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Original Article

Predictive factors for bleeding that require a blood transfusion after percutaneous nephrolithotomy

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Abstract: *Background and aims:* Percutaneous nephrolithotomy is the preferred technique for treating large kidney stones. One of the most frequent complications after percutaneous nephrolithotomy is renal bleeding, which requires blood transfusion. The aim of the present study was to determine the risk factors associated with blood transfusion following percutaneous nephrolithotomy. *Methods:* In order to determine the risks factors associated with blood transfusion, we retrospectively reviewed the medical records of 341 patients that underwent percutaneous nephrolithotomy in our clinic between 2011 to 2016. Patients were categorized into two groups: those that did not received blood transfusion and those that received blood transfusion. The groups were compared in terms of age, sex, body mass index, comorbidity, presence of anatomical abnormalities, history of anticoagulant use, history of urinary tract infection treated at the preoperative period, history of previous renal surgery, history of extracorporeal shock wave lithotripsy, Hounsfield unit value of the stone, degree of hydronephrosis, stone localization, stone opacity, stone size, solitary kidney, puncture site, operation time, thickness of parenchyma, and preoperative hematocrit values. *Results:* Transfusion group had significantly lower degree of hydronephrosis, lower preoperative hematocrit values, bigger stones, greater parenchymal thickness and longer operation time than non-transfusion group ($p < 0.001$). Furthermore, transfusion group had significantly higher median Hounsfield unit value than non-transfusion group ($p < 0.001$). *Conclusions:* It is important to establish risk factors associated with renal bleeding to take necessary precautions like the preparation of sufficient blood product for patients who are likely to have bleeding during the perioperative period of percutaneous nephrolithotomy.

Keywords: Percutaneous nephrolithotomy, kidney calculi, hemorrhage, Hounsfield unit

Introduction

Thomas Hillier (1865) was the first person to describe the percutaneous tract technique for the drainage of the kidney [1]. In 1976, Fernström and Johansson used this technique for the treatment of stone disease [2]. Today, percutaneous nephrolithotomy (PCNL) is one of the most common techniques for the treatment of kidney stones. Despite the common use, complication rates are still around 20% [3]. The most common complication is renal bleeding which will require blood transfusion [4-8]. Renal bleeding that occurs after PCNL can often be managed conservatively; however, in a small portion of patients, it can be life-threatening and requires radiological intervention [9].

The purpose of this study was to determine the risk factors associated with a blood transfusion following PCNL. Preoperative assessment parameters were measured in patients with perioperative blood transfusion in comparison to patients without postoperative blood transfusion. The differences in those parameters were evaluated in order to investigate their association with blood transfusions following PCNL.

Materials and methods

Medical records of 341 patients that underwent PCNL in the Urology Clinic of Adıyaman University Faculty of Medicine between 2011 to 2016 were retrospectively reviewed. Prior to operation, hemogram, bleeding time, creatinine, and urinary culture results were evaluated in each patient. Patients with positive urinary cultures were first treated with the appropriate anti-biotherapy before undergoing the operation. At the preoperative period, all patients underwent intravenous pyelography and non-contrast computed tomography (NCCT) with a Toshiba Aquilion system (Toshiba Medical Systems, Otawara, Japan). The non-contrast imaging parameters were as follows: cross section thickness: 1 mm, voltage: 120 kV, and mAS: 150-250. All patients were evaluated for the presence of retrorenal colon. Additionally, maximum diameter of stone size, Hounsfield unit (HU) value and thickness of renal parenchyma [measurement of parenchyma over accessed calyx (upper/middle/lower)] were calculated using the NCCT.

Blood transfusion was performed in patients with haemodynamic instability associated with hemorrhage during the intraoperative and postoperative period (systemic blood pressure < 90/60 mmHg, heart beat rate > 100/min) and if hemoglobin (Hb) levels were below 10 g/dL. Patients were categorized into two groups. Group 1 consisted of the patients that did not receive a blood transfusion whereas group 2 did received blood transfusion. Age, sex, body mass index (BMI), comorbidity (diabetes mellitus (DM), hypertension (HT), renal dysfunction), anatomical abnormality (horseshoe kidney, rotation anomaly), mean Hb drop, anticoagulant use, history of urinary tract infection treated at preoperative period, history of previous renal surgery, history of extracorporeal shock wave lithotripsy (SWL), HU value of the stone, degree of hydronephrosis, stone localization, stone opacity, stone size, solitary kidney, puncture site, operation time, thickness of parenchyma, and preoperative hematocrit values were compared between the two groups.

Surgical technique

Under general anesthesia, a 6-Fr open-ended ureteral catheter was inserted in the lithotomy position with the patients in the prone position. A radio-opaque fluid was administered via a ureteral catheter and the pelvicalyceal system was visualized via fluoroscopy. After identifying the most suitable posterior calyx, access was achieved using an 18-G percutaneous needle. A guide wire was inserted through the needle into the collecting system following the flow of urine through the needle. Following dilatation of the tract using Amplatz dilatators (Microvasive/Boston Scientific, Natick, MA), a 25-Fr nephroscope was inserted into the kidney via a 30-Fr sheath. All patients were treated by a single tract approach. A pneumatic lithotripter (Swiss Lithoclast, EMS Electro Medical System, Nyon, Switzerland) was used to fragment the stones. At the end of the procedure, a re-entry nephrostomy tube was inserted in each operated renal unit.

Statistical analysis

Data analysis was performed by using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, United States). The distributions of continuous variables were determined be using the Kolmogorov Smirnov test. The continuous variables were shown as mean ± standard deviation (SD) or median (min-max), number of cases and percentages were used for categorical data. While, the mean differences between groups were analyzed by Student's t test, the Mann Whitney U test was applied for comparisons of the medians. Categorical data were analyzed by Pearson's Chi-square or Fisher's exact test where applicable. Multiple Logistic Regression models were used to determine the best predictor(s) for blood transfusion complications after PCNL. A univariable test *p*-value less than 0.05 was accepted as a candidate for the multivariable model along with all variables of known clinical importance. Odds ratios, 95% confidence intervals, and Wald statistics for each independent variable were also calculated. A *p*-value less than 0.05 was considered statistically significant.

Results

Of the 341 patients that underwent PCNL, 36 (10.5%) received a blood transfusion. Six patients (1.7%) developed postoperative bleeding that caused hemodynamic instability which could not be managed with conservative therapies (nephrostomy obstruction, fluid support, and blood transfusion). Therefore, angioembolization was performed in those patients. The drop in Hb (preoperative levels to postoperative) was significantly higher in group 2 ($p < 0.001$). There was no statistically significant difference between group 1 and group 2 regarding age and sex ($p = 0.763$ and $p = 0.779$) or in terms of laterality, mean BMI, DM, HT, chronic renal failure, renal abnormality, anticoagulant use, history of urinary tract infection treated at the preoperative period, and history of previous renal surgery and SWL ($p > 0.05$) (**Table 1**). Furthermore, group 2 had significant-

Table 1. Comparison of demographic and clinical factors between non-transfusion and transfusion groups

Parameters	Group 1 (n = 305)	Group 2 (n = 36)	*p*-value
Age (yr)	44.8 ± 12.0	44.1 ± 14.5	0.763†
Sex			0.779‡
Male	202 (66.2%)	23 (63.9%)	
Female	103 (33.8%)	13 (36.1%)	
Laterality			0.999‡
Right	161 (52.8%)	19 (52.8%)	
Left	144 (47.2%)	17 (47.2%)	
Body mass index (kg/m^2)	26.1 ± 2.9	26.6 ± 3.5	0.371†
Diabetes mellitus	31 (10.2%)	6 (16.7%)	0.254¶
Hypertension	18 (5.9%)	2 (5.6%)	1.000¶
Hb drop (g)	1.32 ± 1.08	4.08 ± 1.42	< 0.001†
Chronic renal failure (serum creatinine > 1.4 mg/dl)	10 (3.3%)	1 (2.8%)	1.000¶
Renal abnormality (horseshoe kidney, rotation abnormality)	9 (3.0%)	2 (5.6%)	0.327¶
Anticoagulant medication	9 (3.0%)	1 (2.8%)	1.000¶
Pre-existing urinary infection	20 (6.6%)	3 (8.3%)	0.722¶
Previous renal surgery	37 (12.1%)	5 (13.9%)	0.788¶
Previous SWL	52 (17.0%)	7 (19.4%)	0.719‡

†Student's t test, ‡Pearson's Chi-square test, ¶Fisher's exact test.

Table 2. HU values according to groups, area under curve for HU measurements for predicting blood transfusion requirement, 95% confidence interval and diagnostic performance indicators at optimum cut-off point

	HU
Group 1	630 (310-970)
Group 2	930 (580-1360)
p-value†	< 0.001
Area under curve	0.907
95% confidence interval	0.842-0.973
Optimum cut-off point	> 925
Sensitivity	88.9%
Specificity	92.5%
Positive predictive value	58.2%
Negative predictive value	98.6%

†Mann Whitney U test.

ly higher median HU value than group 1 (p < 0.001). The receiver operating characteristic (ROC) analysis showed that HU values could discriminate the 2 groups (AUC = 0.907, 95% CI: 0.842-0.973 and p < 0.001). Based on the constructed ROC curve, a threshold value of 925 HU in NCCT was established as cut-off in determining whether a patient underwent blood transfusion or not (AUC = 0.907, sensitivity 89%, specificity 93%, positive predictive 58%, negative predictive 99% (**Table 2**). No statistically significant difference between the groups were found regarding stone localization, opacity, presence of solitary kidney, and puncture site (p > 0.05). Group 2 had significantly lower degree of hydronephrosis, lower preoperative hematocrit values, bigger stones, greater parenchymal thickness and longer operation time than group 1 (p < 0.001, **Table 3**).

A multivariate logistic regression analysis was performed with all the possible risk factors associated with blood transfusion requirement. According to the results of multivariate logistic regression analysis, HU value, operation time, thickness of renal parenchyma, degree of hydronephrosis, and stone size were factors associated with blood transfusion requirement (**Table 4**).

Discussion

PCNL was first performed in 1976 by Fernström and Johansson and has become one of the most frequently performed minimally invasive surgical methods for treatment of kidney stone today [2]. Compared to open kidney stone surgery, PCNL is associated with shorter hospital stay, less pain, a quicker return to daily activi-

Table 3. Comparison of other clinical factors

Parameters	Group 1 (n = 305)	Group 2 (n = 36)	*p*-value
Degree of hydronephrosis			0.010†
Absent	46 (15.1%)	13 (36.1%)	
Mild	64 (21.0%)	10 (27.8%)	
Moderate	82 (26.9%)	7 (19.4%)	
Severe	113 (37.0%)	6 (16.7%)	
Stone localization			0.521†
Staghorn	76 (24.9%)	13 (36.1%)	
Renal pelvis	110 (36.1%)	11 (30.6%)	
Calyx	104 (34.1%)	11 (30.6%)	
Upper ureter	15 (4.9%)	1 (2.8%)	
Stone opacity			1.000‡
Opaque	268 (87.9%)	32 (88.9%)	
Nonopaque	37 (12.1%)	4 (11.1%)	
Stone size (cm)	3.5 (1.4-7.6)	5.5 (1.5-8.2)	< 0.001¶
Solitary kidney	12 (3.9%)	3 (8.3%)	0.203‡
Puncture site			0.117†
Lower calyx access	71 (23.3%)	14 (38.9%)	
Middle calyx access	184 (60.3%)	18 (50.0%)	
Upper calyx access	50 (16.4%)	4 (11.1%)	
Operation time (min)	75 (17-159)	133.5 (42-174)	< 0.001¶
Thickness of renal parenchyma (mm)	12 (8-22)	20 (10-25)	< 0.001¶
Preoperative hematocrit level	44.2 ± 5.0	40.0 ± 6.2	< 0.001$

†Pearson's Chi-square test, ‡Fisher's exact test, ¶Mann Whitney U test, $Student's t test.

Table 4. Multivariate logistic regression analysis of all risk factors associated with blood transfusion requirement

	Odds ratio	95% Confidence Interval		*p*-value
		Lower limit	Upper limit	
Degree of hydronephrosis	0.572	0.187	0.794	0.042
Stone size	0.470	0.226	0.677	0.046
Operation time	1.942	1.026	3.677	< 0.001
Renal parenchyma thickness	1.490	1.036	1.720	0.027
Preoperative hematocrit level	1.009	0.866	1.174	0.913
HU value	2.073	1.490	2.885	< 0.001

ties, smaller incision, and lower rates of postoperative complications [10, 11]. As a result, a decline in open kidney stone surgery is notice in most surgical centers [12, 13]. Despite the advantage of PCNL, complications are still around 20% [3]. The complications after PCNL include fever, perforation of the collecting system, neighboring organ damage (ex: intestines, spleen, liver), and renal bleeding. Renal bleeding is the most common complication (1% to 55%) [4-9] but can often be managed conservatively. Arteriovenous fistula and pseudoaneurysms are the most common lesions leading to late postoperative period renal bleeding [14]. Endovascular interventional procedures, like angioembolization, may be required in severe bleeding conditions. Angioembolization after PCNL is between 0.3% to 2.4% [10, 14-16] with a success rates above 90% [9, 14].

Previously studies have shown that stone size, BMI, inferior calyx access, DM, staghorn stone, patient age, degree of hydronephrosis, and presence of preoperative urinary tract infection are associated with renal bleeding following PCNL [1, 8, 10, 17]. Our study did not found statistically significant associations between postoperative renal bleeding, BMI and staghorn stone (p > 0.05). However we found that the degree of hydronephrosis was inversely related with the blood transfusion rate. We speculated that the higher degree of hydronephrosis provides easier access to the renal collecting system and tract creation. Furthermore, we also found that prolonged operation time was associated with increased incidence of blood transfusion. This is may be due to the prolongation of the trauma to the kidney. Furthermore, increased bleeding during prolonged operations results in poor visualization during the operation, which may further prolong the duration of the operation and increases the amount of bleeding. In addition, the application of ultrasonic lithotripter may reduce the operation time by preventing fragments of broken stone from escaping to other calices, resulting in less bleeding. However, the pneumatic lithotripter is only used in PCNL operations in our clinic and therefore was not included in our evaluation.

Tan *et al.* indicated that severe postoperative bleeding is associated with inferior calyx puncture access ($p < 0.001$) [17]. They attributed this finding to the fact that inferior calyx access requires a more oblique and longer tract, leading to an increase risk of laceration to the renal parenchyma. Our study showed that lower calyx access was performed in 39% of patients with transfusion, and only in 23% of patients without transfusion. However no statistically significant difference was found ($p = 0.117$). Stoller *et al.* investigated the effects of telescopic metal and balloon dilatation and found no significant difference between the two methods in terms of resulting blood loss [7]. Bellman and Davidoff showed that Amplatz dilatation caused more frequent renal bleeding compared to balloon dilatation [18]. On the other hand, Kukreja *et al*. reported that renal bleeding occurred less frequently with Amplatz dilators as compared to telescopic metal dilators and balloon dilators [19]. In this study, we only used Amplatz dilators, therefore the effects of dilatation methods on renal bleeding could not be evaluated. Several studies did not found any risk factor associated with renal bleeding [9, 20]. It is important to establish risk factors associated with renal bleeding to take necessary precautions such as preparation of sufficient blood product for patients who are likely to have bleeding during the perioperative period. In our study, we found that thickness of renal parenchyma, degree of hydronephrosis, stone size and HU value of the stone were factors associated with blood transfusion.

To our knowledge, this is the first study that links higher HU value with higher probability of blood transfusion requirement. We speculate that this associate is based on the fact that lithotripsy of the denser stones requires longer procedure time and more energy which leads to a higher risk of trauma to the kidney. Future studies with prospective designs and increased patient numbers are needed.

Disclosure of conflict of interest

None.

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