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## REVIEW

# Advances in percutaneous stone surgery





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Received 15 July 2014; received in revised form 11 August 2014; accepted 18 August 2014 Available online 16 April 2015

#### KEYWORDS

Nephrolithiasis; Kidney calculi; Percutaneous nephrolithotomy **Abstract** Treatment of large renal stones has changed considerably in recent years. The increasing prevalence of nephrolithiasis has mandated that urologists perform more surgeries for large renal calculi than before, and this has been met with improvements in percutaneous stone surgery. In this review paper, we examine recent developments in percutaneous stone surgery, including advances in diagnosis and preoperative planning, renal access, patient position, tract dilation, nephroscopes, lithotripsy, exit strategies, and post-operative antibiotic prophylaxis.

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## 1. Introduction

Nephrolithiasis presents a significant health concern for a large number of individuals throughout the world. Increasing rates of comorbidities known to correlate with urinary stone disease, such as diabetes mellitus, hypertension, and obesity, have all led to an increase in the incidence of new stones in these individuals. For example, as the prevalence of diabetes in the United States has nearly doubled in the past 20 years, the number of presentations to the Emergency Department for stone episodes rose from 178 per 100,000 patient visits to 340 per 100,000 patient visits roughly over the same time period [1,2]. This increase in overall stone prevalence has been met with a similar increase in large renal stones.

Recent studies have shown that environmental factors may also play a significant role in the development of nephrolithiasis. For example, Chi et al. [3] demonstrated significant differences in the stone composition of Chinese patients living in North America compared to Chinese patients living in China. They found that patients in China were more likely to have a lower body mass index (BMI), present approximately 9 years earlier than Chinese Americans, and form calcium oxalate stones. This suggests that environmental factors may play a significant role in stone formation, in addition to genetic factors.

Oberlin et al. [4] recently looked at patterns of treatment for upper tract calculi. They found that during 2003–2012 the number of patients treated with ureteroscopy rose from 40.9% to 59.6%, while the number of

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Peer review under responsibility of Chinese Urological Association and SMMU.

http://dx.doi.org/10.1016/j.ajur.2015.04.010

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patients treated with extracorporeal shock wave lithotripsy (ESWL) correspondingly decreased from 54% to 36.3%. The rate of percutaneous nephrolithotomy (PCNL) stayed roughly the same.

Our aim is to review the literature on PCNL and examine new developments in percutaneous stone surgery in recent years.

## 2. Diagnosis

A number of imaging modalities have been described to diagnose nephrolithiasis, including ultrasound (US), computerized tomography (CT), and plain X-rays. Noncontrast CT has emerged as the imaging study of choice because of relative cost-effectiveness, sensitivity for diagnosing nephrolithiasis, and speed at which it can be performed [5]. Low-dose CT is an acceptable option in patients with a favorable body habitus. In cases in which percutaneous surgery is anticipated for a large stone burden, CT scans aid in classification of stone size, location within the collecting system, and density. Additionally, they help in planning the operative approach a surgeon may take in accessing a stone. In regions in which CT is not readily available, renal US is a reasonable alternative for diagnosing renal calculi, though the sensitivity and specificity of US is not as high as that of CT [6].

Okhunov et al. [7] recently proposed their S.T.O.N.E. nephrolithometry scoring system to standardize reporting for percutaneous nephrolithometry. In 117 patients from a single institution, they measured five variables relating to stone complexity based on pre-operative CT scan, including stone size (S), tract length (T), obstruction (O), number of calvces involved (N), and essence or stone density (E). They found that pre-operative stone score correlated to postoperative stone-free rate, estimated blood loss, operative time, and length of stay. In follow-up, the group recently validated the S.T.O.N.E. scoring system in a multiinstitutional study comprising 706 patients. Their results confirmed their prior findings that a greater S.T.O.N.E. score correlated with lower stone-free rates, increased bleeding and estimated blood loss, operative time, length of hospital stay, fluoroscopy time, and overall complication rate [8].

Labadie et al. [9] recently compared three stone scoring systems, including the S.T.O.N.E. scoring system, Guy's stone score, and the CROES (Clinical Research Office of the Endourological Society) nephrolithometric nomogram to determine which was the most predictive of surgical outcomes. They found that each was significantly associated with stone-free status, however Guy's stone score and the S.T.O.N.E. scoring system were significantly associated with estimated blood loss (EBL) and hospital length of stay (LOS), whereas the CROES nomogram was not predictive of EBL or LOS.

Mishra et al. [10] also recently used CT urography and three-dimensional volume rendering to assess staghorn stone volume and correlate stone morphometry with the number of tracts and stages needed to clear patients of their staghorn stones. They then defined stones as one of three types, with type 1 stones having a volume of less than 5000 mm<sup>3</sup> with less than 5% of the stone volume in an

unfavorable calyx, while type 3 stones were those with a total volume greater than 20,000  $\text{mm}^3$  and greater than 10% of the stone in an unfavorable calyx. Type 2 stones were those that fell between these two extremes. Through their model they predict that type 1 stones necessitate a single tract and single stage for stone clearance, type 2 stones necessitate single tract-single/multiple stages or multiple tracts within a single stage, and type 3 stones require multiple tracts and stages for clearance.

These results argue that one of the recently developed stone scoring systems should be used in preoperative planning and patient counseling, and that this scoring system should be universally used as a way to standardize PCNL-planning across institutions.

### 3. Preoperative planning

The number of patients requiring PCNL who are on longterm anticoagulation or antiplatelet therapy with warfarin. aspirin, clopidogrel, and heparin derivatives has increased in recent years due to the use of more drug-eluting cardiac stents, heart valve replacements, treatment of atrial fibrillation, and cardioprotective measures [11,12]. Controversy exists as to which patients may be safely taken off of anticoagulation for a period of time, as well as how to best manage patients who need to remain on anticoagulation perioperatively. In patients with a significant stone burden and in whom cessation of anticoagulation poses an unacceptable risk, performing staged ureteroscopies may be preferable to PCNL. In patients with significant cardiac risk factors, cessation of aspirin may have adverse cardiac consequences during the perioperative period due to the rebound period off of aspirin. Recent studies have also shown that low-dose aspirin can safely be continued in the perioperative period without a significantly increased risk of bleeding [13,14].

In patients undergoing procedures with a high risk of bleeding such as PCNL, it is recommended that they discontinue the use of warfarin 3–5 days prior to the intended procedure. Kefer et al. [15] specifically recommends stopping warfarin 5 days prior to PCNL and waiting to restart it for 5 days following the procedure. Low molecular weight heparin may be used for bridging in the perioperative period. The authors demonstrated this regimen to be safe, with an acceptable major bleeding risk of 7%. The same group demonstrated that stopping clopidogrel 10 days prior to undergoing PCNL and resuming it 5 days postoperatively incurred an acceptable bleeding risk, as well.

Sepsis secondary to urinary tract infection can significantly increase morbidity and mortality in patients who have undergone PCNL. It is standard practice for patients to have a urinalysis and urine culture (UCx) checked prior to undergoing surgery to reduce the risk of sepsis. Gutierrez et al. [16] examined 5354 patients who underwent PCNL and who had preoperative UCx available, and found that 865 (16.2%) patients had a positive UCx. Of the patients with a positive culture, 18.2% developed a post-operative fever in comparison to 8.8% of patients with a negative pre-operative UCx. The type of microorganism was also found to play a role, with as low as 9.7% of patients whose urine was colonized with *Staphylococcus* species developing a fever, compared to a high of 23.8% of patients whose urine was colonized with *Enterobacter species*. In patients who have a contaminated UCx, however, treatment decisions become somewhat more difficult. Leavitt et al. [17] recently reported on the use of urinalysis (UA) and urine dipstick analysis (UDA) to predict the risk of sepsis after PCNL. They found that of 291 patients with a negative UA or UDA, none developed sepsis after undergoing PCNL. They concluded that a negative UA or UDA may be sufficient as a screening test prior to undergoing PCNL. At this time, however, we continue to recommend obtaining a UCx prior to PCNL in order to prevent sepsis.

Larson et al. [18] recently compared the bacterial species between stone cultures (SCx) and UCx in patients undergoing PCNL. They found that SCx and UCx correlated in 79% of cases. SCx was positive in 12.5% of patients who had a negative UCx, and they therefore recommended obtaining a stone culture at the time of PCNL in order to more effectively tailor antibiotic treatment of sepsis after surgery in patients with a negative UCx.

Controversy exists as to the best duration of preoperative antibiotic treatment in patients scheduled to undergo PCNL. Although many patients will have a negative UCx preoperatively, approximately one-third of stones harbor bacteria, despite the presence of antibiotic treatment. Previous studies have demonstrated that one week of preoperative antibiotic therapy may reduce the risk of serious infectious complications in patients who are at high risk for infection but have sterile UCx. Larson et al. [19] recently examined the differences in infectious complications in patients with sterile urine who underwent PCNL and received between 2 and 7 days of preoperative antibiotic prophylaxis and who were deemed to be at high risk for infectious complications. They found that there were no patients who developed an infectious complication in either group, including fever >38.5 °C, SIRS criteria, or sepsis after PCNL. They concluded that either 2 or 7 days of prophylactic antibiotics are effective at preventing infectious complications in high-risk patients with sterile urine who undergo PCNL.

### 4. Access

Access to the collecting system for PCNL may be obtained either in interventional radiology (IR) prior to definitive stone management, or by the urologist at the time of PCNL. Oftentimes, urologists who perform less percutaneous stone surgeries will proceed with PCNL after access is obtained by IR, while dedicated endourologists will gain access by themselves. Ingimarsson et al. [20] compared access obtained in IR to access obtained at the time of PCNL by a urologist, examining differences in complications and stone-free rates when access is obtained by each of these groups. They found that endourologists were significantly more likely to gain access in the 10th or 11th intercostal spaces than interventional radiologists (47% vs. 14%, p < 0.001). There was no difference in the rate of complications between the two groups, including pneumothorax requiring intervention, transfusion, or failed access. They did, however, find that patients for whom access was obtained by an interventional radiologist underwent more secondary procedures to become stone-free (38% vs. 21%, p < 0.01). They concluded that access may safely be obtained by either group, however these results argue that urologists who gain access at the time of PCNL may achieve a stone-free state with fewer procedures. This is likely due to goal-directed access by endourologists to achieve stone-free states, rather than to simply access the collecting system.

Total fluoroscopy time and radiation exposure have also come into scrutiny recently, especially amongst endourologists performing PCNL. The traditional "bullseve" technique for obtaining renal access has been criticized for long fluoroscopy times. Lightfoot et al. [21] examined a novel technique, utilizing laser-guided renal access and compared the fluoroscopy time to traditional bullseye access in a benchtop kidney model. They found that fluoroscopy time was significantly reduced among all groups examined, including attendings/fellows, residents, and medical students when using laser-guided access. The least experienced users, medical students and residents, reported that laser-guided access was significantly easier to learn than conventional access. These results argue that laser-guided access may significantly reduce fluoroscopy time when gaining renal access for PCNL, however these results need to be confirmed in *in vivo* experiments, as kidney models do not move with respiration as do in vivo kidneys.

In a similar attempt to reduce fluoroscopy time during PCNL, Alsyouf et al. [22] examined ureteroscopic-assisted access in a recent feasibility study. Instead of using fluoroscopy, the authors placed a ureteroscope in the desired calyx under direct visualization and then used ultrasound to guide the access needle into that calyx. They found that fluoroscopy time was significantly decreased in the ureteroscopy-ultrasound group (4.6 s vs. 790 s, p < 0.001), while operative time, stone-free rates, mean hospital stay, estimated blood loss, and complication rates were not significantly different between the two groups. Future studies with a greater number of patients need to be performed to confirm these findings.

Kawahara et al. [23] recently performed another study utilizing ureteroscopy to gain renal access. In their study, they inserted a nephrostomy puncture wire through the ureteroscope and gained retrograde access to the collecting system. While they used fluoroscopy and did not report on fluoroscopy times or a comparison of radiation exposure to conventional renal access, they did report that retrograde renal access was successful in 77.3% of patients.

Controversy also exists as to the safety of upper pole renal access as compared to lower and middle pole access. Some urologists believe that upper pole access may lead to increased pain and complications, including thorascopic complications. Lightfoot et al. [24] examined complications, narcotic use, stone burden, operative time, and estimated blood loss between patients undergoing upper pole access compared to lower pole access. They found that patients undergoing upper pole access had an overall greater stone-free rate (94.4% vs. 85.5%, p = 0.024) compared to patients undergoing lower pole access, although complication rate, estimated blood loss, narcotic requirements and operative time were similar between the two groups. These results argue that for patients in whom upper pole access may be beneficial, it is safe to perform and may lead to greater stone-free rates.

### 5. Position

Percutaneous nephrolithotomy has traditionally been accomplished in the prone position. This requires first performing a cystoscopy and ureteral catheter placement in the lithotomy position and later repositioning the patient in the prone position, or performing cystoscopy and ureteral catheter placement in the prone position, a technique that many urologists are not comfortable performing. Alternatively, PCNL may be performed in the supine position, performing ureteral stent placement in lithotomy and proceeding with PCNL without significant repositioning. The advantage of this technique is also to be able to work both from above and below at the same time.

Controversy exists, however, as to which technique is superior in terms of operative time, stone-free rates, and complications. Astroza et al. [25] recently published on these topics, looking at 1311 patients who either underwent supine (232 patients) or prone (1079 patients) PCNL. They found that the stone-free rate was greater (p < 0.001) and surgical time was shorter (p < 0.001) in patients who underwent prone PCNL. They found that there was no difference in the complication rates between the two groups. Conversely, a number of studies have examined the differences between the two methods of PCNL and found that operative time is shorter in patients undergoing supine PCNL [26-29]. Numerous studies have also found that the complication rates are similar between modalities [26,28,29], transfusion rates or estimated blood loss are similar [27,28], and stone-free rates are similar [26-29].

As it is easier to gain access to all calyces ureteroscopically than with a flexible nephroscope in patients with multiple small stones in different calyces, it may be beneficial to grasp these stones with the flexible ureteroscope and release them in the renal pelvis. This then allows these stones to be retrieved with the nephroscope more easily. This is most easily accomplished with patients in the supine position. This is especially relevant for PCNL performed in the supine position as the tract is much longer than the prone PCNL tract and consequently the long tract makes it difficult to maneuver the nephroscope from one calyx to another. We believe that endourologists should be comfortable with performing PCNL in both the supine and prone positions.

## 6. Tract dilation

Traditional tract dilation using successive Amplatz or Alken dilators has recently been replaced by some urologists with the use of balloon dilators. By rapidly dilating with a single balloon rather than successively using different dilators, balloon dilation is thought to be faster than successive fascial dilation. Additionally, some believe that balloon dilation may result in less renal trauma and a reduced risk of dislodging the safety wire [30]. Fuller et al. [31] recently examined the influence of BMI on PCNL outcomes and found that, in obese patients, tract dilation was more commonly performed via balloon dilation (p < 0.0001).

One of the major criticisms of balloon dilators is their relatively low burst pressure at 17 ATM. Recently developed balloons have improved upon this, allowing pressures up to 30 ATM before concern for bursting exists. Hendlin and Monga [32] reported a 100% success rate after dilating 60 nephrostomy tube tracts with a Bard X-Force 30 ATM balloon, as opposed to the reported 5%–10% failure rate with standard 17 ATM balloons.

Another new development in tract dilation has been the introduction of the pathway access sheath (PAS), a device that allows for tract dilation and sheath placement at the same time. In a small study of only 21 patients, Pathak and Bellman [33] compared access time between traditional standard balloon dilation and the PAS system. They found significantly reduced access time in those tracts dilated with the PAS system (3 min vs. 5.7 min). These results need to be confirmed in larger, prospective trials, but are promising in potentially reducing the operative and fluoroscopy times amongst patients undergoing PCNL.

### 7. Nephroscopes

The standard rigid nephroscope has many advantages and disadvantages related to its size. This scope requires a calvceal tract to be dilated to 30 French, either via serial fascial dilation or by balloon dilation. The large diameter of the scope allows for excellent visualization within the collecting system by providing good flow of irrigation and a large visual field. The scope allows standard PCNL instruments to pass through it, such as more powerful ultrasonic lithotripters and graspers that can be used to remove large stones. The 30 French calvceal tract allows for removal of larger stone fragments intact, ostensibly allowing for quicker stone clearance. However, the large tract required by the standard rigid nephroscope possibly results in more renal trauma upon dilation of the tract, creating a higher risk of intraoperative and postoperative complications. Standard PCNL may have a higher risk of intraoperative blood loss, a higher postoperative risk of pseudoaneurysm or arteriovenous malformation, and the larger tract may contribute to more postoperative pain and higher requirements for narcotics postoperative. Should multiple percutaneous tracts be necessary, standard PCNL is likely to increase the requirement for intraoperative and postoperative transfusions and increase the bleeding risk.

Flexible nephroscopy provides a convenient way to survey the renal collecting system with direct visualization without creating another tract. Using a standard flexible cystoscope, one can survey the renal pelvis and most of the calyces for residual stones, and even perform laser lithotripsy and use stone baskets to extract small residual stones. If a large residual stone burden is noted, another percutaneous tract may be created, however it is best to limit the number of tracts as much as possible to lower the risk of bleeding. While flexible nephroscopy is not perfect and its reliability is user dependent, in skilled hands the combination of rigid and flexible nephroscopy can effectively clear a large stone burden while limiting the number of percutaneous tracts required.

"Mini"-perc is a term used to describe a method of percutaneous stone extraction utilizing a smaller

percutaneous tract. In a mini-perc, access is gained into the calyx and the tract is usually dilated to 12-14 French, large enough to accommodate a ureteral access sheath. Ureteroscopic instruments are then utilized, including flexible and rigid ureteroscopes. Pediatric cystoscopes may also be helpful. Smaller rigid nephroscopes, such as 12 French nephroscopes, are available and can be used through a 14-16 French Amplatz sheath as well. Li et al. [34] described the use of an endoscopic pulsed perfusion pump combined with retrograde flushing via a previously placed ureteral catheter for removal of small fragments. The pump, which irrigates via the endoscope, generates a pressure up to 300 mmHg for 3 s with a 2 s respite. This pressure, combined with retrograde flushing, distends the collecting system. With properly timed removal of the endoscope, a relative vacuum is created within the sheath, forcing small fragments out via the sheath. Guohua et al. [35] investigated whether such a device contributed to high intrarenal pressures, promoting pyelovenous backflow. They found that the device created intrarenal pressures that were generally lower than the level required for backflow. When the level was reached, the pressure lasted only for a few seconds and was soon relieved.

Mini-perc was originally designed for children with large stones requiring percutaneous stone extraction [36], but it has been shown to be useful for adults as well [37]. Generally used for stones less than 2 cm, mini-perc reduces the morbidity of standard PCNL. The smaller tract potentially creates a lower bleeding risk, both intraoperatively and postoperatively. The smaller tract may also decrease postoperative pain level, narcotic requirements, and hospital length of stay. However, given the smaller tract, visualization of the collecting system is worse than standard PCNL and efficiency of lithotripsy is limited by instruments available that fit through such small working channels, including lasers, baskets, small suction devices, and small grasping forceps. The stone fragments that are removed must be much smaller to pass through the calyceal tract. Thus, this technique is best for use in children or for stones less than 2 cm in size.

Standard PCNL combined with mini-perc can be an effective method to maximize stone-free rates while minimizing complications. In a recent study, Wang et al. [38] compared standard PCNL combined with mini-perc versus single access standard PCNL, showing greater stone-free rate in the PCNL/mini-perc group with similar operative time, complication rate, and lower re-operation rate.

Micro-PCNL is a new technique designed to minimize the diameter of the calyceal tract. Micro-PCNL utilizes a 4.85 French optic needle, dubbed the "all-seeing needle", originally designed to obtain quicker percutaneous calyceal access prior to dilation. This technique takes advantage of the optic capability of the needle and uses this direct access for lithotripsy [39], reducing the risk associated with tract dilation. Given that the tract is approximately 16 Gauge, this technique seems to be best suited for small to moderate size stones. However, it limits much of the morbidity associated with standard PCNL and may be useful for stones difficult to access ureteroscopically. Additionally, this technique may find a niche in treating lower pole stones which have poor clearance rates with ESWL.

## 8. Lithotripsy

There are many different types of intracorporeal lithotripsy modalities that can be used with PCNL. The most common modalities are homium:YAG laser, pneumatic lithotripter, ultrasonic lithotripter, and combination devices. Individually, ultrasonic lithotripters have been shown to be more efficient for stone clearance than pneumatic lithotripters [40]. However, combination ultrasonic-pneumatic devices are more efficient for stone clearance than either device individually [41]. These devices are also combined with suction capability allowing for greater efficiency. Laser lithotripsy is less efficient than the other modalities, however its main advantage is the flexibility of the laser fiber. This allows for lithotripsy to be performed during flexible nephroscopy and antegrade flexibly ureteroscopy. A novel laser with suction capabilities is under investigation. Another novel device under investigation, PercSac, is a polyethylene sack used to entrap a stone, controlling all of the stone's fragments during lithotripsy [42]. This device has been shown to improve efficiency in stone fragmentation and improve stone free rates in in vitro models.

## 9. Exit strategies

Renal drainage upon termination of PCNL has evolved over time with a trend toward leaving smaller nephrostomy tubes, and even with some urologists leaving patients tubeless. Generally there are three main categories: large nephrostomy tube drainage, small nephrostomy tube drainage, and "tubeless" renal drainage in which the patient is left with a ureteral stent or ureteral catheter instead of a nephrostomy tube.

For the most part, the large nephrostomy tube of choice is a 24 French malecot re-entry nephrostomy tube. This is accommodated within the calyceal tract of a standard PCNL, its large diameter providing some tamponade of bleeding from the tract. The large diameter also provides low-pressure direct drainage of the kidney. The malecot sits comfortably within the renal pelvis, helping to keep the tube in place. The ureteral portion of the tube allows for quick through-and-through access in cases where staged procedures or re-operation is necessary. Thus, this tube is preferred when the need for re-operation or staging is suspected, after complicated cases with a large blood loss, when gross stone is visible, or when there is complicated anatomy [43].

An effort has been made to use smaller nephrostomy tubes when possible. Smaller nephrostomy tubes have been associated with less postoperative pain and narcotic requirements when compared to 24 French malecot re-entry tubes [44]. Different sizes of tubes can be used, from 8.5 French to 14 French. After uncomplicated cases, small nephrostomy tubes are a safe alternative for renal drainage.

"Tubeless" PCNL has recently become more popular and has proven to be safe and viable. There are two ways to promote renal drainage after tubeless PCNL: with a double-J stent and Foley catheter, or with a ureteral catheter and Foley catheter. When using a double-J stent, the Foley catheter is removed after 24 h and the stent removed approximately 5–10 days after surgery. When using a ureteral catheter, both the Foley catheter and ureteral catheter are removed 23–48 h after surgery. Zilberman et al. [45] reviewed the use of tubeless PCNL and found this technique decreased the need for pain medication in the postoperative period, shortened hospital stay, and reduced time to return to normal activities with no increase in complications. It is recommended that tubeless PCNL be reserved for straightforward, uncomplicated cases.

Tract sealants have been used in tubeless PCNL as surrogates for nephrostomy tubes in an effort to facilitate hemostasis and to prevent urinary extravasation. Agents such as fibrin glue and FloSeal have been applied to calyceal tracts with these objectives in mind. However, the advantage to this practice remains theoretical. Shah et al. [46] performed a prospective randomized trial utilizing fibrin sealant after PCNL, finding no difference in blood transfusion requirement and a trend toward less post-operative pain and less analgesic requirement, though this did not reach statistical significance.

Cryotherapy has also been used to facilitate tubeless PCNL. Okeke et al. [47] utilized a cryoprobe within the renal parenchyma just outside the collecting system, using a 10-min freeze-thaw cycle, then removing the probe and closing the skin incision. They found cryotherapy shortened hospital stay, decreased rates of delayed bleeding, and decreased rates of urinary leak.

The exit strategy for mini-perc has a similar dilemma regarding which method of renal drainage is appropriate. Sabnis et al. [48] performed a randomized controlled trial comparing tubeless mini-perc with ureteral catheter and Foley catheter, tubeless mini-perc with a double-J stent and Foley catheter, and 14 French nephrostomy tube with ureteral catheter and Foley catheter and Foley catheter after mini-perc. They found lower pain levels and pain medication requirements in patients who underwent tubeless procedures and were left with ureteral and Foley catheters, with no change in drop in hemoglobin, urine leakage, or perioperative complications.

## 10. Postoperative antibiotics

There are no clear guidelines for postoperative prophylactic antibiotic choice and duration. In patients with positive urine or stone cultures, these cultures should guide antibiotic choice. Patients with postoperative fevers and sepsis should be treated according to their clinical condition. Regarding routine prophylaxis post-PCNL, the AUA recommends an initial perioperative prophylactic dose of antibiotics, with prophylaxis continuing for 24 h postoperatively [49]. There is some consideration given to prolonging prophylaxis in anticipation of manipulating an indwelling urinary tract catheter (Foley or nephrostomy tube), however, in general prophylaxis should continue for only 24 h.

## **Conflicts of interest**

The authors declare no conflict of interest.

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