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The Rise of AI in Endourology and Robotic Surgery

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The Application of Next-Generation Sequencing in Preoperative Evaluation for Urologic Stone Surgery

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Abstract

Introduction: Next-generation sequencing (NGS) is a new molecular technique for identifying microorganisms. Treating bacteriuria in patients undergoing stone removal procedures is important for preventing postoperative urinary tract infection (UTI). The objective of this study is to assess the usefulness of preoperative urine NGS testing by comparing NGS with standard urine culture in predicting postoperative UTI after ureteroscopic lithotripsy (URSL) and percutaneous nephrolithotomy (PCNL).

Materials and Methods: This prospective study was conducted from February 16, 2022, to January 11, 2024. Sixty subjects who underwent URSL or PCNL were included. Preoperative voided urine samples were collected for urine culture and tested by MicroGenDX for urine polymerase chain reaction (PCR) and urine NGS. Stone specimens obtained intraoperatively were also sent for stone culture and MicrogenDx. Patients were monitored for 4 weeks post-operation for recording clinical outcomes related to infections and complications.

Results: Twenty-six (43.3%) male and 34 (56.7%) female participants were included. Twenty-six (43.3%) patients underwent PCNL (15 standard PCNL and 11 mini PCNL), and 34 (56.7%) underwent URSL. Standard urine culture identified positive results in 26 cases (43.3%), PCR for 17 cases (28.3%), and NGS for 31 cases (51.7%). The overall postoperative UTI rate was 6 (10%). Standard urine culture demonstrated a sensitivity of 50%, specificity of 57.4%, and accuracy of 56.7%. Positive predictive value (PPV) was notably poor at 11.5%. Urine NGS showed a higher sensitivity of 83.3%, specificity of 53.7%, accuracy of 55%, and PPV of 16.7%.

Conclusion: Urine NGS significantly improves the sensitivity of detecting microorganisms in preoperative urine compared with standard urine culture. Despite its high sensitivity and capability to identify nonculturable bacteria, using NGS alongside standard urine culture is recommended. This parallel approach harnesses the strengths of both methods. Integrating NGS into standard practice could elevate the quality of care, especially for patients at high risk of UTIs, such as those undergoing invasive stone removal procedures.

Keywords: next-generation sequencing, preoperative evaluation, urologic stone surgery, ureteroscopic lithotripsy, percutaneous nephrolithotomy

Introduction

Urinary tract infections (UTIs) are a burden on patients and health care. The established method for diagnosing a UTI, urine culture, necessitates an incubation period exceeding 48 hours for results. This delay in appropriate antibiotic (ATB) treatment can impact patient outcomes. Recognizing these limitations, novel approaches such as polymerase chain reaction (PCR) and next-generation sequencing (NGS) have emerged for bacterial identification in urine, aiming to provide faster and more precise diagnostic information. PCR, a molecular technique, amplifies specific DNA sequences unique to certain bacteria by using designed primers targeting these sequences. The amplified DNA is subsequently analyzed against known bacterial and ATB resistance databases. In UTI, PCR-based tests swiftly

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and accurately identify the multiple infecting bacteria and ATB resistance genes, offering immediate results from urine samples.[1] Despite its ability to detect nonculturable and small amounts of bacterial DNA, including remnants of dead bacteria, PCR's high sensitivity may also detect nonpathogenic microorganisms, reducing its specificity for UTI.

NGS is another molecular technique for identifying microorganisms in urine. In the laboratory, using high-throughput sequencing technologies, millions of DNA fragments from diverse microorganisms are sequenced simultaneously. Post-sequencing, bioinformatics tools analyze the generated sequences, comparing them against microbial databases to identify and characterize the microbial composition. NGS offers a comprehensive analysis, providing insights into the diversity, abundance, and types of microorganisms present in the urine sample, aiding in the identification of potential pathogens causing infections.[2]

MicroGenDX testing includes both PCR and NGS results. The Level 1 report provides PCR results immediately upon specimen arrival, offering quick insights. In contrast, the Level 2 report, using NGS, takes 2–3 days to deliver results. Despite its precision, the overall suitability of NGS for routine UTI diagnoses is controversial with concerns regarding its cost-effectiveness and lower specificity. The test may offer a focused benefit in specific high-incident UTI populations, such as kidney stone patients in the perioperative setting.

UTI commonly arises following stone removal procedures, contributing to urosepsis in about 7.6% of postoperative infections. Incidence rates of UTI post-ureteroscopic lithotripsy (URSL) range from 2.2% to 20% and up to 20% in percutaneous nephrolithotomy (PCNL).[3–6] Ensuring sterile urine before surgery is crucial, and preoperative urine cultures guide ATB treatment, although standard cultures have limitations. With a sensitivity in diagnosing UTI of 50%–60%,[7,8] standard urine cultures often miss anaerobic, slow-growing, and fastidious bacteria, potentially allowing unidentified pathogens to spread during surgery. To address these issues, our prospective study aimed to compare MicroGenDX (PCR and NGS) with standard urine culture to detect pathogens in preoperative voided urine and stones among patients undergoing stone removal procedures (URSL and PCNL). The primary outcome of the study was the ability of NGS to predict a UTI within 30 days post stone removal. Secondary outcomes included the effectiveness of PCR in predicting postoperative UTI, surgical complications, unplanned additional surgical visits, and readmissions.

Materials and Methods

This prospective study aimed to compare urine culture and urine NGS analysis for postoperative infection following stone removal procedures. The study was conducted from February 16, 2022, to January 11, 2024, post Institutional Review Board approval. Sixty subjects who underwent URSL or PCNL and met the eligibility criteria were recruited from urology clinics after informed consent was obtained during the planning of the stone removal procedure.

Eligibility and exclusion criteria

Eligible participants were individuals aged 18 years or older planning stone removal surgery (URSL or PCNL) and able to provide informed consent. Patients with indwelling ureteral stents, ileal conduits, practicing Clean Intermittent Catheterization, or having an indwelling Foley catheter were not excluded. Exclusion criteria comprised those unwilling or unable to provide consent, individuals under 18, failure to meet inclusion criteria, and pregnancy.

Sample collection and analysis

Preoperatively, 30–50 mL voided urine samples were collected using the clean catch or catheterized technique. One portion was sent to the institutional laboratory for urine culture following validated reference ranges, whereas the remaining was deidentified and forwarded to MicroGenDX for urine PCR and urine NGS analysis. Stone specimens obtained intraoperatively were crushed, cultured, and subjected to MicroGenDX stone testing. Patients with positive urine cultures were treated preoperatively. PCR and NGS data were not used for immediate clinical decisions by treating providers and were treated as research specimens.

Clinical follow-up

Patient demographic data and operative events were recorded and de-identified in REDCap. Patients were monitored for 4 weeks post-operation, recording clinical outcomes related to infections, complications, postoperative ATBs, emergency room visits, and patient calls. The criteria for the diagnosis of postoperative UTI are defined in Figure 1.

Statistical analysis

All statistical analyses were performed using IBM SPSS software, version 28 (Armonk, NY, USA). For sample size calculation, we estimated that 40% of patients would have a positive preoperative urine culture, and 70% would have a positive urine NGS.[9] We defined concordance between tests as either both being positive or both being negative for any microorganisms. Using McNemar's test for paired proportions with a 0.2 and 0.5 probability of discordance, a two-sided 5% significance level, and 80% power, we required 58 patients for this study.

Results

Demographics

In this prospective study conducted from February 16, 2022, to January 11, 2024, a total of 60 patients were enrolled. Table 1 presents demographic data, illustrating 26 (43.3%) male and 34 (56.7%) female participants. The cohort had a mean age of 57.36 years, with a median stone burden of 14 mm. Among the patients, 26 (43.3%) underwent PCNL (comprising 15 standard PCNL and 11 mini PCNL), whereas 34 (56.7%) underwent URSL.

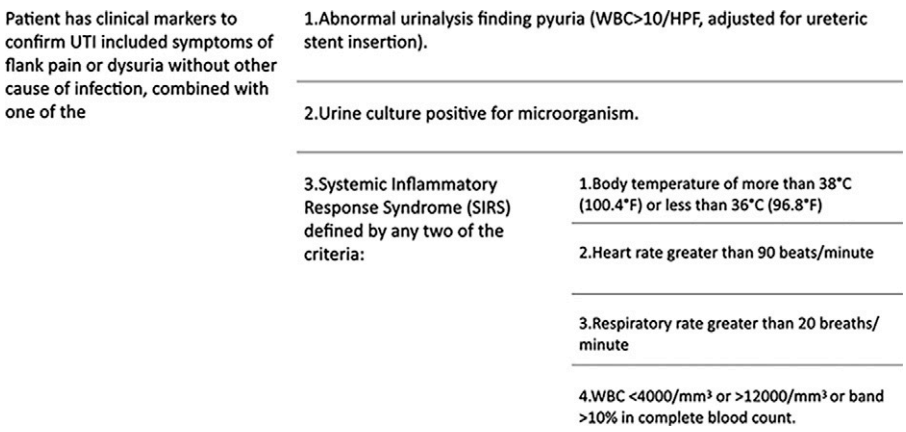

FIG. 1. Criteria for the diagnosis of postoperative urinary tract infection.

Pathogen detection rates

The comparison between preoperative urine and stone tests revealed varying detection rates of preoperative bacteriuria among different testing methods. Standard urine culture identified positive results in 26 cases (43.3%), which included mixed urogenital flora in 15 cases. All patients with identified pathogens in urine culture were treated with ATBs preoperatively. Patients with urine cultures revealing mixed urogenital flora were treated with ATBs in 2 out of 15 cases; however, these 2 cases did not experience postoperative UTI. Urine PCR and NGS detected positives in 17 cases (28.3%) and 31 cases (51.7%), respectively. Among the cases detected by urine NGS, 1 out of 31 cases exclusively contained only known nonpathogenic organisms.

Regarding stone tests, standard culture methods yielded positive results in 9 cases (15%), whereas PCR showed positives in 6 cases (10%), and NGS exhibited a higher detection rate with positives in 18 cases (30%). These results indicate that NGS consistently displayed higher detection rates compared with both standard urine and stone culture methods, with PCR demonstrating a lower level of detection (Fig. 2).

Comparison of tests

The relationship between standard culture and NGS is illustrated in Tables 2 and 3. The *p*-value of the McNemar test for both urine and stone cultures compared with NGS exceeds 0.05, indicating that the NGS test cannot substitute the standard culture method. The concordance between tests is shown in Table 4.

Although NGS demonstrated a higher detection rate compared with standard urine culture, it is essential to note that NGS also provided negative results in 7 cases (18.3%) that tested positive in urine culture. These cases included organisms like *Candida albicans, Proteus mirabilis, Enterococcus faecalis*, and four cases with mixed urogenital flora; none of these patients experienced postoperative UTI.

Similar to urine NGS, stone NGS exhibited a superior detection rate compared with standard stone culture. Stone NGS provided a negative result in two cases (22%) that tested positive in stone culture. The cases missed by stone NGS revealed the presence of *Candida glabrata* and *Staphylococcus epidermidis* in stone culture. Notably, none of these patients experienced postoperative UTI, and these findings from stone culture did not align with either urine culture or urine NGS results.

Patient predictive factors

Female patients exhibited a higher rate of culture positivity, as well as NGS and PCR positivity for both urine and stone tests. Despite these differences, the postoperative infection rate remained consistent across genders. However, the rate of prescribed postoperative ATBs was higher in females (44.1% vs. 15.4%), with a significant *p*-value of 0.025.

The overall postoperative UTI rate was 6 (10%), including cases of sepsis affecting 5/6 (83.3%) patients (Table 5). Among the six, three had a positive urine culture result upon revisiting, and two out of the three also had a positive blood culture with the same organism. Only one of the three positive blood culture cases showed the same organism between the preoperative urine culture and the urine culture while having postoperative UTI. Although urine NGS showed the same result as postoperative urine organism (*Escherichia coli*) in two of three cases, the other case's urine culture revealed no growth, urine NGS revealed *Bacillus subtilis* and *Sphingomonas leidyi*, and the urine culture while having postoperative UTI showed mixed urogenital flora.

Test performance

The performance of tests to detect postoperative UTI is outlined in Table 6. Standard urine culture demonstrated a sensitivity of 50%, specificity of 57.4%, and accuracy of 56.7%. However, its positive predictive value (PPV) was notably poor at 11.5%. Urine culture that defined mixed urogenital flora as negative has a sensitivity of 16.7%, specificity of 81.5%, accuracy of 75%, and PPV of 9.1%. Urine PCR exhibited the same sensitivity as urine culture at 50% but a higher specificity at 74.1%, with an accuracy of 71.7% and PPV of 17.6%. On the contrary, urine NGS showed a higher sensitivity at 83.3% but a lower specificity at 53.7%, accuracy of 55%, and PPV of 16.7%.

Standard stone culture had a sensitivity of 33.3% for detecting postoperative UTI, with a specificity of 87%, an accuracy of 81.7%, and a PPV of 22.2%. Stone NGS displayed the same sensitivity of 33.3% and accuracy of 80%. However, its specificity and PPV were lower at 70.4% and

Table 1. Demographic Data

Characteristic	*Total,* N *(%)*	*No UTI*	*UTI*	p-*Value*
	60 (100)	54 (90)	6 (10)	
Gender				0.602
Male	26 (43.3)	24 (44.4)	2 (33.3)	
Female	34 (56.7)	30 (55.6)	4 (66.7)	
Age: year (SD)	57.36 (14.05)	57.33 (14.47)	57.67 (10.46)	0.957
BMI: mean (SD)	31.00 (7.37)	30.67 (7.53)	34 (5.30)	0.293
ASA				0.950
1	2 (3.3)	2 (3.7)	0 (0)	
2	28 (46.7)	25 (46.3)	3 (50)	
3	29 (48.3)	26 (48.1)	3 (50)	
4	1 (1.7)	1 (1.9)	0 (0)	
DM status				0.904
Nondiabetic	51 (85)	46 (85.2)	5 (83.3)	
Diabetic	9 (15)	8 (14.8)	1 (16.7)	
History of UTI				0.076
No	47 (78.3)	44 (81.5)	3 (50)	
Yes	13 (21.7)	10 (18.5)	3 (50)	
Urinalysis				
Nitrite positive	8 (13.3)	8 (14.8)	0 (0)	0.311
Leukocyte positive	34 (56.7)	31 (57.4)	3 (50)	0.728
WBC > 3	20 (33)	20 (37)	0 (0)	0.068
Bacteria positive	42 (70)	16 (29.6)	2 (33.3)	0.851
Preoperative urine culture				
Positive	26 (43.3)	23 (42.6)	3 (50)	0.728
Identified pathogen	11 (18.3)	10 (18.5)	1 (16.7)	0.911
Urogenital flora	15 (25)	13 (24.1)	2 (33.3)	0.619
Negative	34 (56.7)	31 (57.4)	3 (50)	0.728
Preoperative drainage status				
Ureteral stent	12 (20)	12 (22.2)	0 (0)	0.197
PCN	1 (1.66)	1 (1.9)	0 (0)	0.737
Median stone burden: mm (IQR)	14 (9, 23.75)	13.5 (7.75, 24.00)	16.00 (12.5, 20)	0.674
Operation				
PCNL	26 (43.3)	22 (40.7)	4 (66.7)	
Mini PCNL	11 (18.3)	9 (16.7)	2 (33.3)	0.317
Standard PCNL	15 (25)	13 (24.1)	2 (33.3)	0.619
URS	34 (56.7)	32 (59.3)	2 (33.3)	0.224
Operative time: minute (SD)	71.76 (28.76)	70.50 (28.77)	83.17 (28.53)	0.310
Post operative ATB	13 (21.7)	12 (22.2)	1 (16.7)	0.754

ASA, American Society of Anesthesiologists Physical Status Classification; ATB, antibiotic; BMI, body mass index; DM, diabetes mellitus; IQR, interquartile range; PCN, Percutaneous nephrostomy; PCNL, percutaneous nephrolithotomy; SD, standard deviation; UTI, urinary tract infection; WBC, white blood cell.

11.1%, respectively, compared with standard stone culture. Stone PCR was inadequate as an indicator of postoperative UTI because of poor sensitivity and PPV.

The logistic regression analysis, which considered the history of UTI as a factor, demonstrated that none of the tests could reliably serve as a significant correlate with postoperative UTI.

Discussion

Postoperative UTI after a stone removal procedure is one of the most concerning complications. Although the standard evaluation of bacteriuria is via urine culture, it shows a sensitivity of only 30%–60% in acute symptomatic UTI.[10] Thus, many studies are focusing on development of new tests. Urine PCR shows higher sensitivity and specificity than urine culture,[1,11,12] demonstrating noninferiority to urine culture at a discrepancy rate of 90%.[7] Another test, NGS, enhances microorganism detection in urine, including fastidious and anaerobic organisms that might be missed in standard cultures. Some literature found that the detection rate of NGS in symptomatic UTI patients is as high as 100%, compared with 30% in urine culture.[13] However, patients without infectious symptoms showed 51% positivity in NGS despite consistently negative urine cultures.[14] This disparity is attributed to NGS's inclination to identify all microbiomes, including nonpathogenic organisms, leading to reduced specificity. Consequently, the utilization of NGS in the general population remains limited, but it may hold benefits for high-incidence UTI populations.

In our study, we assessed the clinical utility of MicrogenDx in the preoperative evaluation for stone removal procedures (PCNL and URSL). The study was designed to compare standard urine culture and MicrogenDx (PCR and

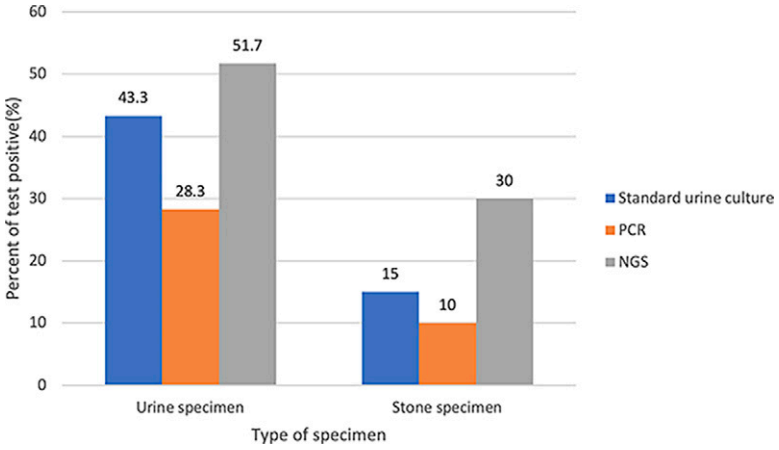

FIG. 2. Preoperative bacteriuria detection rate of the tests. NGS, next-generation sequencing; PCR, polymerase chain reaction.

NGS) for preoperative voided urine in PCNL and URSL patients. We found that urine NGS demonstrated a higher organism detection rate in urine compared with standard culture (51.7% vs 43.3%), consistent with previous literature.[2]

Urine culture necessitates a larger number of organisms in the specimen to yield a positive result, whereas NGS has the capability to detect even minute amounts of organisms. Furthermore, NGS can identify multiple organisms in a single specimen, unlike standard culture, which typically identifies only one organism at a time. Urine culture often categorizes multiple organisms as contamination or reports them as mixed urogenital flora. As is known, polymicrobial findings can occur in 39% of UTI cases.[15] Notably, NGS provides the actual names of organisms, offering more valuable information for ATB selection compared with the classification of mixed urogenital flora. Thus, despite its superior detection rate, NGS might complicate ATB selection. Moreover, in the judgment of ATB selection for multiple organisms, the concordance of organisms between standard urine and NGS was 63.3%, suggesting that 36.7% of patients might encounter challenges in preoperative ATB selection if both tests were conducted.

PCR, despite its speed, demonstrated a lower detection rate (28.3%) than standard urine culture, not meeting the high sensitivity reported in previous literatures.[1,7,11,12,2] This discrepancy might be because of organism mutations over time, making it difficult to recommend using PCR alone in preoperative evaluation and limiting its role in this context.

Existing literature highlights discrepancies between urine and stone cultures. Stone cultures demonstrate a more pronounced association with sepsis than urine cultures, displaying a concordance rate of 64% between stone culture and readmission culture.[16,17] In our study, the detection rate of organisms in stones was the highest with NGS (30%), followed by standard stone culture (15%) and PCR (10%). However, the time required (2–3 days) to obtain results from stone culture and NGS limits their utility in the early detect postoperative UTI particularly for first-time stone removal patients. Although stone PCR offers rapid reporting within 24 hours, its lower detection rate and poor sensitivity to postoperative UTI render it nonapplicable in this scenario.

The overall postoperative urinary infection rate was 10% (six patients), with five cases (8.3%) developing sepsis. Urine NGS demonstrated better performance in predicting postoperative UTI compared with standard urine culture. Standard urine culture displayed a sensitivity of 50% and a specificity of 57.4% in predicting postoperative UTI, whereas urine NGS showed a notably higher sensitivity at 83.3% but a slightly lower specificity at 53.7%. Interestingly, seven cases that tested positive with urine culture were reported as negative in NGS. None of these patients experienced postoperative UTI, indicating that urine NGS may be more clinically relevant than standard urine culture.

Among the six postoperative UTI patients, only one of them could identify the actual organism in urine culture, whereas the results for the others showed two cases with mixed urogenital flora and three with no growth. Among the two patients with preoperative mixed urogenital flora in urine culture, NGS identified these organisms. This finding suggests that the presence of mixed urogenital flora in urine culture might signify pathogens because of dysbiosis, holding clinical significance beyond the assumption of mere contamination. In addition, three of these patients had no organisms detected in preoperative urine culture. Urine PCR

Table 2. Correlation Between Urine Culture with Urine NGS

Urine	*NGS positive*	*NGS negative*	*Total*
Culture positive	19 (73.1%)	7 (26.9%)	26 (100%)
Culture negative	12 (35.3%)	22 (64.7%)	34 (100%)
Total	31 (51.7%)	29 (48.3%)	60 (100%)

$p = 0.359$, Kappa 0.369.
NGS, next-generation sequencing.

Table 3. Correlation Between Stone Culture with Stone NGS

Stone	*NGS positive*	*NGS negative*	*Total*
Culture positive	6 (66.7%)	3 (33.3%)	9 (100%)
Culture negative	12 (23.5%)	39 (76.5%)	51 (100%)
Total	18 (30.0%)	42 (70.0%)	60 (100%)

$p = 0.791$, Kappa 0.162.

Table 4. Concordance Between the Two Tests, Test Matching Includes Negativity in Both Tests

The number and percentage of matching organisms between the tests	N *(%)*
Standard urine culture VS	
Stone culture	35 (58.3)
Urine NGS	38 (63.3)
Stone NGS	38 (63.3)
Stone culture VS	
Urine NGS	31 (51.7)
Stone NGS	42 (70)
Urine NGS VS	
Stone NGS	32 (53.3)

also failed to detect any organisms in all cases, but urine NGS managed to identify organisms in two cases previously undetected.

In the postoperative UTI sepsis workup, urine culture was positive in three patients. The results of this culture were consistent with only one of the three preoperative urine cultures but matched with two of three cases in urine NGS. The patient initially had a mixed urogenital flora in preoperative urine culture without ATB treatment. Subsequently, urine NGS and PCR detected several pathogenic organisms, including *E. coli*, corroborated by postoperative sepsis workup that identified *E. coli* in urine culture. Another patient, for whom urine NGS did not match, had a urine culture for postoperative UTI workup that did not reveal the organism's name but reported mixed urogenital flora, in contrast to urine NGS, which detected *B. subtilis* and *S. leidyi.* This demonstrates the superior performance of urine NGS in the preoperative evaluation for infectious prevention after surgery, particularly in cases where urine culture reports mixed urogenital flora. Two out of 13 (15.4%) patients with untreated preoperative mixed urogenital bacteriuria developed UTI after the operation. Many vaginal bacterial species, such as *Gardnerella vaginalis, Aerococcus* sp., and *Ureaplasma* sp., are considered potential causes of UTI[18] but are difficult to isolate and commonly reported as urogenital flora. At this stage of research, urine NGS can serve as a useful adjunction to conventional testing. The utility of NGS may therefore have more value postoperatively when a UTI has developed as it will identify any potential pathogen. This combination would be extremely valuable as it will allow for direct treatment more quickly.

As for limitations, we do not use MicroGenDX for urine diagnosis in postoperative UTI cases when patients revisit the hospital. The absence of this data leads to a lack of a head-to-head NGS comparison of organisms causing infection before and after the operation.

One potential advantage of MicrogenDx is its ability to detect ATB resistance genes. Among the 31 cases, 18 showed ATB-resistant organisms, none of which corresponded with the ATB resistance results from the standard urine culture. This contrasts with previous literature,[2] reporting greater similarity between urine NGS ATB resistance and urine culture. The discrepancy may arise from ATB resistance mechanisms not solely dependent on genes, especially in polymicrobial infections, where one resistant strain

Table 5. Diagnostic Test Results of the Six Patients Who Experienced Postoperative Urinary Tract Infection

	Preoperative			*Intraoperative*			*Postoperative*	
Patient	*Urine culture*	*Urine PCR*	*Urine NGS*	*Stone culture*	*Stone PCR*	*Stone NGS*	*Urine culture*	*Hemoculture*
1	*E. coli*	*E. coli* *K. pneumoniae*	*E. coli* *K. pneumoniae* *E. hormaechei*	No growth	No growth	No growth	*E. coli*	*E. coli*
2	Mixed urogenital flora	*P. bivia* *E. coli* *G. vaginalis* *U. parvum*	*P. bivia* *E. coli* *G. vaginalis* *U. parvum*	No growth	No growth	No growth	*E. coli*	*E. coli*
3	No growth	No growth	*B. subtilis* *S. leidyi*	*A. europaeus*	No growth	*C. acnes* *S. epidermidis*	Mixed urogenital flora	N/A
4	No growth	No growth	*S. haemolyticus* *S. epidermidis* *S. mitis*	No growth	No growth	No growth	No growth	N/A
5	No growth	No growth	No growth	No growth	No growth	No growth	No growth	N/A
6	Mixed urogenital flora	*P. bivia*	*S. saprophyticus* *P. timonensis* *P. bivia*	*C. acnes*	No growth	*S. hominis*	No growth	N/A

PCR, polymerase chain reaction.

Table 6. The Tests' Performance to Predict Postoperative Urinary Tract Infection

Test characteristic	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*Accuracy*
Urine culture	50	57.4	11.5	91.2	56.7
Urine culture (excluding mixed urogenital flora)	16.7	81.5	9.1	89.8	75
Urine PCR	50	74.1	17.6	93	71.7
Urine NGS	83.3	53.7	16.7	96.7	55
Stone culture	33.3	87	22.2	92.2	81.7
Stone PCR	0	88.9	0	88.9	80
Stone NGS	33.3	70.4	11.1	90.5	66.7

NPV, negative predictive value; PPV, positive predictive value.

can confer ATB resistance to another.[19] In addition, it is essential to note that NGS reports ATB resistance genes, representing genotypic ATB susceptibility, rather than phenotypic susceptibility as seen in urine culture. Hence, interpreting ATB resistance results from MicrogenDx should be approached with caution. Using the local antibiogram for ATB selection is advisable in this context.

The American Urological Association's and European Association of Urology's guidelines[20,21] advocate prophylactic ATB use for PCNL and URS but do not recommend extended postoperative ATB therapy. Clinically, 13 patients were discharged with ATBs, including those with high-risk symptoms requiring treatment. Including patients who revisited with postoperative UTI, 19 cases received postoperative ATBs. In predicting the necessity of postoperative ATBs, urine NGS exhibited the highest sensitivity at 78.9%, followed by urine culture at 63.2% and urine PCR at 52.6%. For specificity, urine PCR displayed the highest rate at 82.9%, followed by urine culture at 65.9% and urine NGS at 61%. The application of urine MicrogenDx may be beneficial in anticipating the need for postoperative ATBs, with the highest PPV of 58.8% for urine NGS. However, although stone NGS showed a sensitivity of 57.9%, specificity of 82.9%, and a PPV of 61.1%, its results might arrive too late to guide the necessity for postoperative ATBs.

The limitations of this study include being underpowered because of a small sample size and the perioperative ATB not being standardized but dependent on physician consideration. A larger sample size study should be conducted to further support the benefits of NGS.

Although NGS demonstrates better performance in predicting postoperative UTI, it cannot replace urine culture. The McNemar test and the consideration of nonphenotypic susceptibility suggest that NGS should be used alongside standard urine culture in preoperative evaluation. Urine NGS and PCR are combined in the MicrogenDx UTI test service, which costs 259 USD, whereas a standard urine culture costs around 69–88 USD and can go up to 500 USD for special cultures. The cost–benefit of adding an NGS test to standard urine culture is apparent in patients with clinically suspected UTI where no organism is identified or when there is mixed urogenital flora.

Conclusion

Urine NGS significantly improves the sensitivity of detecting microorganisms in preoperative urine compared with standard urine culture. Despite its high sensitivity and capability to identify nonculturable bacteria, using NGS alongside standard urine culture is recommended. This parallel approach harnesses the strengths of both methods. NGS also shows promise for predicting which patients may benefit from postoperative ATBs (a decision commonly based solely on clinical intuition). Integrating NGS into standard practice could elevate the quality of care, especially for patients at high risk of UTIs, such as those undergoing invasive stone removal procedures.

Authors' Contributions

K.J.: Writing—original draft (lead), formal analysis (lead), writing—reviewing and editing (equal). T.S.: Writing—reviewing and editing (equal). J.F.: Resource (lead). S.K.B.: Investigation (equal). R.L.S.: Investigation (equal). M.M.: Conceptualization (lead), writing—reviewing and editing (equal), and investigation (equal).

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Abbreviations Used

ATB = antibiotic
BMI = body mass index
DM = diabetes mellitus
IQR = interquartile range
NGS = next-generation sequencing
NPV = negative predictive value
PCNL = percutaneous nephrolithotomy
PCR = polymerase chain reaction
PPV = positive predictive value
SD = standard deviation
URSL = ureteroscopic lithotripsy
UTI = urinary tract infection
WBC = white blood cell