Original Article

Predictive factors for fever and sepsis following percutaneous nephrolithotomy: A review of 580 patients

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Abstract

Aims: There has been much speculation and discussion about the infective complications of percutaneous nephrolithotomy (PCNL). While fever is common after PCNL, the incidence of it progressing to urosepsis is fortunately less. Which patient undergoing PCNL is at risk of developing urosepsis and in whom aggressive treatment of fever postoperatively may prevent the progression to severe sepsis becomes a very important question. This study aims to answer these vital questions.

Settings and Design: This is a single institutional, retrospective study over a period of 3 years.

Materials and Methods: Retrospective analysis of medical records of the patients undergoing PCNL from August 2012 to July 2015 was done. A total of 580 patients were included in the study, and the study variables recorded were analyzed statistically.

Statistical Analysis Used: Statistical analysis was performed by Chi-square test.

Results: Three factors significantly correlated with postoperative severe sepsis, namely, stone size >25 mm, prolonged operative time >120 min, and significant bleeding requiring transfusion. Factors associated with fever after PCNL which did not progress to sepsis were the presence of staghorn calculi and multiple access tracts in addition to the factors listed above for sepsis.

Conclusions: Fever after PCNL is not uncommon but it has a low incidence of progressing to life-threatening severe sepsis and multiorgan dysfunction syndrome. Special precautions and monitoring should be taken in patients with bigger stone (>25 mm) and patients with severe intraoperative hemorrhage requiring blood transfusion. It is better to stage the procedure rather than prolong the operative time (120 min). Identifying these factors and minimizing them may decrease the incidence of this life-threatening complication.

Keywords: Fever, percutaneous nephrolithotomy, sepsis, systemic inflammatory response syndrome

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INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is presently the mainstay of treatment for most large renal calculi. Since its inception in 1976,[1] PCNL has stood the test of time. It is, however, not free of complications. The most common complications of PCNL are a fever of no clinical significance and bleeding not requiring transfusion. Urosepsis is infrequent but a dreaded complication with

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an incidence ranging from 0.25% to 4.7% in various series.[2,3] Urosepsis can progress to multiorgan dysfunction syndrome (MODS), which has a high mortality. Therefore, predicting and preventing factors leading to urosepsis become of utmost importance.

Conventionally, infected urine and stone were implicated as possible causes of urosepsis,[4] with recent articles stressing other factors also to be important for the same.

Which patient undergoing PCNL is at risk of developing urosepsis and in whom aggressive treatment of fever postoperatively may prevent the progression to severe sepsis becomes a very important question. This single institutional retrospective review of 580 patients over a period of 3 years aims to answer these vital questions.

MATERIALS AND METHODS

Retrospective analysis of medical records of all the patients undergoing PCNL from August 2012 to July 2015 was done. A total of 580 patients fulfilled the inclusion criteria for this study. Exclusion criteria were compromised renal function, untreated urinary tract infection, intraoperative purulent urine, fever before surgery, multiple stones more than 5, and residual stone more than 4 mm.

The recorded data included age, gender, stone size, stone location, medical comorbidity, American Society of Anesthesiologists (ASA) score, subcostal or intercostal tract, number of access tracts used, operative time, blood transfusion, pre- and post-operative hemoglobin, pre- and post-operative total leukocyte count, postoperative maximum and minimum body temperature, postoperative maximum heart rate (HR), and postoperative maximum respiratory rate (RR). Patients with positive urine culture were treated adequately with antimicrobials. The intravenous antibiotic cover was given at induction of anesthesia depending on previous urine culture report or injection cefotaxime if urine was sterile.

The diagnosis was made on either intravenous urography or computed tomography (CT) urography. Stone size was calculated as the maximum diameter on plain X-ray kidney, ureter, and bladder (KUB) or CT KUB plain for radiolucent stones. For multiple stones, diameters of all stones were taken separately and added. Staghorn calculi were defined as stones occupying the pelvis and two or more calyces.

The standard PCNL procedure was used for all the patients. Under anesthesia, ureteric catheter was kept and fixed to Foley catheter. The patient was turned prone. The initial puncture was taken with an 18-gauge needle and tract dilated with Alkens dilators. A 24 or 26 Fr Amplatz sheath was placed. A 22 Fr rigid nephroscope was used. The operative time was calculated from turning patient prone till placement of nephrostomy tube. Patients were divided into four categories depending on the operative time: <60 min, 60–90 min, 90–120 min, and >120 min.

Systemic inflammatory response syndrome (SIRS) or sepsis was defined as having two or more of the following:[5]

- Body temperature <36°C odds ratio (OR) >38°C
- HR >90 beats/min
- RR >20 breaths/min or $PaCO_2$ <32 mmHg
- White blood cell >12,000/dl <4,000/dl, or >10% immature (band) forms.

Severe sepsis was termed in case of systolic blood pressure (BP) <90 mmHg OR systolic BP drop >40 mmHg.

Statistical analysis was done with Chi-square test, and $P < 0.05$ was considered statistically significant.

RESULTS

Table 1 depicts the demographic data and the relevant preoperative parameters of the patients. This study included 580 patients comprising 343 (59.10%) males and 237 (40.90%) females. The age of patients ranged from 7 to 71 years (mean - 43.3 years). Eighty-four (14.4%) patients were diabetic. Totally, 330 (56.8%) patients had a stone size more than 25 mm, and 175 (30.17%) patients had a staghorn stone. Seventy-two (12.4%) were ASA 3 or 4. One hundred and forty (24.1%) patients had a positive urine culture preoperatively.

Table 2 depicts the relevant intraoperative factors of the patients. The operative time taken was from 30 to 150 min (mean - 90 min). In 209 (36%) patients, an operative time of more than 120 min was taken. Multiple access tracts were

Table 1: Preoperative data of patients

Observation	Value
Total patients	580
Age (years)	
Mean	43.3
Range	7-71
Sex (%)	
Males	343 (59.1)
Females	237 (40.69)
Comorbidity: Diabetes mellitus	84
Stone size >25 mm	330
Staghorn calculus	175
ASA score 3/4	72
Preoperative positive urine culture	140

ASA: American Society of Anesthesiologists

used in 241 (41.55%) patients while 111 (19.1%) patients required a supracostal tract. Blood transfusion was required in 18 (3.1%) patients.

Statistical analysis was done using Chi-square test, and $P > 0.05$ was considered statistically significant. Table 3 shows the factors studied in context to fever and sepsis. We found three factors to be significantly correlated with postoperative severe sepsis, namely, stone size >25 mm, prolonged operative time >120 min, and significant bleeding requiring transfusion. Factors associated with fever after PCNL which did not progress to sepsis were the presence of staghorn calculi and multiple access tracts in addition to the factors listed above for sepsis.

A total of eight patients went into severe sepsis; however, fortunately, all responded to fluid resuscitation and antibiotics. There was no mortality.

Figures 1 and 2 depict the relation of fever and severe sepsis, respectively, with different factors studied.

DISCUSSION

PCNL is a relatively safe procedure for treating upper tract calculi. However, the procedure has to be done with utmost care and only by trained urologists. The pathophysiology of fever and sepsis is multifactorial including proinflammatory cytokines,[6] ischemia-reperfusion injury, and response to blunt trauma to the kidney.[7] There is an increasing interest in the role of noninfectious factors leading to SIRS and severe sepsis. In a study of 209 patients undergoing PCNL by Chen *et al.*,[8] the incidence of SIRS was reported as 23.4%. Contributory factors were number of tracts, blood transfusion, stone size, and presence of pyelocaliectasis. Similarly, Gonzalez-Ramirez *et al.* in a study of 280 patients found the incidence of severe sepsis to be 2.14%.[9] Significant bleeding during the procedure was the only factor implicated in severe sepsis while staghorn stones, body mass index <18.5, bleeding, and prolonged surgical time were associated with fever.

Intraoperative bleeding hampers vision prolonging operative time, and increased operative time is a risk factor for bleeding, making it a vicious cycle. Shear and blunt injury to kidney parenchyma releases cytokines and inflammatory mediators which may play a role in causing fever and sepsis. It is clear that prolonged operative time is a risk factor for postoperative fever and severe sepsis, but there are no clear, definite guidelines regarding the same. Wang *et al.*[10] found 90 min to be

Table 2: Perioperative data of patients

Observation	Value
Operative time >120 min	209
Multiple access tracts	241
Supracostal tract	111
Intraoperative bleeding requiring blood transfusion	18

Table 3: Incidence of fever and systemic inflammatory response syndrome in different risk factor groups

	Fever	*P*	SIRS	*P*
Total (%)	96 (16.55)	-	8 (1.37)	-
Sex (%)				
Males	56 (16.32)	0.9167	4 (1.67)	0.9912
Females	40 (16.87)		4 (1.69)	
Patients with diabetes mellitus	19	<0.001	3	0.0625
Stone size >25 mm	76	<0.001	7	<0.001
Staghorn calculus	45	<0.001	2	0.9989
ASA score 3/4	14	0.4804	2	0.2769
Preoperative positive urine culture	18	0.1769	1	0.4386
Operative time >120 min	74	<0.001	6	0.0197
Multiple access tracts	72	<0.001	2	0.3388
Supracostal tract	20	0.6439	1	0.6464
Intraoperative bleeding requiring blood transfusion	12	<0.001	4	<0.001

SIRS: Systemic inflammatory response syndrome, ASA: American Society of Anesthesiologists

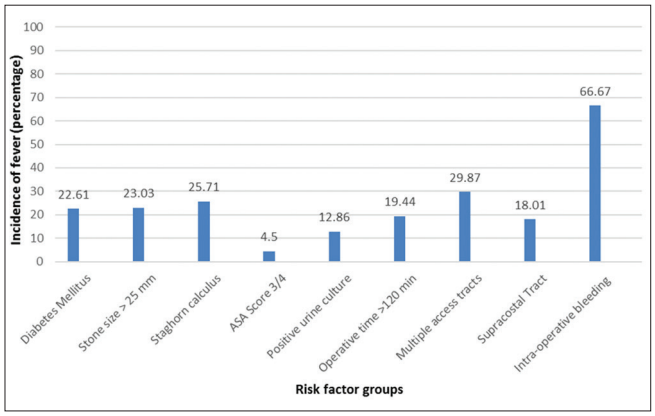

Figure 1: Bar diagram showing incidence of fever in different risk factor groups

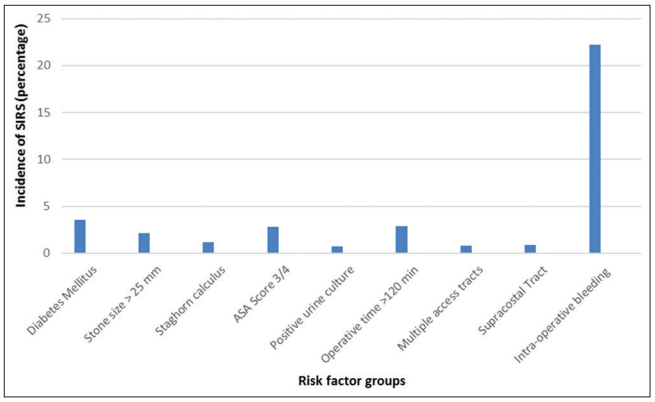

Figure 2: Bar diagram showing incidence of systemic inflammatory response syndrome in different risk factor groups

the upper limit of safety in their study of 303 patients. However, in this study, we found that the procedure can be safely carried on up to 120 min, starting from turning the patient prone.

Bigger stones including staghorn stones increase the operative time and propensity of bleeding. There is a greater manipulation during the procedure. We found that a stone size of more than 25 mm was associated with both fever and severe sepsis; however, staghorn stone had a positive association with fever but not severe sepsis. A negative preoperative urine culture is desirable but not always possible, especially with a stent or nephrostomy tube *in situ*. In a prospective trial by Mariappan *et al*.,[11] where 1 week of prophylactic preoperative ciprofloxacin was compared to control, they found a three-fold decreased risk of infection in the treatment arm.

Multiple access tracts lead to greater manipulation along with more traumas to the kidney with the release of inflammatory cytokines. There is also an added risk of bleeding. Sharma *et al*.[12] concluded a higher rate of blood transfusion in patients where multiple access tracts were used.

CONCLUSIONS

Fever after PCNL is not uncommon but it has a low incidence of progressing to life-threatening severe sepsis and MODS. Special precautions and monitoring should be taken in patients with bigger stone (>25 mm) and patients with intraoperative hemorrhage requiring blood transfusion. It is better to stage the procedure rather than prolong the operative time (120 min). Identifying these factors and minimizing them may decrease the incidence of this life-threatening complication.

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Conflicts of interest

There are no conflicts of interest.

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