

## CONTINUOUS PERIOPERATIVE USE OF ASPIRIN AS SINGLE THERAPY DURING PERCUTANEOUS NEPHROLITHOTOMY: A SMALL RETROSPECTIVE, SINGLE-CENTER EXPERIENCE

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### Abstract

**Introduction:** The rates of heart disease and nephrolithiasis continue to increase in the United States, and aspirin is increasingly prescribed for varying indications. Current recommendations in the urologic literature are to stop aspirin before percutaneous nephrolithotomy (PCNL); however, this is based on expert opinion. This study aims to determine the safety of PCNL performed on patients who took aspirin in the perioperative period.

**Methods:** This study was a retrospective review of 27 consecutive PCNLs for patients who took aspirin in the perioperative period (January 2013–September 2016). Pre- and postoperative hemoglobin was recorded, as were age, sex, BMI, operative duration, skin-to-stone distance, stone size, aspirin dose, aspirin indication, number of blood transfusions, and Clavien–Dindo complication classification. Correlations between hemoglobin and explanatory variables were then explored with linear regression and the Wilcoxon rank-sum test.

**Results:** Of the 199 PCNLs performed, 27 procedures on 23 patients were conducted without discontinuing aspirin perioperatively. Coronary artery disease was the most common indication for aspirin use (81%). Patients experienced a median hemoglobin decline of 1.4 g/dl perioperatively. No significant associations were found between hemoglobin decline and age, sex, BMI, operative duration, skin-to-stone distance, or stone size. There were no Clavien–Dindo grade III or higher complications, and no patients required a blood transfusion or angio-embolization. There were no thrombo-embolic or cardiac events in our series.

**Conclusions:** In our single-center experience, PCNLs performed on patients taking aspirin perioperatively were not associated with the need for blood transfusion nor the occurrence of high-grade complications.

**Keywords:** *Kidney Stone, Aspirin, Antiplatelet, percutaneous nephrolithotomy (PCNL)*

### INTRODUCTION

Nephrolithiasis is an increasing problem in the United States, with one in eleven people reporting a history of kidney stones.<sup>1</sup> As the incidence of nephrolithiasis has increased, so has the use of percutaneous nephrolithotomy (PCNL).<sup>2,3</sup> The rate of heart disease has risen concurrently in recent years and is predicted

to continue to increase with estimations that more than 40% of Americans will have cardiovascular disease by 2030.<sup>4</sup> The American Heart Association recommends lifetime aspirin therapy for secondary prevention in patients with coronary artery disease in order to reduce subsequent morbidity associated with the diagnosis.<sup>5</sup>

As the incidence of both heart disease and nephrolithiasis rise, the problem of antiplatelet management during surgical stone treatment is increasingly important.<sup>6</sup> The American College of Chest Physician’s Clinical Practice Guidelines recommend that those patients on aspirin who are at high risk of cardiovascular events should not stop aspirin at the time of surgery.<sup>7</sup> In contrast, current urologic consensus guidelines recommend stopping antiplatelet agents before PCNL.<sup>8</sup> Ureteroscopy remains an option for surgical stone management in those patients who cannot withdraw their anticoagulant regimens, but this is a non-ideal option for larger or complex renal stones.<sup>6</sup> Additionally, stopping aspirin in the perioperative period has been linked with an increased risk of thrombotic events and death.<sup>9</sup>

Very little evidence exists in the current literature on the perioperative continuation of aspirin during PCNL. Three series reported in the literature have shown that aspirin usage did not result in more blood transfusions or complications in patients who continued aspirin perioperatively.<sup>10-12</sup>

This study aims to determine the safety and efficacy of PCNL performed while continuing aspirin throughout the perioperative period in the high-risk cardiovascular patient population.

**METHODS**

***Patient Selection***

After receiving institutional review board approval, we retrospectively reviewed our single-center, single-surgeon (BK) the experience of PCNLs performed between January 2013 and September 2016. Those patients with either nursing intake documentation or operative report documentation supporting aspirin use in the immediate pre-operative period were included in the study. Aspirin use was therefore not interrupted before, during, or after surgery. Patients under the age of 18, pregnant women, wards of the state, and patients on other antiplatelets (such as clopidogrel) or anticoagulants (such as warfarin) were excluded.

Our technique of split-leg, prone PCNL was performed in all patients. Briefly, cystoscopy is first performed in the prone position, and a 5F ureteral catheter is advanced to the renal pelvis. A retrograde pyelogram is performed. The urologist obtains

access under fluoroscopic guidance in the calyx of choice, and the tract is dilated to 30F with a balloon dilator. The stone is removed by rigid and flexible nephroscopy using the ShockPulse-SE dual action lithotripsy system (Olympus, Center Valley, PA, USA) and Holmium laser as necessary. The renal unit is drained with either an 8F nephrostomy tube or a 7F indwelling ureteral stent. The nephrostomy tube would be removed on postoperative day 1 following a successful clamp trial, whereas the stent would be removed one week postoperatively in the outpatient setting. We have transitioned throughout the time course of this study to placing stents preferentially over nephrostomy tubes. Patients are generally discharged on postoperative day 1.

Demographic information, operative measures, and outcome-related metrics were recorded. These included: age, sex, BMI, operative duration, skin-to-stone distance, stone size, aspirin dose, aspirin indication, drainage type (nephrostomy tube or indwelling ureteral stent), pre- and postoperative hemoglobin levels, and Modified Clavien-Dindo complications within the first 30 days postoperatively by documentation review in the patient record. The pre-operative hemoglobin measure was the most recent measure available and not confined to a time range. The postoperative hemoglobin measure was taken on postoperative day 1. See Table 1.

***Endpoints***

The study’s primary objective was to determine the prevalence of bleeding associated complications

**TABLE 1** Demographic Information

Characteristic	Value
Number of procedures	27
Number of patients	23
Age (median [IQR]), yrs.	67 [59-73]
Sex (male, female) (%)	22 (81), 5 (19)
Laterality (left, right) (%)	18 (67), 9 (33)
BMI (median [IQR]), kg/m <sup>2</sup>	32 [29-35]
Indication for aspirin use, n (%)	
Coronary artery disease	22 (81)
Atrial fibrillation	5 (19)
Abdominal aortic aneurysm	1 (4)
Stroke	1 (4)
IQR = interquartile range, BMI = body mass index	

following PCNL on patients taking ASA in the immediate pre-operative period, including transfusion and angio-embolization. The secondary objectives of this study were to determine the overall prevalence of associated complications and the effect of PCNL on hemoglobin perioperatively as associated with various patient and case parameters.

**Statistics**

Descriptive statistics were reported as median and intraquartile range (IQR). Correlations between hemoglobin and explanatory variables were then explored with linear regression for continuous variables and the Wilcoxon rank-sum test for factor variables. A p-value of < 0.05 was considered significant. Analyses were performed with the use of the R statistical package version 3.2.3 and Excel 2013 Professional Edition.

**RESULTS**

Of 199 PCNLs performed at our institution in the range of our study, 27 procedures on 23 patients were conducted by a single surgeon (B.K.) on patients with documented use of aspirin in the immediate pre-operative setting. Patient demographics and indications for aspirin are outlined in Table 1. Three patients (13%) were on aspirin 325 mg daily. All other patients were on aspirin 81 mg daily.

Operative parameters are listed in Table 2. The median hemoglobin decline was 1.4 g/dL. The largest decline was 4.1 g/dL, but the lowest post-operative hemoglobin was 8.2 g/dl (above the transfusion threshold). No significant associations were found between hemoglobin decline and age (p = 0.73), sex (p = 0.42), BMI (p = 0.17), operative duration

**TABLE 2** Operative Parameters

Parameter	Value
Operative Time (median [IQR]), min	61 [46-61]
Stone size (median [IQR]), cm	2.2 [1.7-2.7]
Drainage type (stent, nephrostomy tube) (%)	9 (33), 19 (66)
Skin-to-stone distance (median [IQR]), cm	12.2 [10.1-14.5]
Length of stay (median), days	1
Hemoglobin decline (median [IQR]), g/dL	1.4 [0.3-2.1]

**TABLE 3** Postoperative Complications

Complications	Number
Clavien-Dindo Grade	
I	(5)
Urinary retention	1
Postural hypotension, conservative treatment	1
Acute kidney injury, hydration	1
Traumatic Foley removal	1
Gross hematuria post stent removal requiring admission and continuous bladder irrigation	1
II	(2)
Stent colic managed with tamsulosin	1
Renal colic due to residual stone fragment managed conservatively	1
III-V	0

(p = 0.054), skin-to-stone distance (p = 0.75), drainage type (p = 0.79), or initial stone size (p = 0.82).

Seven patients (30%) experienced a Clavien-Dindo grade I or II complication (Table 3). There were no Clavien-Dindo grade III or higher complications. Notably, no patients required a blood transfusion or angio-embolization. In addition, there were no cardiac or thrombo-embolic events in our series.

**DISCUSSION**

Evaluating the competing risks in patients on antiplatelet therapy is critical. The risk of hemorrhage due to the procedure must be weighed against a significant cardiac or cerebrovascular event risk. As a complicated and potentially troublesome condition, kidney stone treatment can often be deferred and/or treated conservatively until these other competing risks are evaluated and fully elucidated. Often, a multidisciplinary approach, including cardiologists, neurologists, or other health care providers, is necessary to adequately evaluate and stratify the risk of a thrombo-embolic event in these high-risk patients. There is a continuous balance of surgical bleeding risk and thrombo-embolic risk, which all involved clinicians needs to be weighed by all involved clinicians.

This study demonstrates that PCNL is safe and feasible to perform in patients who remain on aspirin in the perioperative period. This should help clinicians gain confidence in the management of these patients. No blood transfusions or angio-embolization were required in our series, and the average hemoglobin drop and length of stay compared very favorably to previously published series.<sup>10-12</sup> In addition, there were no thrombo-embolic events in our study. It is important to stress that the evidence presented relates only to patients on one antiplatelet therapy (aspirin in this series) and cannot be extrapolated to other antiplatelet therapies.

The current recommendation for peri-procedural management of aspirin from the urological literature is to withhold it before PCNL temporarily; however, this is based solely on expert opinion.<sup>6,8</sup> A growing body of evidence supports the continued use of aspirin throughout the perioperative period. A recent meta-analysis of the impact of aspirin, clopidogrel, and dual antiplatelet therapy on bleeding complications in non-cardiac surgery concluded that antiplatelet therapy at the time of non-cardiac surgery conferred minimal bleeding risk with no difference in thrombotic complications.<sup>13</sup> Discontinuing aspirin may prove to be harmful in some patients, with evidence suggesting a “rebound phenomenon” or “aspirin withdrawal syndrome”<sup>9</sup> where there is increased activity of thromboxane A<sub>2</sub> and decreased fibrinolysis, which, along with the pro-inflammatory state induced by the surgery itself, promotes an overall pro-thrombotic state. This was demonstrated in a randomized, double-blind, placebo-controlled study comparing the effect of low-dose aspirin to placebo in high-risk patients undergoing non-cardiac surgery (about 30% urological surgery). Ten patients (9.0%) in the placebo group compared to 2 patients (1.8%) in the aspirin group experienced a major adverse cardiac event at 30 days postoperatively ( $p=0.02$ ). Continuing aspirin in the perioperative period resulted in a 7.2% absolute risk reduction (95% CI, 1.3-13%), without any significant difference in bleeding complications.<sup>14</sup>

Moreover, several studies looking at renal procedures performed while on antiplatelet therapy have shown no increased risk of bleeding complications, including native<sup>15</sup> and transplant<sup>16</sup> kidney biopsies

and laparoscopic<sup>17</sup> and robot-assisted<sup>18-21</sup> partial nephrectomy. Two series published by Leavitt et al.<sup>10,11</sup> looked at PCNL performed while on aspirin. In their preliminary series, they performed 16 PCNL procedures in 14 high-risk cardiovascular patients continuing aspirin perioperatively. Three patients required a blood transfusion postoperatively, but there was no angioembolization or cases of delayed bleeding. They concluded that PCNL on aspirin is a viable treatment option for this population and was associated with an acceptably low transfusion rate compared with the potential sequelae of a thrombo-embolic event. Their second series compared 17 PCNL procedures performed on patients taking aspirin to 42 PCNL procedures performed on patients temporarily withholding aspirin. There were no differences between groups in terms of hemoglobin drop ( $p=0.522$ ), transfusion rates ( $p=0.703$ ), length of stay ( $p=0.642$ ), and no patient experienced a thrombo-embolic event. More recently, Otto et al.<sup>12</sup> compared outcomes and complications of 285 consecutive PCNL procedures, 67 (24.5%) of whom were maintained on aspirin 81 mg daily. There was no difference in blood loss, residual stone fragment size, length of stay, hemoglobin drop, and complication rates, including transfusions. Our outcomes compare very favorably to these previously published series and are consistent with historic published outcomes,<sup>22</sup> supporting the safety and feasibility of PCNL performed without discontinuing aspirin.

Limitations of this study include its retrospective nature and the small patient population. Exploratory analyses into the relationship between hemoglobin change and operative parameters were not powered a priori. In addition, the data is from a single surgeon with significant expertise in stone disease and PCNL, and may not be generalizable to all urologists performing PCNL. Also, formal cardiac evaluation was not conducted routinely postoperatively, and silent cardiac events may have occurred and been missed. Additionally, data from the 172 patients who did not take aspirin perioperatively was not extracted, and future research could prospectively or retrospectively compare these two groups for additional insights. To our knowledge, this is the second-largest published series looking at PCNL performed without discontinuing aspirin and provides further evidence

to help clinicians gain confidence that PCNL can be performed safely in this high-risk patient population while continuing aspirin.

### CONCLUSION

In our single-center experience, PCNLs performed on patients taking aspirin as monotherapy perioperatively were not associated with the need for blood transfusion nor the occurrence of high-grade complications. There is a need for a larger, randomized trial to corroborate these findings, and perhaps studies aiming to identify subgroups most likely to benefit from aspirin continuation. Our experience is that the continuation of aspirin is safe when performed by a high-volume surgeon in a high-volume center.

### DISCLOSURE

A portion of the content from this study was presented at the American Urological Association annual meeting in Boston, MA in May 2017.

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