

Peer Review File

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Reviewer A

Comment 1: Definition of Urosepsis: Please mention that the reference of the qSOFA score for defining sepsis originates from the Sepsis-3 criteria.

Reply 1: Thank you for your advice, I have modified our text as advised (see Page 4, line 116). Changes in the text: **According to the Sepsis-3 criteria,** urosepsis was defined as the qSOFA (quick sepsis-related organ failure assessment) score ≥ 2 consequent upon suspected or confirmed urinary system infection, the qSOFA score included: (1) Respiratory rate ≥ 22 /min; (2) Alteration in mental status (Glasgow Coma Scale (GCS) score < 13); (3) Systolic blood pressure ≤ 100 mmHg(12).

Comment 2: Definition of Bladder Urine Culture: Does this term refer to preoperative urine cultures?

Reply 2: Yes, all of our patients with kidney stones are routinely admitted to the hospital for urine culture, which we have mentioned in the paper “Bladder Urine Culture” is preoperative relevant clinical data(see Page 4, line 80-81).

Changes in the text: None

Comment 3: qSOFA Sensitivity: It is shown in guidelines that qSOFA has low sensitivity and is not recommended for use as a single screening tool. For example, was lactate measured in this study?

Reply 3: Thank you for your advice, in patients with suspected sepsis, we also measure the procalcitonin (PCT), C-reactive protein (CRP) and lactate to assist with screening and blood cultures were performed if necessary. I have modified our text as advised (see Page 5, line 119-121).

Changes in the text:

We also measured the procalcitonin (PCT), C-reactive protein (CRP) and lactate to assist with screening, and blood cultures were performed if necessary.

Comment 4:Urosepsis and Urine Culture Results: I would like to know the profile of urine cultures in patients who developed urosepsis. If there was no effect of preoperative antibiotics, this could be considered an independent factor for sepsis.

What was the incidence of septic shock and bacteremia? I am also interested in the proportion of patients who developed bacteremia. It is likely that urosepsis with bacteremia is more severe and indicates bacteria entering the bloodstream during surgery, compared to urosepsis without bacteremia.

Reply 4: Thank you for your advice, I have modified our text as advised (see Page 5, line 143-146).

Changes in the text: **A total of 19 cases of urosepsis patients showed a positive bladder urine culture in the training cohort, among which the most common pathogenic bacteria were Escherichia coli (57.9%), followed by enterococci (10.5%). The incidence of septic shock and bacteraemia was 2.2% and 2.4%, respectively.**

Comment 5:Urine Culture Bacterial Species: What was the proportion of ESBL-producing bacteria and carbapenem-resistant bacteria detected in urine cultures? It is important to extract these results as they are critical factors for sepsis. The proportion of resistant bacteria varies between China and other countries. It would also be beneficial to list the preoperative antibiotics used.

Reply 5: Thank you for your advice, I have modified our text as advised (see Page 5, line 141-

143; see Page 5, line 147 and Page 4, line 92-93).

Changes in the text:

In urine cultures, the most common type was *Escherichia coli* (61.7%) in the training cohort, including 56.7% of ESBL-producing bacteria and 1.1% of carbapenem-resistant bacteria.

All urosepsis patients were treated with active antibiotic therapy (piperacillin-tazobactam or carbapenem antibiotics).

Patients with positive urine WBC or urine nitrite were immediately given antibiotics (second-generation cephalosporins) for 3-7 days. Antibiotic prophylaxis (second-generation cephalosporins) was given to all patients 30 minutes prior to surgery and was continued for 48 hours after surgery if the urine culture was positive.

Reviewer B

Comment 1: Interesting study on an important topic. From a stone clearance perspective, pcnl is the gold standard and though usually well tolerated, the complications, including urosepsis, can be severe and thus mitigation is important so I applaud the authors for addressing the important topic. Renal pressure monitoring is an area of active investigation, especially with the advent of new pressure sensing ureteroscopes. My biggest concern with the study, is, was the pressure sensing apparatus utilized validated, and if so how? If it was indeed validated this needs to be addressed in the manuscript as the entire novelty of the study hinges on the RPP measurements.

Reply 1: Thanks for your valuable suggestions, the principle of this pressure sensing apparatus has been reported in many literatures and has a certain accuracy. I have modified our text as advised (see Page 4, line 97-102).

Literature 1 :

Measurement of renal pelvic pressure

Intra-operative RPP was measured in the way as presented in previous studies. The 6 Fr open-ended ureter catheter which inserted retrogradely into the renal collecting system was connected to a pressure transducer. The baroreceptor was fixed on the horizontal plane of renal pelvis, and connected to the invasive blood pressure measurement channel of electrocardiogram monitor. Real-time RPP was measured by the baroreceptor and recorded each second.

[1]Zhong W, Wen J, Peng L, Zeng G. Enhanced super-mini-PCNL (eSMP): low renal pelvic pressure and high stone removal efficiency in a prospective randomized controlled trial. *World J Urol.* 2021;39(3):929-934.

Literature 2 :

Measurement of Renal Pelvic Pressure (RPP) In-Vivo: After the retrograde insertion of an open-ended ureteral catheter, it was connected to an invasive blood pressure channel of PM9000 patient monitor (Maidray Medical Corporation, Shenzhen, China) with a baroreceptor.

[2]Alsmadi J, Fan J, Zhu W, Wen Z, Zeng G. The Influence of Super-Mini Percutaneous Nephrolithotomy on Renal Pelvic Pressure In Vivo. *J Endourol.* 2018;32(9):819-823. doi:10.1089/end.2018.0239

Changes in the text:

After the patient underwent general anesthesia induction, a catheter that was self-designed (Figure. S1) for renal pelvic pressure measurement was retrogradely inserted into the renal pelvis through a ureteroscope in the lithotomy position. Then the tail connector was connected to the pressure measurement module of the external anesthesia machine through pressure transducer to monitor changes in renal pelvic pressure in real time during the surgery for collecting RPP data every second (Figure. S2). The way of measuring the RPP as presented in previous studies(13, 14).

Comment 2:Also, how you explain the correlated increase risk of urosepsis in both degree of hydro and time of elevated RPP? With more hydro, I would expect there to be more space in

the kidney and lower RRP. Is it related to stone complexity? I think including a stone complexity metric in the model beyond staghorn and not staghorn would help.

Reply 2: In my opinion, firstly, I think the higher degree of hydronephrosis in the patient indicates that the obstruction time is longer and more severe, so the patient is more susceptible to urosepsis after surgery; Secondly, during surgery, we will inject water into the renal pelvis to help flush out the stones so that some patients with severe hydronephrosis may have a transient or prolonged increase in intrapelvic pressure, but the mean intrapelvic pressure may not be high; Thirdly, I think stone complexity may be a factor, so I agree with your valuable suggestion to include the “Guy’s stone score”, I have modified our text as advised (see Table 1,2; see Page 4, line 86-91).

Changes in the text: I have modified our text as advised (see Table 1,2; see Page 4, line 86-91).

Comment 3: You note the study is retrospective... is it your standard practice to monitor intrarenal pressure during pcnl?

Reply 3: Yes, the pressure sensing apparatus is convenient, so we routinely measure intrarenal pressure during PCNL.

Changes in the text: None.
