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Lithotrites and Postoperative Fever: Does Lithotrite Type Matter? Results from the Clinical Research Office of the Endourological Society Percutaneous Nephrolithotomy Global Study

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Abstract

Objective—To compare the risks of fever from different lithotrites after percutaneous nephrolithotomy (PNL).

Materials and Methods—The Clinical Research Office of the Endourological Society (CROES) PNL database is a prospective, multi-institutional, international PNL registry. Of 5,803 total patients, 4,968 received preoperative antibiotics, were supplied with complete information and included in this analysis. The lithotrites assessed included no fragmentation, ultrasonic, laser, pneumatic and combination ultrasonic/pneumatic. Risk of fever was estimated using multivariate logistic regression with adjustment for diabetes, steroid use, a history of positive urine culture, the presence of staghorn calculi or preoperative nephrostomy, stone burden and lithotrite.

Results—The overall fever rate was 10%. Pneumatic lithotrites were used in 43% of the cohort, followed by ultrasonic (24%), combination ultrasonic/pneumatic (17.3%), no fragmentation (8.4%) and laser (7.3%). Fever rates were no different between patients who underwent no or any fragmentation ($p = 0.117$), nor among patients when stratified by lithotrite ($p = 0.429$). On multivariate analysis, fragmentation was not significantly associated with fever [Odds Ratio (OR) 1.17, $p = 0.413$], while diabetes (OR 1.32, $p = 0.048$), positive urine culture (OR 2.08, $p < 0.001$), staghorn calculi (OR 1.80, $p < 0.001$) and nephrostomy (OR 1.65, $p < 0.001$) increased fever risk. Fever risk among lithotrites did not differ ($p = 0.128$).

Conclusions—Risk of post-PNL fever was not significantly different among the various lithotrites used in the CROES PNL study.

Keywords

Percutaneous nephrolithotomy; Lithotrites; Fever

Introduction

One of the more common complications following a percutaneous nephrolithotomy (PNL) procedure is the development of postoperative fever. Recent estimates of post-PNL fevers range from 21–32%, despite administration of preoperative antibiotics [1]. In some cases, pyrexia may be secondary to bacteria contained inside the renal stones. Although a few studies have shown the bactericidal effects of lithotripsy on bacteria contained within urinary stones [2–4], the release of endotoxin may still result in postoperative fever or, even worse, urosepsis.

Currently, there is a wide range of technologies and intracorporeal lithotrites available and in use throughout the world, including pneumatic, ultrasonic, dual combination ultrasonic/pneumatic, electrohydraulic, holmium: YAG laser or pulsed dye laser. However, to our knowledge, no study has compared rates of post-PNL fever as stratified by lithotrite in a patient population, which is important because of global variability in the availability and usage of these technologies. Furthermore, to our knowledge, no prior study has compared whether simple stone extraction without fragmentation has a risk of fever different from that with intrarenal fragmentation of stones from lithotripsy. As smaller stone fragments would have a greater surface area and thereby theoretically release more bacteria and endotoxins, we hypothesize that lithotripters with an ultrasonic component, with their proven ability to fragment stones into smaller pieces [5], may be associated with higher post-PNL fever rates. We also hypothesize that, due to the increased release of bacteria and endotoxins, any form of lithotripsy would increase the risk of postoperative fever over that with simple stone extraction.

Materials and Methods

The Clinical Research Office of the Endourological Society (CROES) PNL Global Study is a prospective, multi-institutional, international registry of PNL cases from 96 centers on 5 continents. Details of the database are as previously described [6]. In brief, clinical data on a total of 5,803 patients who underwent PNL, including preoperative, perioperative and postoperative information, were prospectively collected between November 2007 and December 2009. The data were stored in a central data repository at the CROES office. At participating centers, IRB approval was obtained if necessary.

Types of lithotrites used in the database included ultrasonic, laser, pneumatic, electrohydraulic lithotripsy and combination ultrasonic/pneumatic. A small percentage of patients underwent no fragmentation when their stones could be removed in their entirety. Fever was defined as any temperature $>38.5^{\circ}\text{C}$ that occurred ≥ 24 h postoperatively; neither urosepsis nor systemic inflammatory response syndrome (SIRS) were defined outcomes in the database. Stone burden was grouped into tertiles using the formula: $\text{length} \times \text{width} \times \text{Pi}/4$ in mm^2 as follows: low ($< 159 \text{ mm}^2$), medium ($159\text{--}394 \text{ mm}^2$) and high ($>394 \text{ mm}^2$).

The CROES database contains information on 5,803 patients. As we were examining the risks of post-operative fever, we excluded patients who did not receive any perioperative antibiotics (2%). Furthermore, because of the very low numbers of patients who underwent

electrohydraulic lithotripsy (n = 57, <1%), this group was also excluded. Finally, we excluded patients who did not have complete information, leaving a final cohort of 4,968 patients (86%).

We compared postoperative fever rates as stratified by fragmentation status (no fragmentation vs. any fragmentation) using the χ^2 test for categorical variables and the Student t test for continuous variables which had normal distribution. Otherwise, the Mann-Whitney U test was performed. We then assessed odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of postoperative fever conferred by fragmentation status using multivariable logistic regression with adjustment for diabetes status (categorical), steroid use (categorical), a history of previous positive urine culture (categorical), the presence of staghorn calculi (categorical), the presence of preoperative nephrostomy tube (categorical) and stone burden (categorical). We repeated our analyses with stratification by specific lithotrite. Data were analyzed using SPSS version 16.0 with a two-tailed alpha of 0.05.

Results

Of the cohort, 92% of the patients underwent stone fragmentation, with pneumatic lithotrites being the most commonly used (43%), followed by ultrasound (24%), combination ultrasound/pneumatic (17%) and laser (7%) (table 1). These patients were no different from those who underwent no fragmentation with respect to age, BMI, diabetes status, steroid use or a history of positive urine culture (all p = 0.100). Patients with no fragmentation, however, were more likely to be female, have a preoperative nephrostomy tube and have less stone burden (all p = 0.018).

The overall fever rate was 10%. Patients who underwent stone fragmentation had no statistically significantly different fever rates compared to those patients who underwent no fragmentation (10.3 vs. 7.9%, respectively, p = 0.117; table 2). Fever rates when stratified by lithotrite type were also not significantly different (p = 0.429).

On multivariable logistic regression analysis comparing fever risk by fragmentation status, stone fragmentation of any kind did not confer a significantly higher risk of post-PNL fever than no fragmentation (OR 1.17, 95% CI 0.77–1.77, p = 0.413; table 3). Neither stone burden nor steroid use were significant independent predictors of postoperative fever. However, diabetes diagnosis, a history of positive urine culture during workup, the presence of staghorn calculi and the presence of a preoperative nephrostomy tube were all significant independent predictors of developing fever after PNL, with positive urine culture conferring the greatest risk (OR 2.08, 95% CI 1.64–2.62, p < 0.001).

When risk for postoperative fever was stratified by specific lithotrite type, no significant differences in risk were found across lithotrites, relative to pneumatic lithotripsy as the reference group (all p = 0.128; table 4). Again, diabetes, positive urine culture, staghorn calculi and a preoperative nephrostomy tube were all noted to be significantly associated with an elevated risk of post-PNL fever (all OR = 1.33, all p = 0.039), while stone burden and steroid use were not (all p = 0.470).

Discussion

Postoperative fever is not an uncommon occurrence after PNL, even in a setting of routine preoperative antibiotics. Importantly, this study suggests that the rates and risk of fever did not vary with the type of lithotrite used during the procedure, nor even with whether fragmentation occurred at all. Instead, the presence of a positive urine culture, staghorn calculus, a preoperative nephrostomy tube and a diabetes diagnosis were the significant risk factors for post-PNL fever. These findings suggest that patient characteristics, rather than technology, have a greater impact on the risk of postoperative fever in patients undergoing PNL.

Currently, various types of lithotrites are being used around the world [6]. In the CROES database, pneumatic lithotriptors were implemented the majority of the time, followed by ultrasonic-only, then combination ultrasonic/pneumatic and, lastly, holmium-based laser lithotrites. Pneumatic lithotriptors work via ballistic properties like a jackhammer, requiring direct contact with stones and a generator attached to a compressed air tank or CO₂ cartridge. Ultrasonic devices utilize an electric current passed through piezoceramic crystals that generate ultrasonic waves. These waves are then transmitted along a probe and converted to mechanical energy at the tip that then fragments stones upon direct contact. Often ultrasonic devices can be coupled to a suction pump to allow for the evacuation of the stone fragments. Combination ultrasonic/pneumatic lithotrites allow for a surgeon choice between the two modalities with theorized benefits of both. The high-power holmium laser can rapidly vaporize large-volume stones during rigid or flexible nephroscopy [7].

Thus far, several clinical comparisons among these intracorporeal lithotrites have been performed in prospective randomized trials. To date, however, while these studies have examined stone-related outcomes such as operative times and stone-free rates [8], none has stratified technologies by postoperative fever risk. Similarly, certain reviews of the literature have shown an estimated risk of post-PNL fever of as high as 30%, likely due to lower thresholds of temperatures defining fever, but, again, no previous study to our knowledge has stratified according to lithotrite modality.

Our study is therefore the first large-scale review to examine post-PNL fever risks by fragmentation status and lithotrite modality. We found no significant differences in postoperative fever risk by fragmentation status. This finding suggests that percutaneous access into a potentially obstructed collecting system may itself be a source of post-PNL fever, and that stone fragmentation makes little difference. One hypothesis for the incidence of fever following PNL is that unrecognized or incidental hematogenous seeding may occur during percutaneous access, and this is consistent with historical data showing that any endourologic manipulation of the urinary tract in the presence of urolithiasis has the potential to spiral into full-blown urosepsis [9]. While other studies have included complete stone extraction with no lithotripsy in their analyses for overall post-PNL fevers, none has stratified according to fragmentation status. In our study, complete stone extraction with intact stone removal revealed a postoperative fever rate (8%) that was not statistically significantly different from that following intra-corporeal lithotripsy (10%). Thus

intracorporeal lithotripsy, routinely utilized to break up larger stones unable to be simply extracted, does not appear to contribute to a higher risk for postoperative fever.

Furthermore, we found no significant differences in post-PNL fever risk by lithotrite modality. Several in vitro studies have shown a direct bactericidal effect of lithotripsy, but they also theorize that release of endotoxins from bacterial cell lysis may potentially still cause deleterious effects in the patient [2–4]. A previous in vitro study found significantly smaller fragment sizes produced by the ultrasonic lithotrite compared to the pneumatic lithotrite [5]. This led to the theory that greater fragmentation by an ultrasonic lithotrite may lead to higher fever rates due to the increased surface area and greater potential for release of endotoxins. However, given our results, we conclude that increased fragmentation by different lithotrite technologies does not clinically elevate the risk of infection or fever from endotoxin release. As such, more attention should be paid to managing patient-level factors such as diabetes diagnosis or positive preoperative urine culture to minimize postoperative fever risk, rather than to the surgeon's choice of technology for stone treatment.

Our study has certain limitations. First, the primary outcome measure of our study was postoperative fever risk and not true SIRS or urosepsis. Studies have shown post-PNL fevers to occur much more frequently than true urosepsis [1], possibly due to other causes such as atelectasis or wound infection. Thus postoperative fever should not serve as a surrogate for life-threatening complications such as urosepsis. In addition, the clinical significance of post-PNL fever has been questioned, particularly if patients are otherwise clinically stable [10]. Given the very low incidence of post-PNL urosepsis overall and the low number (<20 events) within the CROES PNL database [11], fever served as a better-powered outcome measure for the purposes of this study. We had also originally sought to explore the impact of different intracorporeal lithotrite technologies on patient safety, with fever serving as a fairly common postoperative complication.

Secondly, some studies have indicated that longer operative times, high-pressure flow systems and positive stone or renal pelvis cultures are additional risk factors for postoperative infectious complications [1, 12–14]. These data, though promising, were not prospectively recorded and are therefore not available in the CROES PNL database. Finally, the cohort that was analyzed consisted of only 86% of the overall patient population of 5,803 PNLs in the database. These data, however, consisted only of patients who received preoperative antibiotics, which is important when our outcome is postoperative fever. All our data were prospectively recorded and the study still constitutes the largest dataset of PNL procedures worldwide.

Conclusions

PNL alone is a procedure with comparable risks for the development of postoperative fever, regardless of the device used for stone fragmentation or if the calculus is removed intact. Therefore, the stone removal technology itself does not appear to influence the development of post-PNL fever. This information suggests that postoperative infectious complications may not be based on the method of stone removal during PNL.

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Table 1

Cohort characteristics by fragmentation status

Characteristic	No fragmentation (n = 418)	Any fragmentation (n = 4,550)	p value
Age, years (mean $\pm$ SD)	49.3 $\pm$ 14.9	49.0 $\pm$ 15.7	0.650 [*]
Male gender, n	212 (50.8)	2,588 (56.9)	0.016 [§]
BMI, kg/m ² (mean $\pm$ SD)	26.6 $\pm$ 5.4	26.6 $\pm$ 5.6	0.190 [*]
Diabetes, n	50 (12.0)	622 (13.7)	0.362 [§]
Steroid use, n	3 (0.7)	50 (1.1)	0.634 [§]
Positive urine culture, n	77 (19.1)	695 (15.8)	0.100 [§]
Preoperative nephrostomy, n	45 (11.0)	340 (7.6)	0.018 [§]
Stone burden, mm ² (mean $\pm$ SD)	152.0 $\pm$ 158.1	330.0 $\pm$ 258.2	<0.001 ⁺
Lithotrite type, n			
Pneumatic	–	2,135 (43)	–
Ultrasound	–	1,193 (24)	–
Combination (ultrasound/pneumatic)	–	859 (17)	–
Holmium laser	–	363 (7)	–

Values in parentheses are percentages, unless otherwise indicated.

^{*} Student t test;⁺ Mann-Whitney U test;[§] χ^2 test.

Table 2

Fever rates (>38.5° C) stratified by fragmentation status and lithotrite

	Fever	No fever	p value*
By fragmentation status, n (%)			
No fragmentation	33 (7.9)	385 (92.1)	0.117
Any fragmentation	469 (10.3)	4,081 (89.7)	
By lithotrite, n (%)			
No fragmentation	33 (7.9)	385 (92.1)	0.429
Pneumatic	215 (10.1)	1,920 (89.9)	
Ultrasound	118 (9.9)	1,075 (90.1)	
Combination	94 (10.9)	765 (89.1)	
Laser	42 (11.6)	321 (88.4)	

* χ^2 test.

Table 3

Predictors of postoperative fever stratified by fragmentation status

Variable	OR	95% CI	p value
Fragmentation			
None	1.0	–	–
Any	1.17	0.77–1.77	0.413
Diabetes			
No	1.0	–	–
Yes	1.32	1.00–1.72	0.048
Steroid use			
No	1.0	–	–
Yes	1.35	0.59–3.07	0.471
Urine culture			
Negative	1.0	–	–
Positive	2.08	1.64–2.62	<0.001
Staghorn stone			
No	1.0	–	–
Yes	1.80	1.43–2.28	<0.001
Nephrostomy			
No	1.0	–	–
Yes	1.65	1.21–2.25	<0.001
Stone burden			
Low	1.0	–	–
Medium	1.06	0.81–1.38	0.697
High	0.99	0.76–1.28	0.917

Table 4

Predictors of postoperative fever stratified by lithotrite modality

Variable	OR	95% CI	p value
Lithotrite			
Pneumatic	1.0	–	–
No fragmentation	0.88	0.57–1.35	0.474
Ultrasound	0.89	0.69–1.16	0.398
Combination	1.16	0.88–1.53	0.321
Laser	1.36	0.93–1.99	0.128
Diabetes			
No	1.0	–	–
Yes	1.33	1.02–1.75	0.039
Steroid use			
No	1.0	–	–
Yes	1.35	0.59–3.07	0.470
Urine culture			
Negative	1.0	–	–
Positive	2.31	1.70–3.12	<0.001
Staghorn stone			
No	1.0	–	–
Yes	1.90	1.45–2.48	<0.001
Nephrostomy			
No	1.0	–	–
Yes	1.62	1.18–2.22	0.003
Stone burden			
Low	1.0	–	–
Medium	1.08	0.82–1.41	0.594
High	0.99	0.77–1.29	0.968