

**Reply letter to: Gorgotsky I, Shkarupa D, Shkarupa A et al. A Feasibility of Percutaneous Nephrolithotomy in Positive Urine Culture: A Single Center Retrospective Study**

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We read with interest the study by Gorgotsky et al<sup>(1)</sup> regarding the outcomes of percutaneous nephrolithotomy (PCNL) performed in patients with preoperative positive urine culture. The authors concluded that infected urine is not an independent risk factor of post-operative infectious complications after PCNL in low risk patients with (non-obstructive) kidney stones. They also suggested that a 24-hours antibiotic administration before the surgery can be considered as alternative to 1-week treatment and allow to perform PCNL with sufficient safety in selected patients.

These considerations, especially in low infectious risk population with sterile urine culture, can be also borrowed from the randomized control trial from the EDGE Consortium<sup>(2)</sup> that demonstrated no advantage to providing 1 week of preoperative oral antibiotics in PCNL candidates. These results are in line with antimicrobial stewardship recommendations orientated in reducing antibiotic treatment duration in the antibiotic resistance era.

As underlined by Gorgotsky et al<sup>1</sup>, EAU Guidelines states that an obstructed kidney with all signs of urinary tract infection (UTI) is a urological emergency<sup>(3)</sup> and instrumentation in the setting of an active infection can lead to an increased risk of post-procedural UTI.

However, a positive urine culture does not imply necessarily an active UTI.

The fundamental point is to distinguish between symptomatic UTI and asymptomatic bacteriuria (ASB) and, in patients with indwelling ureteral stent or nephrostomy tube, a bacterial colonization. This difference can be figured out by the integration of urine microscopy, complete blood count and C-reactive protein results.

As recently stated by the Best Practice Statement on Urologic Procedures and Antimicrobial Prophylaxis<sup>(4)</sup>, ASB does not need to be managed any differently prior to high-risk procedures (like PCNL) as single-dose antibiotic prophylaxis (AP).

In the current study, the AP was continued in both groups for 3 days, in contrast with the intrinsic concept of prophylaxis and with the current urological guidelines that recommended single dose or 24hours duration.

We know from the literature that bacteria can be cultured from the stones themselves in a variable rate (ranging from 15 to 70%)<sup>(5)</sup> and these results may be underestimated because stone culture is not routinely performed.

In our experience, even when preoperative positive urine cultures were treated appropriately, the stone cultures revealed the same pathogen with similar resistance in the 63,6% of cases (article in press), implying that the pathogen is harbored inside the stone.

In this study, the infectious complications, especially in group 2, are not correlated with intra-operative (i.e. stone culture) or post-operative blood and urine culture results, neglecting the possibility to evaluate the effect of antibiotic therapy on peri-operative cultures.

Moreover, it would have been useful to report the biochemical analysis of the fragments to evaluate the rate of struvite stones in the group 2 of this low risk population for infectious complications.

The authors excluded from the cohort all patients with potential pre-operative risk factors for infectious complications, except the presence of a urinary diversion like nephrostomy or ureteric stent and history of recurrent UTI, potential factors for bacterial colonization. Some intraoperative potential risk factors for infectious complications were not investigated as multiple percutaneous tracts, drainage of purulent urine during the puncture and the intrarenal pressures.

A prolonged use of antibiotics can be associated with an increased risk of acquiring antibiotic-resistance and, in the setting of kidney stones, can be useless because any calcified or non-calcified stone may be colonized by infectious organisms creating a persistent bacterial niche. In this view, the results by Gorgotsky et al<sup>1</sup> may help to reduce the rise of antibiotic resistance, avoiding pre-operative unnecessary treatments. The unsolved question remains how to efficiently treat the patients with risk factors for infectious complications, as they represent a considerable part of the population (34.5% in the series by Gorgotsky et al<sup>1</sup>).

Future large prospective studies are needed to comprehensively investigate the impact of AP on patients that are candidate to stone removal with and without risk factors for infectious complications, both with ASB and negative urine culture.

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## REPLY BY AUTHOR

In fact, our study identified a group of patients with certain specific indications and minimally complicated conditions to assess the impact of positive urine as an independent factor. Majority of such patients typically have a “simple” pelvis or calyx stone, which can be removed through single access without leaving significant residual fragments. Thus, our study estimates the effect of only plankton forms of bacteria contained in urine. Stone culture may play a role in further therapy in complicated patients, but under current conditions, this analysis with assessment of antibiotic resistance takes about 48-72 hours and has questionable feasibility, which limits its routine widespread use<sup>1</sup>.

All patients participated in our study had no signs of acute obstruction or had previously established drainage (stent or nephrostomy tube) in this regard. Of course, it is necessary to take into account the bacterial biofilms on the drainage surface, but it is difficult to assess the degree of colonization and the correlation of this factor on intra- and postoperative results using existing routine methods of analysis. With the development of new experimental methods for rapid assessment of bacterial drainage contamination, this problem is likely to have some solution<sup>2</sup>. It is quite difficult to distinguish objectively between asymptomatic bacteriuria (ASB) and latent manifestations of urinary tract infection. It may be worth excluding from the further study the category of patients who may have other reasons for ASB (postmenopausal women, elder patients, etc.)

If you look carefully at the section on a single dose of antibiotic prophylaxis for PCNL in EAU Guidelines, it refer to an article on ureteroscopy, not percutaneous interventions.

Struvite stone formers tend to have known additional risk factors, so we tried not to include such cases in the study. We absolutely agree that further research on antibiotic prophylaxis and treatment duration in complicated stone patients is needed. The major difficulty in organizing such studies is the impossibility to structure research in a modern, relevant fashion (e.g. double-blind randomized, etc.) primarily for ethical reasons. Taking into account the presence of different local recommendations on antibiotic prophylaxis in each country and institution, detection of heterogenic types of bacteria in different countries, as well as private opinions of high-volume experts, no consensus has yet been reached on this problem<sup>3</sup>. Despite the global tendency to decrease the duration of antibiotic use, some specialists still justify the tactics of long-term pre-operative therapy - 2 weeks or more<sup>4</sup>.

Thus, it is difficult to perform meta-analyses and determine reliable conclusions. There is still hope for the development of bacteriological analysis technologies (modified gene sequencing, advanced polymerase chain reaction, etc.), that will enable fast and accurate determination of both plankton and biofilm pathogens for correlations with other clinical factors.

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