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Original Article

The effects of continuing aspirin on blood loss and postoperative outcomes in percutaneous nephrolithotomy

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Abstract: Background: Percutaneous nephrolithotomy (PCNL) is an effective surgery for complex kidney stones yet with inherent bleeding risks. It remains unclear whether aspirin should be discontinued prior to PCNL. We aimed to further substantiate the safety of continuing aspirin during PCNL surgery and to determine whether aspirin status affects postoperative outcomes following PCNL. Methods: We retrospectively queried our endourology database for patients who underwent PCNL from October 2017 to December 2022 at our high-volume tertiary referral center. The three groups were based on aspirin status at the time of PCNL: no aspirin (NA), discontinued aspirin (DA), and continued aspirin (CA). Data collected included demographics, preoperative characteristics, operative parameters, pre and postoperative lab values, transfusions, and complications. Results: A total 648 patients were divided into these study groups: 525 NA patients (81.0%), 55 DA (8.5%), and 68 CA (10.5%). The DA and CA groups were of similar comorbidities, and both were more comorbid at baseline than NA. Postoperative change in lab values and complications did not differ significantly. Rates of postoperative blood transfusion were higher in the CA and DA groups compared to NA and approached statistical significance. There were no significant differences in any postoperative outcomes between the DA and CA groups alone. Conclusions: In patients on chronic aspirin therapy, continuing aspirin appears equally safe to discontinuing aspirin prior to PCNL. Most patients should not forego the benefits of continuous aspirin for the theoretical risk of bleeding. Patients on prolonged aspirin therapy may be more likely than those who are not on chronic aspirin therapy to require blood transfusions. However, regardless of whether aspirin use is stopped, this may be caused by patient comorbidities rather than higher rates of blood loss.

Keywords: Percutaneous nephrolithotomy, kidney calculi, aspirin, blood loss

Introduction

Percutaneous nephrolithotomy (PCNL) has become the standard treatment for large or complex renal stones [1, 2]. Though effective, PCNL can result in significant blood loss [3]. Special consideration must therefore be taken with patients on long term aspirin therapy, and it remains unclear whether aspirin should be discontinued prior to PCNL.

Low-dose aspirin is recommended for secondary prevention of atherosclerotic cardiovascular disease (ASCVD) and for primary prevention of ASCVD in patients with risk factors such as diabetes, hypercholesterolemia, and hypertension [4-6]. Higher dose aspirin (>100 mg) is generally not recommended as it is equivalent to low-dose aspirin in ASVCD risk reduction but has significantly greater risk of bleeding [4]. Aspirin withdrawal or non-compliance in high-risk patients has been associated with an increased risk of major adverse cardiac events [7] while continuing aspirin in the perioperative period has been associated with a decreased risk [8]. However, due to the perceived risk of bleeding complications, aspirin is often discontinued prior to non-cardiac surgery, including PCNL.

Retrospective studies have suggested that it is safe to continue aspirin during PCNL [9, 10]. Accordingly, given the known benefits of continuous aspirin therapy, we aimed to further

substantiate the safety of continuing aspirin during PCNL. The objective of this study was to determine whether aspirin status affects blood loss and postoperative outcomes following PCNL.

Methods

After institutional review board approval, we retrospectively queried our endourology database for patients who underwent PCNL from October 2017 to December 2022 at our high-volume tertiary referral center. All patients were treated by a single, fellowship-trained endourologist. Patients with documented aspirin status and pre- and post-operative complete blood count were included in the study. The three groups were based on aspirin status at the time of PCNL: no aspirin (NA), discontinued aspirin (DA), and continued aspirin (CA). Patients were evaluated for blood loss based on differences in pre- and post-operative hemoglobin and hematocrit as well as need for blood transfusion.

Data collected included demographics, medical and surgical history, stone history, surgical approach and operative parameters, and complications. The American Society of Anesthesiologists (ASA) physical status was determined by the anesthesiologist prior to PCNL. Lab values were collected from the preoperative period (within 30 days of surgery), in the post-anesthesia care unit (PACU) on postoperative day (POD) 0, and POD1. Complications, including blood transfusion and indication for transfusion, were captured up until the postoperative visit at 1 month. Complications were graded using the Clavien-Dindo classification system [11].

The primary endpoint of the study was the association between aspirin status and postoperative blood loss following PCNL. Secondary endpoints included other postoperative complications unrelated to blood loss. Baseline patient, operative, and postoperative variables were analyzed with a one-way ANOVA and chi-square test for continuous and categorical variables, respectively. Post-hoc testing was performed for all statistically significant results utilizing a Bonferroni correction to control experiment-wise error rate. All statistical analyses were two tailed with $\alpha=0.05$ and performed using Stata/MP 14.1 (College Station, TX, USA).

Results

There were 648 patients included 525 NA patients (81.0%), 55 DA (8.5%), and 68 CA (10.5%). Demographics are summarized in **Table 1**. There were no significant differences in body mass index (BMI) or gender among the three groups. The DA and CA groups were significantly older than the NA group (mean age 65.2, 67.8, and 55.4, respectively; P<0.001) (**Table 1**). Compared to the NA group, the DA and CA groups were more likely to have diabetes (16.2% in NA, 50% in DA, 40% in CA; P<0.001), hypertension (39.2% in NA, 73.5% in DA, 72.7% in CA; P<0.001), hyperlipidemia (18.9% in NA, 51.5% in DA, 49.1% in CA; P<0.001), coronary artery disease (4.8% in NA, 27.9% DA, 41.8% CA; P<0.001), and ASA score ≥3 (88.6% in NA, 100% in DA, 100% in CA; P<0.001). There were no significant differences between the DA and CA groups with regards to these same comorbidities. The DA and CA groups had more patients on a statin (21.8% in NA, 70.2% in DA, 72.6% in CA; P<0.001), with no significant difference between the DA and CA groups.

Comparisons between operative and stone parameters among groups is shown in **Table 2**. There was no significant difference in number of accesses, access site, tract size, stone volume, estimated blood loss (EBL), or operative time. There was no significant difference in the rates of partial or complete staghorn stone. Regarding stone location, patients in the NA group had significantly lower rates of stones in the renal pelvis (35.4%, 49.1%, 50.0%, for NA, DA and CA groups respectively; P=0.039).

Postoperative outcomes and complications are summarized in **Table 3**. There were no significant differences among the three groups in the mean percent change in hematocrit from pre-op to PACU (-1.4%, -1.5%, -1.9%, for NA, DA and CA groups respectively; P=0.659) or to POD 1 (-4.7%, -4.8%, -5.2%, for NA, DA and CA groups respectively; P=0.791), or in the mean change in hemoglobin from pre-op to PACU (-0.4, -0.5, -0.6, for NA, DA and CA groups respectively; P=0.620) or to POD 1 (-1.7, -1.6, -1.8, for NA, DA and CA groups respectively; P=0.771). There was also no significant difference in mean length of stay, postoperative fever, infective complications, or major complications (Clavien grade IIIa or higher). Rates of postoperative blood transfusion were higher in the CA and

Table 1. Demographic and clinical parameters stratified by aspirin group

	No Aspirin n=525	Discontinued Aspirin n=68	Continued Aspirin n=55	*p*
Mean (SD)*				
Age	55.4 (15.0)†,‡	65.2 (11.7)†	67.8 (8.5)‡	<0.001
BMI, kg/m^2	28.3 (6.4)	29.8 (6.6)	28.5 (7.7)	0.216
N (%)**				
Gender				0.726
Male	266 (51.9)	37 (56.1)	29 (55.8)	
Female	247 (48.2)	29 (43.9)	23 (44.2)	
ASA				<0.001
1	1 (0.2)	0 (0.0)	0 (0.0)	
2	44 (8.6)	0 (0.0)	0 (0.0)	
3	359 (70.4)	40 (61.5)	30 (57.7)	
4	93 (18.2)	25 (38.5)	19 (36.5)	
Diabetes Mellitus	85 (16.2)†,‡	34 (50.0)†	22 (40.0)‡	<0.001
Hypertension	205 (39.2)†,‡	50 (73.5)†	40 (72.7)‡	<0.001
Hyperlipidemia	99 (18.9)†,‡	35 (51.5)†	27 (49.1)‡	<0.001
Coronary Artery Disease	25 (4.8)†,‡	19 (27.9)†	23 (41.8)‡	<0.001
Hypertriglyceridemia	67 (13.4)†,‡	18 (29.5)†	21 (38.2)‡	<0.001
History of UTI	70 (35.4)	5 (18.5)	7 (46.7)	0.128
Positive Urine Culture	139 (28.4)	16 (27.6)	12 (22.6)	0.671
History of Nephrolithiasis	134 (67.3)	16 (59.3)	8 (53.3)	0.418
Immunocompromised	38 (8.7)	4 (7.6)	3 (6.3)	0.826
Statin Use	68 (21.8)†,‡	33 (70.2)†	37 (72.6)‡	<0.001
Preoperative Drains				0.857
Stent	52 (12.2)	9 (19.6)	7 (14.9)	
Nephrostomy Tube	17 (4.0)	1 (2.1)	2 (4.3)	
Both	1 (0.2)	0 (0.0)	0 (0.0)	
Calcified Stent	25 (6.7)	3 (7.7)	3 (6.8)	0.972

*One-way ANOVA. **Chi-Square. SD: Standard Deviation; BMI: Body Mass Index; UTI: Urinary Tract Infection. †Significant difference (Bonferroni corrected *P*-value <0.008) between No Aspirin and Discontinued Aspirin groups. ‡Significant difference (Bonferroni corrected *P*-value <0.008) between No Aspirin and Continued Aspirin groups.

DA groups compared to the NA group, and approached statistical significance (0.66% in NA, 1.7% in DA, 4.0% in CA; P=0.08).

An exploratory post-hoc test was performed to determine whether there was a statistically significant difference in transfusion rates between CA and NA, NA and DA, and CA and DA. After using a Bonferroni correction, no significant differences between individual groups were noted.

Among those who required blood transfusion, indications varied. Three patients in the NA group (0.66%) were transfused. One transfusion was given for hemoglobin 7.4 g/dl and hematocrit 25.6% in the setting of gross hematuria and postoperative non-ST-elevation myocardial infarction (NSTEMI) in a patient on warfarin (stopped six days pre-op) for mechanical heart valve. The second was for acute blood loss anemia (hemoglobin 5.8 g/dl, hematocrit 18%) on POD4 secondary to gross hematuria in a patient on warfarin, which was stopped pre-op and bridged with enoxaparin. The third was transfused at a hemoglobin of 7.9 g/dl and hematocrit 24% following PCNL with EBL of 500 cc in a patient with a history of iron deficiency anemia. In the CA group, two patients received blood transfusion: one for NSTEMI due to demand ischemia in the setting of septic shock with hemoglobin 8.2 mg/dl and hematocrit 24.8%, and the other for 16% drop in hematocrit with hemodynamic instability fol-

Table 2. Operative and stone parameters stratified by aspirin group

	No Aspirin Use	Discontinued Aspirin	Continued Aspirin	*P*
Mean (SD)*				
Number of Accesses	1.4 (0.6)	1.4 (0.5)	1.4 (1.0)	0.845
Tract Length, cm	9.2 (2.8)	9.4 (2.9)	8.0 (2.1)	0.376
Number of Calyces	2.6 (2.4)	2.1 (1.7)	3.1 (2.1)	0.320
Number of Stones	5.0 (9.9)	3.5 (2.4)	5.8 (8.8)	0.799
Estimated Blood Loss, mL	43.0 (30.2)	55.0 (24.0)	42.5 (32.5)	0.458
Operative Time, min	94.2 (56.6)	100.4 (43.5)	97.2 (58.2)	0.707
Stone Volume, mm^3	1,420.5 (2,364.0)	796.9 (950.7)	2,058.0 (2,092.7)	0.539
N (%)**				
Patient Position				0.507
Prone	449 (89.4)	59 (89.4)	51 (94.4)	
Supine	53 (10.6)	7 (10.6)	3 (5.6)	
Tract Size				0.247
24 French	244 (89.7)	29 (80.6)	29 (90.6)	
16/17 French	28 (10.3)	7 (19.4)	3 (19.4)	
Access Type				0.835
Fluoroscopy	223 (73.6)	25 (71.4)	27 (79.4)	
Ultrasound	47 (15.5)	7 (20.0)	5 (14.7)	
Both	33 (10.9)	3 (8.6)	2 (5.9)	
Access Site				0.210
Upper Pole	32 (18.6)	8 (40.0)	2 (22.2)	
Interpolar	36 (20.9)	3 (15.0)	2 (11.1)	
Lower Pole	104 (60.5)	9 (45.0)	12 (66.7)	
Stone Location				
Upper Pole	79 (20.2)	13 (24.5)	10 (22.7)	0.732
Interpolar	75 (19.1)	11 (20.8)	5 (11.4)	0.418
Lower Pole	264 (65.7)	32 (60.4)	26 (59.1)	0.550
Renal Pelvis	140 (35.4)	26 (49.1)	22 (50.0)	0.039
UPJ	83 (21.3)	11 (20.8)	11 (25.0)	0.844
Kidney Abnormalities	41 (7.8)	7 (10.3)	4 (7.3)	0.760
Staghorn				0.320
No	147 (34.8)	19 (40.4)	11 (25.0)	
Partial	149 (35.2)	15 (31.9)	22 (50.0)	
Complete	127 (30.0)	13 (27.7)	11 (25.0)	
Inflammation				0.362
None	28 (30.4)	3 (17.7)	3 (37.5)	
Mild	45 (48.9)	11 (64.7)	2 (25.0)	
Moderate	12 (13.0)	2 (11.8)	3 (37.5)	
Severe	7 (7.6)	1 (5.9)	0 (0.0)	
Hydronephrosis				0.724
None	107 (41.5)	14 (36.8)	8 (34.8)	
Mild	66 (25.6)	11 (29.0)	5 (21.7)	
Moderate	57 (22.1)	11 (29.0)	8 (34.8)	
Severe	28 (10.9)	2 (5.2)	2 (8.7)	
Stent Placed	203 (70.0)	29 (74.4)	24 (80.0)	0.466
Tract Closure				0.459
Nothing	151 (50.7)	14 (38.9)	20 (58.8)	
Sealant	47 (15.8)	5 (13.9)	4 (11.8)	

Sealant & Marcaine	66 (22.2)	12 (33.3)	6 (17.7)	
16 French PCN	33 (11.1)	4 (11.1)	4 (11.8)	
Other	1 (0.34)	1 (2.8)	0 (0.0)	
Collecting System Injury	2 (2.4)	1 (8.3)	1 (12.5)	0.264
Stricture	3 (3.8)	0 (0.0)	1 (12.5)	0.365
Positive Stone Culture	79 (18.1)	12 (21.8)	6 (12.2)	0.438
Stone Composition				0.725
Calcium Oxalate	226 (45.1)	29 (48.3)	26 (47.3)	
Uric Acid	100 (20.0)	13 (21.7)	14 (25.5)	
Mixed/Other	175 (34.9)	18 (30.0)	15 (27.3)	

*One-way ANOVA. **Chi-Square. SD: Standard Deviation. PCN: Percutaneous Nephrostomy Tube.

Table 3. Post-operative outcomes and complications stratified by aspirin group

	No Aspirin Use	Discontinued Aspirin	Continued Aspirin	*P*
Mean (SD)*				
Days to Discharge	1.3 (1.4)	1.4 (1.1)	1.3 (1.0)	0.925
Change in Hematocrit, %				
PACU	-1.4 (3.7)	-1.5 (4.0)	-1.9 (3.1)	0.659
Post-op Day One	-4.7 (4.1)	-4.8 (4.7)	-5.2 (4.2)	0.791
Change in Hemoglobin, gm/dl				
PACU	-0.4 (1.5)	-0.5 (1.1)	-0.6 (0.9)	0.620
Post-op Day One	-1.7 (1.4)	-1.6 (1.3)	-1.8 (1.4)	0.771
N (%)**				
Blood Transfusion	3 (0.66)	1 (1.7)	2 (4.0)	0.08
Post-Op Fever	35 (7.4)	2 (3.6)	4 (7.8)	0.561
Infective Complications				0.174
SIRS	30 (6.3)	1 (1.8)	0 (0.0)	
Septic	4 (0.9)	0 (0.0)	1 (2.0)	
Major Complications§	10 (2.1)	1 (1.9)	2 (4.0)	0.682

*One-way ANOVA. **Chi-Square. SD: Standard Deviation. §Clavien IIIa or higher.

lowing a prolonged surgery for a complete staghorn stone with seven access tracts (lowest hemoglobin 10.7 g/dl, hematocrit 33%). One patient in the DA group required transfusion for acute on chronic anemia (hemoglobin 6.6 g/dl, hematocrit 22.9%) with NSTEMI also found to have gastric and duodenal ulcers on endoscopy.

Discussion

To our knowledge, this is the largest retrospective study of aspirin use in PCNL. We found no difference in blood loss indicated by change in hemoglobin and hematocrit or EBL with respect to perioperative aspirin status. There were no significant differences in the rate of major complications among those that continued aspirin up until surgery compared to those that did not. Although patients that discontinued aspirin at least 7 days prior to surgery and those that continued aspirin perioperatively had a higher rate of postoperative blood transfusion compared to those never on aspirin, this difference did not reach significance.

The American Heart Association and American College of Cardiology recommend continuous aspirin for patients with known ASCVD given the benefits of long-term aspirin therapy [4]. Their guidelines on perioperative management of patients on aspirin undergoing elective noncardiac surgery recommend continuing aspirin in patients with a history of coronary stenting (and discontinuing P2Y12 inhibitors) and that it may be reasonable to continue aspirin in

patients without a history of stenting based on individual cardiac event risk assessment [12]. Yet the evidence is conflicting. Observational studies suggest that discontinuing aspirin preoperatively is associated with increased risk of thromboembolic events [13-16]. Aspirin withdrawal syndrome may further increase the risk of thromboembolic complications [17]. This is thought to be related to a platelet rebound phenomenon in which increased thromboxane and decreased fibrinolysis following aspirin withdrawal contribute to a prothrombotic state [18, 19]. However, the landmark prospective POISE-2 randomized controlled trial evaluating aspirin in patients undergoing non-cardiac surgery found that continuation of low-dose aspirin in the perioperative period had no significant impact on the rate of mortality or nonfatal MI but did increase the risk of major bleeding [20].

Factors associated with increased risk of postoperative hemorrhage specifically following PCNL include hypertension, diabetes, staghorn stone, urinary tract infection, multiple tracts, and prolonged operative time [21-24]. Hypertension and diabetes affect ASCVD risk and likelihood to be on aspirin. Thus, patients who take aspirin are less likely to be healthy at baseline and more likely to have some of the comorbidities independently associated with blood loss in PCNL. These comorbidities are present regardless of whether the patient discontinues aspirin perioperatively. Accordingly, patients with an indication for long-term aspirin therapy are typically assigned ASA score 3 or above, which is reflected in our population, **Table 1**.

Our findings that there was no significant difference in preoperative to postoperative change in hemoglobin or hematocrit between the NA, DA, and CA groups is consistent with what is previously reported in the literature. In an earlier retrospective review of consecutive PCNL cases, Leavitt et al. similarly found no difference in blood loss, transfusion rate, total complications or thromboembolic events between patients who continued aspirin perioperatively and those who temporarily discontinued aspirin [10]. Another retrospective study by Otto et al. comparing patients on chronic low-dose aspirin who continued therapy for PCNL to those not on chronic aspirin also found no significant difference in blood loss and complications [9]. However, there was no study arm of patients on chronic aspirin who discontinued use for surgery. By comparing not only those that continued aspirin, but also patients on antiplatelet therapy at baseline who discontinued aspirin prior to surgery, we aimed to understand whether the latter group could be at heightened risk of bleeding versus those not on aspirin. In an earlier study looking at only patients on long-term anticoagulation or antiplatelet therapy, Fernández-Baltar et al, found that with a proper discontinuation protocol (holding aspirin 7 days before surgery), patients on chronic anticoagulant or antiplatelet therapy were not at increased risk of blood loss after PCNL [25]. Though we found no significant differences in hemoglobin or hematocrit decreases among patients following a discontinuation protocol, we did observe relatively higher rates of blood transfusion among those in the CA and DA groups compared to the NA group, though not statistically significant. While patients on long-term aspirin may not be at higher risk for hemoglobin drop after PCNL, they may be more likely to require transfusion given comorbid conditions at baseline, irrespective of whether they discontinue aspirin prior to surgery.

Rates of blood transfusion after PCNL range from 1% to 18% [9, 10, 23, 26]. A large global prospective study on PCNL complications found a transfusion rate of 5.7% [27]. Our transfusion rates were lower than many prior reports. Although changes to hemoglobin were not different among the three groups in our study, those in the DA and CA groups appeared more likely to require blood transfusion than those never on aspirin. There are a number of factors that may explain the higher rates of transfusion. There is a more liberal threshold for transfusion in patients with ASCVD (hemoglobin 8 g/dl versus 7 g/dl in patients without) [28, 29]. Additionally, there may be a bias towards transfusing patients on aspirin due to concern that they may continue to bleed more. Patients with indications for long-term aspirin are also at increased risk for other complications, such as NSTEMI, that might increase the decision to transfuse. There was, importantly, no significant difference in blood transfusion between those that discontinued aspirin and those that continued aspirin perioperatively in our study. Though they differ significantly from the NA group, these two groups have similar baseline

characteristics to one another, further supporting the idea that any potential difference in blood transfusion is better explained by underlying conditions rather than continued aspirin use itself.

Aside from higher rates of stones in the renal pelvis in the aspirin groups (DA and CA) compared to the NA group, there were no significant differences in operative factors among the three groups in our study. Stones in the renal pelvis may result in a more difficult procedure due to challenging access and higher chance of stone migration [30]. However, there is no indication based on the other operative parameters (accesses, operative time, EBL) that operations in the DA and CA groups were more complicated overall.

Important limitations of our study include the retrospective study design and single site/surgeon. While surgeon uniformity may also reduce potential confounding associated with individual surgeon approach and experience, it limits the generalizability of our results. Furthermore, we did not differentiate between low-dose and full dose aspirin use. Despite these limitations, we believe this study adds to the literature on PCNL and aspirin use given our large sample size and three-group analysis (NA vs. DA vs. CA). Future prospective randomized controlled studies are required to verify these findings that continuing aspirin during PCNL is safe.

Conclusion

In individuals on long-term aspirin medication, continuing aspirin appears to be as safe as stopping aspirin before PCNL. Accordingly, in most cases, patients should not forego the benefits of continuous aspirin for the theoretical risk of bleeding. However, patients on chronic aspirin therapy may be more likely to undergo blood transfusion compared to those not on chronic aspirin therapy whether they discontinue aspirin or not, but this may be related to comorbidities and is not related to higher rates of blood loss. We recommend future study in a prospective manner to validate these findings.

Disclosure of conflict of interest

None.

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