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RESEARCH

Heterogeneity in stone culture protocols and endourologist practice patterns: a multi-institutional survey

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Abstract
Kidney stone cultures can be beneficial in identifying bacteria not detected in urine, yet how stone cultures are performed among endourologists, under what conditions, and by what laboratory methods remain largely unknown. Stone cultures are not addressed by current clinical guidelines. A comprehensive REDCap electronic survey sought responses from directed ($n=20$) and listserv elicited ($n=108$) endourologists specializing in kidney stone disease. Questions included which clinical scenarios prompt a stone culture order, how results influence post-operative antibiotics, and what microbiology lab protocols exist at each institution with respect to processing and resulting stone cultures. Logistic regression statistical analysis determined what factors were associated with performing stone cultures. Of 128 unique responses, 11% identified as female and the mean years of practicing was 16 (range 1–46). A specific 'stone culture' order was available to only 50% (64/128) of those surveyed, while 32% (41/128) reported culturing stone by placing a urine culture order. The duration of antibiotics given for a positive stone culture varied, with 4–7 days (46%) and 8–14 days (21%) the most reported. More years in practice was associated with fewer stone cultures ordered, while higher annual volume of percutaneous nephrolithotomy was associated with ordering more stone cultures ($p<0.01$). Endourologists have differing practice patterns with respect to ordering stone cultures and utilizing the results to guide post-operative antibiotics. With inconsistent microbiology lab stone culture protocols across multiple institutions, more uniform processing is needed for future studies to assess the clinical benefit of stone cultures and direct future guidelines.

Keywords Kidney stones · Stone culture · Infection · Sepsis · Antibiotics

Introduction

When stone cultures were first described in 1971 by Nemoy and Stamey [1], it was postulated that culturing the stone material provided utility in distinguishing surface contamination from organisms embedded in the stone. Fast forward to present day and post-operative infection following kidney stone surgery continues to be a common occurrence, with studies reporting 10–38% of patients undergoing percutaneous nephrolithotomy (PCNL) experiencing severe inflammatory response syndrome (SIRS) [2, 3]. To help manage these patients post-operatively, many studies have described performing stone cultures to detect differences in bacterial growth from urine obtained from the bladder, upper urinary tract, and from the stone itself [3, 4]. While they may take 1–2 days to result, these stone cultures are thought to allow urologists to tailor antibiotics in patients who develop post-operative urinary tract infections (UTIs) [5–8].

Despite several studies supporting stone culture as a helpful diagnostic test [2–8], some studies have questioned its utility [9, 10]. With a paucity of data describing the optimal stone culture microbiology protocol [11], guidance regarding the timing and necessity of stone cultures is notably absent from both the European Association of Urology (EAU) [12] and the Endourological Society/American Urological Association (AUA) Guidelines [13]. As such, under which

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clinical scenarios these stone cultures are being performed, how frequently they are ordered across institutions, and how these results influence practice patterns all remain unknown.

This study aims to reveal how stone cultures are performed currently by urologists with specific expertise in kidney stone disease and stone-related procedures from which stone cultures can be obtained. We hypothesized that there are varying methods by which stone cultures are conducted across sites, and that practice patterns differ among endourologists.

Materials and methods

A survey assessing institutional stone culture ordering availability and microbiological processing as well as individual urologist ordering behaviors was created in REDCap® [14]. First, the survey was distributed to a diverse group of 20 Endourological Society fellowship-trained endourologists based in the United States. The responses highlighted a lack of uniformity in stone culture protocols among institutions. Therefore, to further enrich the responding population, the survey was distributed to the Endourological Society listserv. Completed surveys were included, while partially completed surveys were excluded. All the original 20 participants agreed to complete the survey knowing their responses would be associated with their respective institutions. Once the survey was distributed through the Endourological Society listserv, institutional and fellowship information was optional.

Survey structure

Demographic questions included the location of current practice, the institution where an Endourological Society fellowship was completed (if applicable), as well as the approximate number of ureteroscopy (URS)/retrograde intrarenal surgery (RIRS) and PCNL cases performed annually. The first half of questions were related to personal stone practice patterns, as described below. The second half of questions asked endourologists to contact their institution's clinical microbiologist or clinical microbiology laboratory to determine how stone cultures were performed, as described below. The survey utilized branching logic for 24 potential responses. For more details on this survey, please see Supplemental Figure.

Practice patterns

To help identify urologist practice patterns related to stone cultures, questions included specific clinical scenarios and asked respondents to share the situations when they ordered a stone culture. In addition, the survey asked how often a stone culture was ordered and whether concomitant intraoperative bladder urine, upper tract urine, fungal cultures, and Gram stain were routinely performed. Furthermore, the survey assessed utilization of stone culture results in guiding post-operative clinical management—specifically with respect to the prescription and duration of post-operative antibiotics.

Microbiology protocols

Questions concerning institutional microbiology culture protocols focused on whether a 'stone culture' order (either electronic or verbal) was available at each institution. If not, respondents were asked whether the culture was ordered as a 'urine' versus 'tissue' or 'other' type of culture. Additional questions asked which part of the stone is usually taken for the culture, how it is crushed, the quantity of solution added (i.e., saline or culture broth), and what microbiologic media is utilized for the culture. Each microbiology lab was asked which organisms they considered significant and if/how susceptibility testing was performed.

Verifying responses/statistical analysis

The study was approved by the primary investigator's Institutional Review Board. Once all 20 of the original survey responses were received, collective follow-up meetings were arranged to further discuss institutional microbiology protocols and verify individual practice patterns before distributing the survey to the larger Endourological Society listserv. Descriptive statistical analyses were obtained to summarize demographic data among respondents, availability of stone culture orders and microbiology laboratory testing methods, and antibiotic use based on culture results. Then, logistic and Poisson regression analysis was performed using R version 4.1.0 (R Core Team, Vienna, Austria) to determine which factors were associated with the primary outcomes of ordering stone cultures and the number of stone cultures ordered each month. These factors included gender, completion of an Endourological fellowship, number of years practicing, and surgical volume. A p value of < 0.05 was considered statistically significant.

Results

All 20 fellowship-trained endourologists initially invited to participate in this survey responded. Once the survey was distributed to the Endourological Society listserv, an additional 108 complete responses were accrued for 128 unique endourologists, representing 7% of active Endourological society members. Table 1 lists the demographics of all respondents to the survey. Training from 32 different

Table 1 Demographics of surveyed endourologists ($n = 128$)

Gender					
Female	14 (10.9%)				
Male	112 (87.5%)				
Preferred not to answer	2 (1.5%)				
Completed Endourological Society Fellowship	63 (49%)				
Mean number of years practicing	16.2 ± 10.9	Range (1–46)			
# Stone surgeries performed/year	0–30	31–60	61–90	91–120	> 120
URS/RIRS	6	12	20	20	70
PCNL	35	34	25	22	12

Endourological Society accredited fellowship programs were represented by the participants, with 23 of these fellowship programs in North America.

Among the original 20 endourologists surveyed, 8 (40%) reported that a 'stone culture' order existed at their institution. Of the remainder, 4 (20%), 5 (25%), and 1 (5%) reported they had to order the test as a 'tissue,' 'urine' or 'miscellaneous' culture, respectively. For the remaining two endourologists from the same high-volume academic institution, the order had to be labeled as a tissue culture at one campus and a urine culture at another. Once the listserv responses were included, this pattern of heterogeneous stone culture protocols persisted, with only 50% (64/128) reporting that an actual 'stone culture' order existed at their institution. For those who did not have such an order available, the majority reported ordering it as a urine culture (32%), while some described labeling the culture as 'biopsy,' 'foreign body' or 'miscellaneous' culture.

The average number of stone cultures ordered each month by the surveyed endourologists can be found in Fig. 1. Of the 5% of endourologists who perform > 15 stone cultures/month, all had completed an Endourological Society accredited fellowship, and all reported performing at least 90 PCNL cases per year. Meanwhile, among the 58% (74/128) who do not perform stone cultures, 40% (30/74) completed an Endourological Society fellowship and 19% (14/74) reported performing at least 90 PCNL cases annually. For the endourologists not performing stone cultures, not believing that stone cultures are clinically beneficial (31%) was the most reported reason, followed by institutional barriers preventing stone cultures from being performed (28%), increased costs to the patient and healthcare system (26%), and other reasons (15%).

Of the endourologists that routinely order stone cultures, 52% (28/54) perform them for PCNL, RIRS, and URS, while the remainder perform them only during PCNL. In addition, most respondents reported that they do not perform concomitant kidney urine cultures, Gram stains or fungal cultures (Table 2). Regarding the clinical scenarios that prompt stone cultures, there was a near consensus that stone cultures be performed for staghorn calculi (98%) and non-staghorn calculi in the setting of recurrent UTIs (91%). Table 2 further illustrates how frequently other clinical scenarios trigger those who perform stone cultures to order this test.

How stone culture results influenced subsequent post-operative antibiotic therapy also varied among the respondents (Table 2). If the stone culture is positive, the majority reported they would give either 4–7 days (46%)

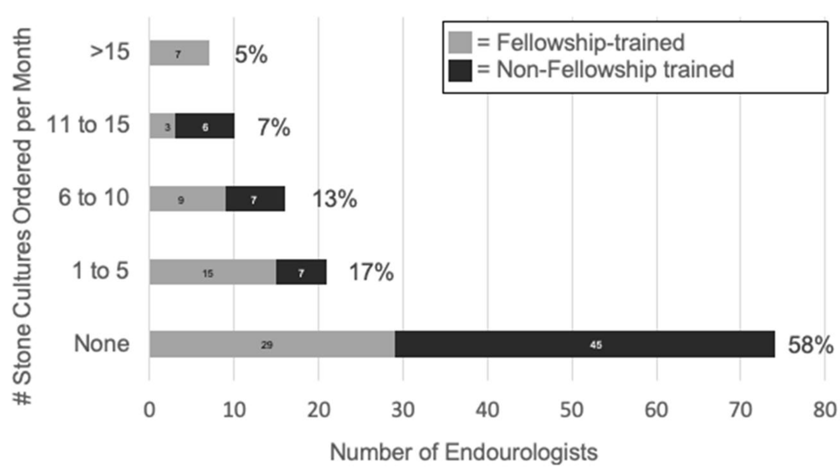

Fig. 1 Number of Stone Cultures ordered per month by Endourologists ($n = 128$)

Table 2 Endourologist practice patterns—types of intraoperative cultures, clinical scenarios prompting stone cultures and post-operative antibiotics based on stone culture results

Intraoperative cultures ($n = 128$)				
# Endourologists who routinely obtain kidney urine cultures:	53/128 (41%)			
# Endourologists who routinely send for Gram Stain:	43/128 (34%)	Urine	Stone	Urine and Stone
If yes, what is sent for Gram Stain?		18	15	10
# Endourologists who routinely send for fungal culture:	15/128 (12%)	Urine	Stone	Urine and Stone
If yes, what is sent for fungal culture?		7	3	5
# Endourologists who routinely order stone cultures:	54/128 (42%)	Outer	Inner	Entire stone
What portion of the stone is sent for stone culture?		9	16	29

Clinical scenarios that prompt stone cultures ($n = 54$)	
Under which clinical scenarios do you perform stone cultures?	
Staghorn calculi	53/54 (98%)
Non-staghorn calculi in context of recurrent UTIs	49/54 (91%)
Pre-op bladder urine culture showing UTI (defined as > 100,000 cfu/ml of specific bacteria)	38/54 (70%)
History of struvite or apatite stone	44/54 (81%)
Patients with chronic indwelling catheters (i.e., urethral Foley, SPT, nephrostomy tube, ureteral stent)	39/54 (72%)
Patients with spinal cord injuries	36/54 (67%)

Post-operative stone culture management ($n = 128$)	
If stone culture is positive, are you more inclined to treat any residual fragments?	Yes
any residual fragments?	101 (79%)
If the stone culture is positive, how many days of post-op antibiotics do you prescribe?	
None	19 (15%)
1–3 days	11 (9%)
4–7 days	59 (46%)
8–14 days	27 (21%)
> 14 days	7 (5%)
Elected not to answer	5 (4%)
If the stone culture is negative, how many days of post-op antibiotics do you prescribe?	
None	59 (46%)
1–3 days	42 (33%)
4–7 days	21 (16%)
8–14 days	2 (2%)
> 14 days	0 (0%)
Elected not to answer	4 (3%)

or 8–14 days (21%) of post-operative antibiotics. A small subset of endourologists (5%) reported they would prescribe > 14 days of antibiotics, and of these, half were fellowship-trained. Meanwhile, most respondents (79%) said that if the stone culture is negative, they will give at most 1–3 days of post-operative antibiotics, if any.

On logistic regression analysis, endourologists with greater time in practice were less likely to order stone cultures and ordered fewer per month, both of which were statistically significant (Table 3). Meanwhile, those who perform higher numbers of RIRS surgeries were more likely to order stone cultures, whereas female gender and more PCNL surgeries performed per year were significantly associated with ordering a higher number of stone cultures per month (Table 3).

Discussion

Variability exists in the performance and utilization of stone cultures among endourologists across multiple institutions. Fewer years in practice and a high-volume surgical stone practice were associated with ordering stone cultures. While 15 of the original 20 fellowship-trained endourologists (75%) reported routinely ordering stone cultures, once the survey was expanded to the Endourological society, the majority of surveyed endourologists (58%) reported that they

Table 3 Association of endourologist characteristics with ordering stone cultures and number of stone cultures ordered per month

	Unadjusted OR (95% CI)	*p* value	Adjusted OR (95%CI)	*p* value
Ordering stone cultures				
Female gender	1.04 (0.37–3.02)	0.93	*	
Completed fellowship	2.46 (1.21–5.10)	0.01	1.25 (0.54–2.86)	0.60
Years in practice	0.93 (0.89–0.96)	< 0.01	0.92 (0.88–0.96)	< 0.01
Number RIRS cases/year	1.39 (1.02–1.93)	0.04	1.48 (1.04–2.20)	0.04
Number PCNL cases/year	1.31 (0.99–1.72)	0.06	*	
Number of stone cultures ordered per month				
Female gender	1.95 (1.07–3.64)	0.03	2.24 (1.10–4.91)	0.04
Completed fellowship	1.68 (1.15–2.47)	< 0.01	1.14 (0.75–1.73)	0.55
Years in practice	0.97 (0.95–0.99)	< 0.01	0.96 (0.93–0.98)	< 0.01
Number RIRS cases/year	1.27 (1.07–1.54)	< 0.01	1.14 (0.93–1.40)	0.22
Number PCNL cases/year	1.41 (1.23–1.62)	< 0.01	1.41 (1.20–1.67)	< 0.01

*Adjusted model only included variables with an unadjusted $p < 0.05$ in the model; therefore these variables were not included in the adjusted model, thus no adjusted OR calculated

do not routinely perform stone cultures, including many of whom had completed fellowship training. These results suggest that there is a lack of consensus among endourologists with regards to the indications for performing stone cultures.

As sepsis is the most common major complication following URS/RIRS and PCNL, appropriate peri-operative antibiotic coverage is a necessity to lower this infectious risk. Recent studies have advocated for the use of differing days of antibiotics prior to specific stone surgeries, with a single dose of preoperative antibiotics sufficient for ureteroscopy [15] and PCNL in low-risk patients [16], and 7 days of preoperative antibiotics prior to PCNL for patients deemed moderate-to-high infectious risk [17]. This is in addition to the 24 hours of post-operative antibiotics recommended by the updated AUA Best Practice Statement [18]. While the current AUA Guidelines emphasize checking preoperative bladder urine for bacteria [13], prior studies demonstrated cultures from the upper urinary tract and the stone itself have greater correlation to pathogenic bacteria in patients who develop more severe infection [2–8]. Absent from the guidelines is when intraoperative bladder urine culture, upper tract urine culture, and/or stone cultures should be performed. The variability in this study's survey results only reinforce that many high-volume endourologists have differing opinions as to what cultures need to be performed.

Among the endourologists surveyed, many described receiving a common response from their microbiology lab that "they do not perform that test' or 'stone cultures are not clinically relevant'. One of the reasons why the data related to stone cultures is not straightforward might be that stone cultures are not being performed consistently across institutions. This study found that only 50% of endourologists surveyed reported having an actual 'stone culture' order available to them, with most resorting to ordering the test as either a 'urine' or 'tissue' culture. Yet, there are inherent problems with this strategy, as urine cultures generally utilize a smaller amount of fluid for the plating process and are quantitative cultures where the workup, identification and susceptibility testing are based on evidence-based guidelines for threshold reporting (i.e., > 100,000 CFU/ml). As such, low abundance organisms in urine cultures will not be fully characterized and will often be lumped into a group of mixed flora (i.e., mixed Gram-positive and Gram-negative organisms). Meanwhile, tissue cultures are often paired aerobic and anaerobic cultures. Depending on the tissue that has been collected, a clinical microbiology laboratory may spend time identifying and performing susceptibility testing on all organisms that are present. We suspect there is a communication gap between the fields of urology and clinical microbiology; each discipline is unaware of the inherent challenges the other field faces. While we highlight the urologic literature on stone cultures, there is little clinical microbiology literature examining the utility of stone culture, leading to a lack of awareness.

Performing a stone culture at the time of stone surgery has been shown to potentially change the antibiotic given to a patient post-operatively [5, 8, 19, 20]. Theoretically, this stone culture serves as a backup plan to guide treatment in the event of post-operative sepsis and poor response to antibiotic treatment. However, the utility of stone culture is limited by the development and treatment of severe post-operative sepsis prior to culture results. In addition, there are studies demonstrating no association between stone culture results and systemic inflammatory response syndrome (SIRS) [7] and that stone cultures may not change peri-operative antibiotic management [9, 10]. Some have even advocated for the use of urine obtained during stone fragmentation as an alternative to stone cultures [20]. This lack of consensus in the literature may further explain why stone cultures have not been universally adopted.

This study also found variation in how stone culture results impact post-operative antibiotic management. Paonessa et al. compared cultures of preoperative bladder urine to that of intraoperative stones and treated positive stone culture results with antibiotics for 3 months post-operatively [19]. Based on the responses in this survey, there is a wide range in the duration of antibiotics prescribed for a positive stone culture, with most (46%) describing 4–7 days, and only 5% reporting they would prescribe over 2 weeks of antibiotics. If the nidus for the infection has been removed, a prolonged course of antibiotics theoretically would treat colonized tissue within the kidney; however, this comes at the risk of antimicrobial resistance, alterations of multiple organ-system microbiomes, and other sequela of prolonged antibiotic use.

Those who have been in clinical practice longer were associated with both not ordering stone cultures and not ordering them as frequently. The reason for this remains unclear; however, it could be that most of the stone culture literature supporting its utility was published within the past 10–20 years [2–8]. Meanwhile performing a higher number of PCNLs annually was associated with ordering more stone cultures. As between 10 and 38% of PCNLs experience SIRS [2, 3], theoretically high-volume endourologists performing more PCNLs would encounter more overall patients experiencing post-operative infections, which might explain their tendency to order stone cultures more frequently. Female endourologists were also significantly associated with higher numbers of stone cultures, though this result may have been confounded by the length of time these respondents have been in practice, as the majority (83%) were within 3 years of completing their training. These findings suggest that those endourologists more recently out of training and who perform more PCNLs are more likely to order more stone cultures.

There are inherent limitations to this study, namely that this was not a validated questionnaire and despite being expanded to the Endourological Society listserv, the survey was still completed by a relatively small number (7%) of endourologists. However, the required granularity about each institution's clinical microbiology stone culture protocols was complex and was completed by the original 20 participants in earnest. The veracity of these responses was reviewed multiple times, confirming the high variability in stone culture processing and practice patterns after positive culture results. The expansion of the survey to the Endourological listserv not only increased the number of responses and provided an international assessment, but also provided perspective on how endourologists who did not complete fellowship approach stone cultures, reinforcing the variability that exists in both protocols and practice patterns.

To our knowledge, this is the first study to reveal the disparity that exists in stone culture microbiology protocols across multiple institutions. It also represents the largest survey of endourologists' practice patterns related to stone cultures to date. As a result, this provides a contemporary glimpse into the practice patterns of not only those well established in their practices, but also those who recently completed their training.

Conclusions

Heterogeneous microbiology stone culture protocols exist across multiple institutions and stone culture practice patterns among endourologists vary widely. Urologists in clinical practice longer order fewer, if any, stone cultures, while those who perform high-volume PCNLs order stone cultures more often. Without a standardized microbiology protocol related to the performance and reporting of stone cultures, the importance of these cultures will remain unclear. Consistent microbiology lab processing of stone cultures is needed to allow for future studies to assess the clinical benefit of stone cultures and direct future guidelines.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article.

Ethical Standards All human studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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