Predictive Factors for Major Bleeding in Patients Undergoing Percutaneous Nephrolithotomy: A Clinical Prediction Study

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ABSTRACT

Objective: To evaluate major bleeding risk factors in percutaneous nephrolithotomy (PCNL) for upper urinary tract calculi and validate a prediction model.
Study Design: Analytical study.
Place and Duration of the Study: The First Affiliated Hospital of Wannan Medical College, Wuhu, China, from January 2019 to August 2023.
Methodology: Major bleeding was defined as a decrease in haemoglobin of ≥20 g/L compared to preoperative levels. A retrospective analysis of 468 PCNL patients identified risk factors for major bleeding using univariate, LASSO, and logistic regression analyses. Nomogram models were developed using R software, with ROC and calibration plots assessing the model's accuracy. The bootstrap method provided internal validation, and DCA evaluated clinical utility.
Results: Independent risk factors included diabetes (OR = 4.17), staghorn calculi (OR = 3.41), operative duration (OR = 1.01), and staged surgery (OR = 2.75). The model showed high discriminative ability (C-statistic: 0.783) and alignment with observed outcomes. Internal validation confirmed robustness (C-statistic: 0.728).
Conclusion: The predictive model for major bleeding during and after PCNL, focusing on diabetes, staghorn calculi, operative duration, and staged surgery, is highly accurate, aiding in the PCNL risk assessment.

Key Words: *Upper urinary tract calculi, Percutaneous nephrolithotomy, Major bleeding, Risk factors, Prediction model*.

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INTRODUCTION

Upper urinary tract calculi are among the most prevalent urological conditions worldwide, significantly impacting the patients' quality of life due to severe pain and potential complications such as urinary tract infections and renal dysfunctions.[1] These calculi impose considerable socio-economic and medical burdens, including increased healthcare costs and loss of productivity. Effective management of upper urinary tract stones is therefore essential to alleviate symptoms and prevent long-term adverse outcomes.

Percutaneous nephrolithotomy (PCNL) has become the standard minimally invasive surgical procedure for the treatment of large or complex renal stones.[2] Compared to open surgery, PCNL offers advantages such as reduced postoperative pain, shorter hospital stays, and faster recovery times.[3]

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However, PCNL is not without risks; one of the most significant complications is major bleeding, which can lead to blood transfusions, extended hospitalisation, additional interventions, and, in rare cases, life-threatening situations.[4] The incidence of significant haemorrhage during PCNL varies across studies, yet it remains a concerning issue for both urologists and patients.

Previous studies have attempted to identify risk factors associated with significant haemorrhage during PCNL, highlighting variables such as patient demographics, comorbidities, stone characteristics (size, location, and type), and surgical techniques (number of access tracts, operative time).[5] Despite these efforts, predicting which patients are at higher risk remains challenging due to the multifactorial nature of bleeding complications and inconsistencies in the study findings. Moreover, many studies have been limited by small sample sizes or have not integrated multiple risk factors into a comprehensive predictive model.

The rationale for this study stemmed from the need to enhance preoperative risk assessment for patients undergoing PCNL. By identifying key risk factors and developing a predictive model for significant haemorrhage, clinicians can better stratify patients according to their bleeding risk, tailor surgical planning, implement preventative measures, and provide informed counselling to patients regarding potential complications. The objective of this study was to identify the risk factors associated with significant haemorrhage during PCNL and to develop a predictive model to estimate the risk of major bleeding in patients undergoing this procedure. By analysing the data of 468 PCNL surgeries performed at the First Affiliated Hospital of Wannan Medical College, the objective was to create a tool to assist clinicians in preoperative decision-making and improve patient outcomes.

METHODOLOGY

This study included 468 adult patients undergoing PCNL for the upper urinary tract calculi at the Wannan Medical College's First Affiliated Hospital, from January 2019 to August 2023. Inclusion criteria were patients diagnosed with upper urinary tract calculi and undergoing PCNL treatment; and surgeries performed by an experienced surgeon with an associate chief physician. Exclusion criteria were coagulation disorders, incomplete data, surgical contraindications, or inability to complete surgery. The study was conducted with institutional ethical approval (No: 20230166) and informed patient consent.

Key patient data collected from electronic hospital records included demographics, body mass index (BMI), medical history, blood creatinine, hydronephrosis severity, stone characteristics, and surgery details, with urinary tract infections defined as $\geq 10^5$/mL bacteria in urine culture, and treated perioperatively with antibiotics. Hydronephrosis severity was classified into three levels: Mild (normal kidney shape / size, parenchyma, and <3 cm collecting system separation), moderate (slight enlargement, thinned parenchyma, 3-4 cm separation), and severe (significant enlargement, misshapen, extremely thinned parenchyma, anechoic renal area). Regarding the size of the stone, the authors used its approximate surface area as a representation. After radiological measurements provided the stone's maximum length (L) and width (W), the stone's surface area (mm^2) was estimated using the formula: Surface area (mm^2) = $L \times W \times \pi^2 \times 0.25$.[6] In this study, significant haemorrhage was defined as a decrease in haemoglobin of ≥20 g/L, determined by comparing the preoperative and postoperative complete blood count, with adjustments for any increase in haemoglobin due to blood transfusions.

Participants were divided into two groups for the analysis: A training set (n = 328) and a validation set (n = 140). The analysis was performed using R software (version 4.2.2) with a 7:3 ratio and a seed value of 468. Statistical analysis was performed using the Chi-square test for gender, hypertension, diabetes, urinary tract infection, SCr (serum creatinine), degree of hydronephrosis, stone location, staghorn calculus, multiple stones, residual calculus, and surgical staging. Wilcoxon rank-sum test was used to compare age and duration of surgery. Welch two-sample t-test was applied for the analysis of other parameters. Statistical methods included LASSO regression for factor selection, logistic regression for evaluating the predictors of significant haemorrhage in PCNL, ROC curve for diagnostic capability, and calibration and bootstrap resampling for model accuracy and precision. DCA assessed clinical utility, with significance set at $p < 0.05$.

RESULTS

Baseline data for the training and validation sets, including gender, age, BMI, hypertension, diabetes, urinary tract infection, creatinine, degree of hydronephrosis, stone location, presence of staghorn calculi, presence of multiple stones, presence of residual stones, surgery duration, and surgery staging, are presented in Table I.

Candidate predictors initially considered for PCNL haemorrhage risk were gender, age, BMI, hypertension, diabetes, urinary tract infection, serum creatinine, hydronephrosis degree, stone location, staghorn stone, multiple stones, residual stones, surgery duration, and staging. LASSO regression in the training cohort narrowed these down to four key factors: Diabetes, staghorn stone, surgery duration, and surgical staging. The LASSO model's cross-validation error and coefficients are illustrated in Figure 1 (A and B), respectively, showing a concise model with minimal error.

Based on the four predictive factors identified through LASSO regression analysis (diabetes, staghorn calculi, surgical duration, and surgical staging), researchers employed binary logistic regression analysis to assess the likelihood of major bleeding during and post-PCNL (not occurred = 0, occurred = 1).

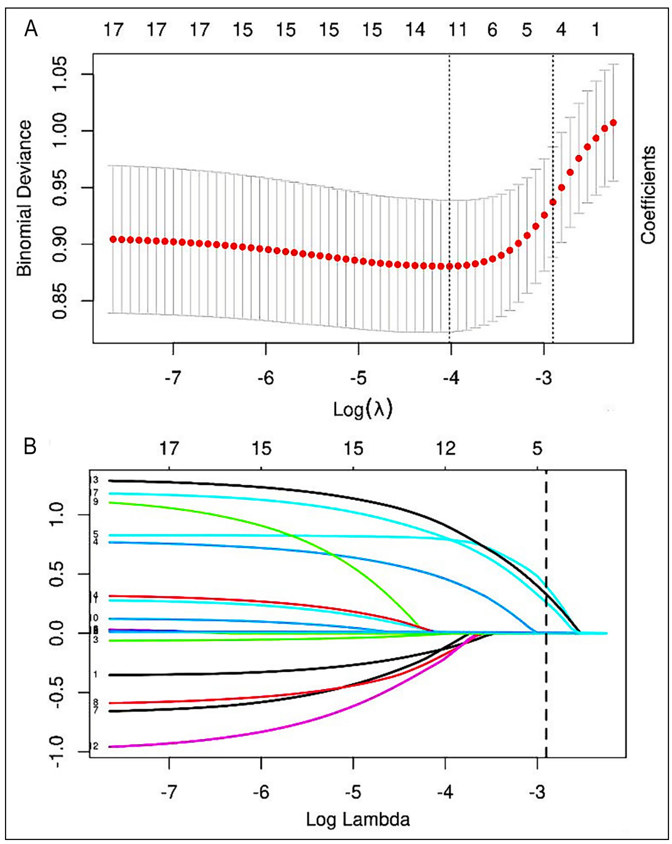

Figure 1: (A) Cross-validation plot for LASSO regression. The vertical lines represent the optimal values by minimum criteria and 1-standard error criteria (B) Variable selection path plot for LASSO regression. The vertical line represents the value chosen by 10-fold cross-validation.

Table I: Patient demographics and baseline characteristics.

Characteristics	Training Cohort, n = 328[1]	Internal Test Cohort, n = 140[1]	p-value[2]
Gender			0.195
Female	143 (44%)	52 (37%)	
Male	185 (56%)	88 (63%)	
Age			0.218
M (Q25, Q75)	55 (49, 62)	54 (47, 59)	
BMI (kg/m)			0.385
($\bar{x}$ ± s)	23.28 ± 3.00	23.02 ± 3.02	
Hypertension			0.470
No	216 (66%)	97 (69%)	
Yes	112 (34%)	43 (31%)	
Diabetes			0.291
No	289 (88%)	128 (91%)	
Yes	39 (12%)	12 (8.6%)	
Urinary tract infection			0.859
No	126 (38%)	55 (39%)	
Yes	202 (62%)	85 (61%)	
SCr			0.665
Abnormal	42 (13%)	20 (14%)	
Normal	286 (87%)	120 (86%)	
Degree of hydronephrosis			0.933
Mildly	127 (39%)	52 (37%)	
Moderately	89 (27%)	36 (26%)	
No	12 (3.7%)	5 (3.6%)	
Severe	100 (30%)	47 (34%)	
Stone location			0.010
Hybrid	52 (16%)	37 (26%)	
Kidney	239 (73%)	95 (68%)	
Ureter	37 (11%)	8 (5.7%)	
Staghorn calculus			0.924
No	207 (63%)	89 (64%)	
Yes	121 (37%)	51 (36%)	
Multiple stones			0.723
No	100 (30%)	45 (32%)	
Yes	228 (70%)	95 (68%)	
Residual calculus			0.119
No	200 (61%)	96 (69%)	
Yes	128 (39%)	44 (31%)	
Duration of surgery (min)			0.145
M (Q25, Q75)	115 (87, 147)	109 (80, 138)	
Surgical staging			0.067
I	271 (83%)	125 (89%)	
II	57 (17%)	15 (11%)	

Note: [1]n (%); [2]Pearson's Chi-squared test; Wilcoxon rank-sum test; Welch two-sample t-test.

Table II: Results of multivariate logistic regression for training cohort.

Characteristics	N	Event N	OR[1]	95% CI[1]	p-value
Diabetes					
No	289	50	—	—	
Yes	39	16	4.17	1.84, 9.42	<0.001
Staghorn calculus					
No	207	29	—	—	
Yes	121	37	3.41	1.86, 6.42	<0.001
Duration of surgery (min)	328	66	1.01	1.01, 1.02	<0.001
Surgical staging					
I	271	45	—	—	
II	57	21	2.75	1.35, 5.55	0.005

Note: [1]OR = Odds ratio, CI = Confidence interval.

Model Optimisation was achieved using a stepwise backward method. The analysis revealed that diabetes, staghorn calculi, surgical duration, and surgical staging were all independent risk factors for significant bleeding, with statistical significance ($p < 0.05$, Table II).

The nomogram for predicting significant bleeding risk in PCNL (Figure 2) shows diabetes, staghorn calculi, surgical duration, and surgical staging as key factors. To evaluate the accuracy and clinical utility of the nomogram, the authors conducted ROC analysis and calibration assessment, which demonstrated satisfactory alignment between predicted and observed bleeding risks. Internal validation using the bootstrap resampling method confirmed the robustness of the model with a high C-statistic (0.783 for the training set and 0.728 for the validation set), indicating strong predictive performance.

The authors selected 100 patients from the Second People's Hospital of Wuhu City, who met the inclusion and exclusion criteria and underwent the same surgical procedure, to serve as the external validation cohort. The Hosmer-Lemeshow test yielded a χ^2 value of 1.836 with a p-value of 0.871, indicating a good model fit. The area under the ROC curve (AUC) was 0.7802 [95% CI: 0.699 - 0.856], and the calibration curve showed good consistency between predicted risks and actual outcomes. These results confirm that the model's external validation accuracy and calibration are satisfactory.

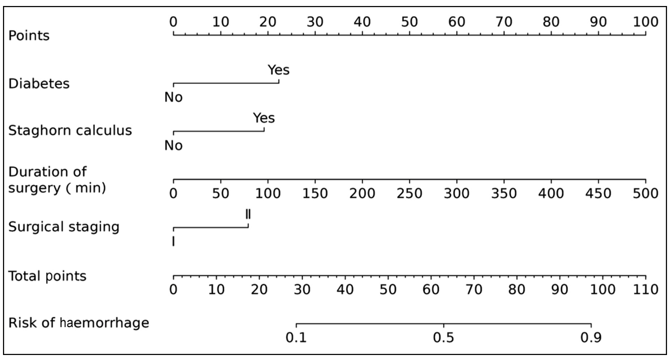

Figure 2: Nomogram risk prediction model for significant bleeding during and post-PCNL.

DISCUSSION

Intraoperative and postoperative bleeding, a serious PCNL complication, requires renal artery embolisation in 0.51 to 41% of cases.[7-9] The observed 18.8% perioperative bleeding rate aligns with previous findings (2% to 45%).[10] Currently, there has been some research on the influencing factors of intraoperative and postoperative bleeding in PCNL treatment for upper urinary tract stones.[11,12] Despite methodological variations in prior research, analysis of 468 patients identified diabetes, staghorn calculi, operative duration, and surgical staging as major bleeding risk factors in PCNL for upper urinary tract stones. The predictive model, with a C-statistic of 0.783, offers clinicians a robust tool for pre-surgical bleeding risk assessment.

Prior research has revealed diabetes as an independent risk factor for bleeding in PCNL.[13] Diabetes can cause nephropathy characterised by microvascular changes, leading to increased vascular fragility and impaired haemostasis, thereby elevating the risk of bleeding during surgical procedures.[14] Additionally, there is a significant association between staghorn calculi and bleeding. It is a risk factor in percutaneous nephrolithotomy (PCNL) surgery,[15] possibly due to the thicker renal cortex associated with this type of calculus, the longer puncture pathway, and the rich renal blood supply.[16] These stones, in combination with the smaller interstitial spaces in the renal tissue, can easily lead to tissue and vascular damage, increasing the risk of bleeding during PCNL. Staghorn calculi are typically large and challenging to manage surgically, leading to increased angles of movement of the nephroscope during stone fragmentation and removal, further increasing the risk of injury and bleeding. Kocan *et al*. also found that a larger stone volume is an independent risk factor for predicting blood loss during PCNL.[17] The influence of operative duration on bleeding in PCNL has been confirmed,[18,19] which aligns with the present study. Longer surgical durations are more likely to damage kidney tissue, resulting in prolonged bleeding. Surgical staging is also an important risk factor. Stage I PCNL is more prone to bleeding compared to Stage II, possibly because in Stage II PCNL, the nephrostomy tube has already been established, avoiding the need for additional punctures. As a result, surgical duration and stone burden are reduced, kidney drainage is improved, and the risk of bleeding is further lowered as the inflammatory factors from infection in the patient have less impact on blood vessels.[20]

Current evidence on the impact of stone location on PCNL bleeding is mixed, with some studies suggesting higher bleeding risks for kidney and upper ureteral mixed stones than for upper ureteral stones alone.[21] This study's univariate analysis found a significant association between stone location and bleeding (p = 0.016), but this was not corroborated in multifactorial logistic regression, likely due to strict inclusion criteria.

Infection has been reported as a significant risk factor for bleeding during PCNL.[22] Positive preoperative urine cultures and urinary tract infections (UTIs) can lead to increased vascularity and inflammation in the renal parenchyma, making the tissue more susceptible to bleeding.[23] Therefore, elective endourological procedures are often deferred in the presence of active infections to minimise complications.[24] In this study, although UTIs were considered, they did not emerge as an independent risk factor in the multivariate analysis. This could be due to the effective preoperative management of infections in the patient cohort or the exclusion of patients with active infections. However, the potential role of infection in the increasing bleeding risk should not be overlooked, and clinicians should continue to adhere to standard practices of managing UTIs before PCNL.

In this study, a nomogram was developed, a visual tool based on multifactorial regression analysis of independent risk factors, to aid clinicians in assessing bleeding risks during and after the PCNL for informed decision-making and early intervention. However, this study has limitations. It is a single-centre retrospective analysis, which may limit the generalisability of the findings. Additionally, other reported factors such as multiple access tracts (multitract-PCNL) and the site of puncture (infundibular *versus* forniceal access) were not included, which have been associated with increased bleeding risk.[25] Including these variables in future studies could enhance the predictive accuracy of the model. Multicentre prospective studies are recommended to validate and refine the predictive model.

CONCLUSION

Diabetes mellitus, staghorn calculi, longer operative duration, and staged surgery are independent risk factors for significant bleeding during and after PCNL. The predictive nomogram developed from these factors is a valuable tool for identifying high-risk patients, aiding in preoperative planning and early intervention.

ETHICAL APPROVAL:
This study was approved by the Hospital's Ethics Committee (Approval No: 20230166).

PATIENTS' CONSENT:
All patients in this study signed a written informed consent form.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
TQ: Research design, surgery, statistical analysis, and manuscript writing.
XTH: Funds management, research design, personnel coordination, and manuscript writing.
All authors approved the final version of the manuscript to be published.

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