Tube	37 (10.4)	6 (13.3)	
Collecting System Injury	4 (3.6)	0 (0.0)	0.608
Operative Time, min	91.09 (86.3, 95.9)	116.1 (102.5, 129.6)	**<0.001**
Stone Composition			0.150
Calcium Oxalate	233 (43.9)	51 (53.1)	
Uric Acid	108 (20.3)	20 (20.8)	
Mixed/Other	190 (35.8)	25 (26.1)	
S.T.O.N.E. Nephrolithometry Score			0.110
Low	24 (10.7%)	4 (16.0%)	
Moderate	146 (65.2%)	11 (44.0%)	
High	54 (24.1%)	10 (40.0%)	
Length of Hospital Stay, days	1.25 (1.1, 1.4)	1.43 (1.2, 1.7)	0.231

Continuous variables reported as mean (95% C.I.) were analyzed with a student's t test. Categorical variables reported as n (%) were analyzed using Chi-square analysis. Significant (*P*<0.05) values denoted in bold font. Fr. = French.

Table 3. Multivariate analysis of factors affecting of significant blood loss during PCNL

	Odds Ratio	95% C.I.	*p*
Operative Time, per min	1.02	1.00, 1.03	**0.006**
Stone Volume, per mm^3	1.00	0.99, 1.01	**0.039**
Number of Accesses, per access	0.23	0.053, 0.98	**0.047**
Staghorn			
No Staghorn	Ref.		
Partial Staghorn	0.33	0.05, 2.24	0.256
Complete Staghorn	2.84	0.63, 12.8	0.173
Wound Closure			
Nothing	Ref.		
Sealant ± bupivicaine	0.19	0.03, 1.44	0.109
16 Fr. Nephrostomy Tube	2.85	0.37, 21.78	0.314
Access Type			
Fluoroscopy	Ref.		
Ultrasound	0.71	0.11, 4.60	0.720
Combined	0.50	0.42, 5.96	0.585
PCNL Patient Position			
Prone	Ref.		
Supine	1.08	0.12, 9.86	0.940

Significant values (*P*<0.05) denoted in bold font. Fr. = French.

noted in a recent meta-analysis [5, 7, 8]. One possible reason of the lower transfusion rate in this study is our routinely use of a 24 French sheath for standard PCNL, considering tract dilation leading to rupture of parenchymal vessels is one of the principal causes of intraoperative bleeding during PCNL and use of a lower diameter dilatory sheath may affect risk of bleeding. Furthermore, given that the present study was performed at a high-volume stone center, surgeon experience may have resulted in fewer complications [20, 21].

In the present study, we found the following three factors to be independently predictive of risk for SBL: stone volume, number of accesses, and operative time. Notably, all three of these factors are related to case complexity in that more complicated PCNLs tend to have larger stone volumes requiring multiple renal accesses and subsequently longer operative times. However, when assessing stone complexity using the S.T.O.N.E. Nephrolithometry scale there were no differences appreciated between the groups across the Low, Moderate, and High-risk categories. A possible explanation for this may be explained by the incomplete operative data required to assign all patients within our sample a S.T.O.N.E. Nephrolithometry score, thus providing insufficient data to fully investigate the association between blood loss and S.T.O.N.E. Nephrolithometry score within our cohort.

Indeed, prior literature does support the association of case complexity with bleeding risk during PCNL. In a similarly sized retrospective study, Akman et al. found both number of accesses and operative time to be associated with risk of blood loss [10]. Similarly, in a prospective study, Kukreja et al. found that number of accesses and case duration was associated with increased risk of blood loss [9]. Importantly, need for multiple accesses and stone volume may be particularly useful clinical parameters, as these can usually be determined with reasonable accuracy in advance of surgery. Prior studies have also identified an association between stone burden and bleeding risk [12, 14]. In our analysis staghorn stones were found to be associated with increased risk of SBL.

Interestingly, there was no association between patient positioning and risk of SBL. Few studies have already compared prone vs. supine PCNL in smaller populations, resulting in no difference in risk of blood transfusion. Our study further validates the notion that patient positioning is not associated with risk of SBL in a large cohort, suggesting surgeon comfort and anesthetic consideration as guidance in selecting patient position.

Although previous studies identified diabetes and high BMI as potential risk factors for increased blood loss, our study did not identify any patient demographic or past medical history factors associated with increased risk of SBL [9, 10, 12, 13, 15-17]. This discordance may be explained with different geographic settings among the populations, considering the variety of diabetes phenotypes and glycemic control according to geographic background [21, 22]. Similarly, two of the studies identifying high BMI as a risk factor for bleeding during PCNL were conducted in South Korea and Pakistan. Asian patients often have higher weight-related disease risks at the same BMI as white patients, suggesting that variation in patient population may be important when comparing our study [10, 11]. In a multi-institutional international study, Fuller et al. found morbidly obese patients with BMI>40 to be at higher risk for bleeding during PCNL; however, there was no difference in blood transfusion rates within our cohort between subjects with a BMI>40 kg/m^2 and those with a BMI<40 kg/m^2, thus calling into question the significance of this greater blood loss [15].

Our study has several limitations, starting from its retrospective nature. Furthermore, given our center's overall low transfusion rate and the challenges in accurately estimating blood loss during endoscopic surgery, adequate powering of the study was achieved by using the median change in hematocrit of those undergoing transfusion to define the SBL group. Additionally, our study was limited to a single high-volume institution and our findings may not be generalizable to lower volume institutions or other patient populations. Lastly, many patients included in the study underwent PCNL introduction of our institutions current EMR system, thus preventing the complete collection of parameters required to accurately assign a S.T.O.N.E. Nephrolithometry score. Indeed, further research is required to validate our findings. Yet, despite these limitations, we believe our study provides an important contribution to the literature supporting the notion that surgical complexity is associated with SBL. Notably, our transfusion rate was low, suggesting that patients with surgically complex stone disease may be best served by treatment at a tertiary care center. Further research in a prospective manner is required to validate these findings and to identify potential causes for the variance between transfusion rates in PCNL between surgical centers.

Conclusions

Stone volume, number of accesses, and operative time, all of which are related to surgical complexity, are associated with increased risk of SBL during PCNL. Stone volume and the need for multiple accesses can usually be determined with reasonable accuracy in advance of surgery; therefore, it is prudent these patients be counseled on the potential for greater risk of bleeding and consideration should be made for referral of these patients to a tertiary care center. Further research in a prospective multi-institutional manner is recommended to validate our findings and to identify potential causes for the variance between transfusion rates in PCNL between surgical centers.

Disclosure of conflict of interest

None.

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