

# Endoscopic lithotripsy in patients with asymptomatic bacteriuria

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## Abstract

**Introduction:** Endoscopic surgery is a highly effective method for treating urolithiasis; however, it carries a risk of postoperative infectious complications. One of the main risk factors for these complications is a positive urine culture. The persistence of asymptomatic bacteriuria (ASB) in patients, combined with the absence of standardized guidelines for its managing prior to endoscopic procedures, highlights the need for further investigation. Thus, conducting a comparative analysis of infectious complications in patients with negative urine culture versus those with persistent ASB undergoing endoscopic surgery for renal and ureteral stones using different regimes of antibiotic prophylaxis seems clinically relevant issue.

**Objective:** To assess the safety of endoscopic stone surgery in patients with persistent asymptomatic bacteriuria and patients' negative urine culture undergoing endoscopic surgery for renal and ureteral stones using different regimes of antibiotic prophylaxis.

**Materials and Methods:** We conducted a retrospective study analyzing data from patients who underwent endoscopic removal of renal and ureteral stones between January 2023 and July 2023. Of the 449 patient records reviewed, 211 patients meeting the inclusion and exclusion criteria were selected for further analysis. Antibacterial prophylaxis was administered as follows: a few hours prior to surgery for patients with an initially sterile urine culture, three days prior to surgery for those with clinically insignificant ASB, and seven days prior to surgery for patients with clinically significant ASB.

**Results:** A preoperative sterile urine culture was identified in 152 patients (72.0%), while 59 patients (28.0%) [95% CI: 22.0%; 34.5%] were diagnosed with bacteriuria. Among these, 28 patients (13.3%) [95% CI: 9.0%; 18.6%] had clinically significant bacteriuria, defined as a bacterial count of  $\geq 10^5$  CFU/mL. Despite culture based antibiotic therapy prior to surgery persistent ASB was observed in six patients (22.0%). Consequently, 37 patients (17.5%) [95% CI: 12.79%; 23.4%] with clinically significant and insignificant ASB along with patients with sterile urine underwent endoscopic surgery. In the postoperative period, leukocytosis alone was observed in 54 patients (25.6%), fever in 17 patients (8.1%), and fever accompanied by leukocytosis in 11 patients (5.2%). Logistic regression analysis demonstrated a statistically significant association between bacteriuria and postoperative fever. A positive urine culture increased the odds of hyperthermia by 4.75 times (OR = 4.75, 95% CI: 1.256; 21.123,  $P = 0.022$ ). Additional factors influencing leukocytosis included maximum stone size ( $P = 0.013$ ), stone volume, and dwelling ureteral stent ( $P = 0.006$ ). Specifically, an increase in stone volume by 1.0 cc raised the odds of leukocytosis by 1.54 times (OR = 1.543, 95% CI: 1.128; 2.158,  $P = 0.008$ ).

**Conclusion:** Our study highlights that a positive urine culture is a significant risk factor for infectious complications following endoscopic surgery. Prolonged antibiotic prophylaxis for patients with clinically significant ASB appears to be an effective strategy to minimize the risk of postoperative infectious complications.

**Keywords:** Kidney stones, ureteral stones, asymptomatic bacteriuria, infection, complications, endoscopy

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## Introduction

Urolithiasis is one of the common urological diseases affecting the adult population [1], accounting for approximately 50.0–60.0% of inpatients [2]. Endourological procedures are the primary treatment for patients with urolithiasis. Currently, ureteroscopy (URS), retrograde intrarenal surgery (RIRS), and percutaneous nephrolithotomy (PCNL) are the most common methods used for treating upper urinary tract stones. The widespread use of these surgical interventions is attributed to their high efficacy and safety. However, the most significant complications are infectious complications, which include fever, pyelonephritis, systemic inflammatory response syndrome (SIRS), and sepsis.

According to current data, the probability of infectious complications after stone surgery might reach up to 19% (up to 13.4% after RIRS and up to 18.9% after PCNL) [3]. Fever is the most frequently observed postoperative complication, typically not necessitating adjustments to the treatment regimen or additional therapeutic interventions. In certain cases, it may reflect reactive or resorptive inflammatory responses rather than an underlying infectious process [4-6]. The incidence of postoperative hyperthermia after endourological procedures ranges from 2.8% to 17.5% [7]. Along with this the risk of systemic inflammatory response syndrome (SIRS) can reach up to 9.7%, while the incidence of urosepsis can be observed in up to 4.7% of cases [2, 8-11]. One of the known modifiable risk factors for infectious complications is bacteriuria [12].

The recommendations of the European Association of Urology (EAU) mandate bacterial urine culture for patients scheduled for endourological procedures. For patients with asymptomatic bacteriuria, antibiotic therapy is recommended to prevent infectious complications during endourological procedures breaching the mucosa [13].

The guidelines of the American Urological Association also emphasize the necessity of performing bacterial urine culture to determine the appropriateness of further antibiotic prophylaxis [14]. Preoperative antibiotic prophylaxis is known to be an effective measure in reducing the incidence of infectious complications in patients with bacteriuria, increasing the rate of sterile cultures of renal pelvis urine and stones obtained intraoperatively [15]. For patients with bacteriuria undergoing endourological procedures, it is recommended to prescribe specific antibiotic prophylaxis based on the results of antibiotic sensitivity testing [16]. As part of antibiotic prophylaxis prior to performing URS or RIRS, a single dose of an antibacterial drug is recommended for patients with sterile urine culture. For planned PCNL, standard antibiotic prophylaxis with continued antibiotic therapy is recommended by many author [17].

Unfortunately, clinical guidelines lack specific algorithms and treatment protocols for managing asymptomatic bacteriuria prior to endoscopic surgery.

Current research evidence suggests that extended courses of antibiotic prophylaxis are more effective in preventing systemic inflammatory response and sepsis in patients

with high-risk factors for infectious complications, such as a positive urine culture [18-20].

Although it is well known that patients with a positive urine culture have an increased risk of infectious complications, approximately 17.0% of patients with a persistent positive urine culture after antibiotic prophylaxis still undergo PCNL [21]. It is also worth noting that repeated courses of antibiotic therapy, administered in an attempt to sterilize the urine culture before surgery, do not always achieve the desired outcome and may contribute to the development of multidrug-resistant bacterial strains.

## Objective of the study

**Primary objective:** To assess the incidence of postoperative infectious complications—specifically fever and leukocytosis—in patients with persistent asymptomatic bacteriuria compared to those with sterile urine cultures undergoing endoscopic surgery for renal and ureteral stones.

**Secondary objective:** To evaluate the influence of different preoperative antibiotic prophylaxis regimens (single-dose, 3-day, and 7-day protocols) on the risk of these complications.

## Methods

### Inclusion and exclusion criteria

The study included patients who underwent endoscopic treatment of upper urinary tract stones and completed a full standard preoperative examination at our clinic. Eligible patients had either positive or negative preoperative urine cultures and received antibiotic prophylaxis strictly in accordance with the standardized protocol adopted in our institution.

Patients were excluded from the study if their medical records lacked complete information regarding the preoperative assessment or if the evaluation was conducted partially or entirely at an external facility. Additional exclusion criteria were deviations from the clinic's standard antibiotic prophylaxis protocols, including cases involving multidrug-resistant bacterial strains, the presence of leukocyturia, congenital or acquired anomalies of the urinary system, HIV infection, ongoing immunosuppressive therapy, and the presence of permanent urethral catheters or cystostomy tubes.

### Grouping

A total of 449 patient records were selected for the analysis. Subsequently, records of 211 patients aged 18 to 75 years, who met the inclusion and exclusion criteria, were analyzed. All patients underwent urine culture with antibiotic sensitivity testing including blood tests, urinalysis, and CT scan before the surgical treatment.

Patients with sterile urine received antimicrobial prophylaxis according to the standard protocol approved by the hospital [ceftriaxone 1000 mg (IM) 2-3 hours before the

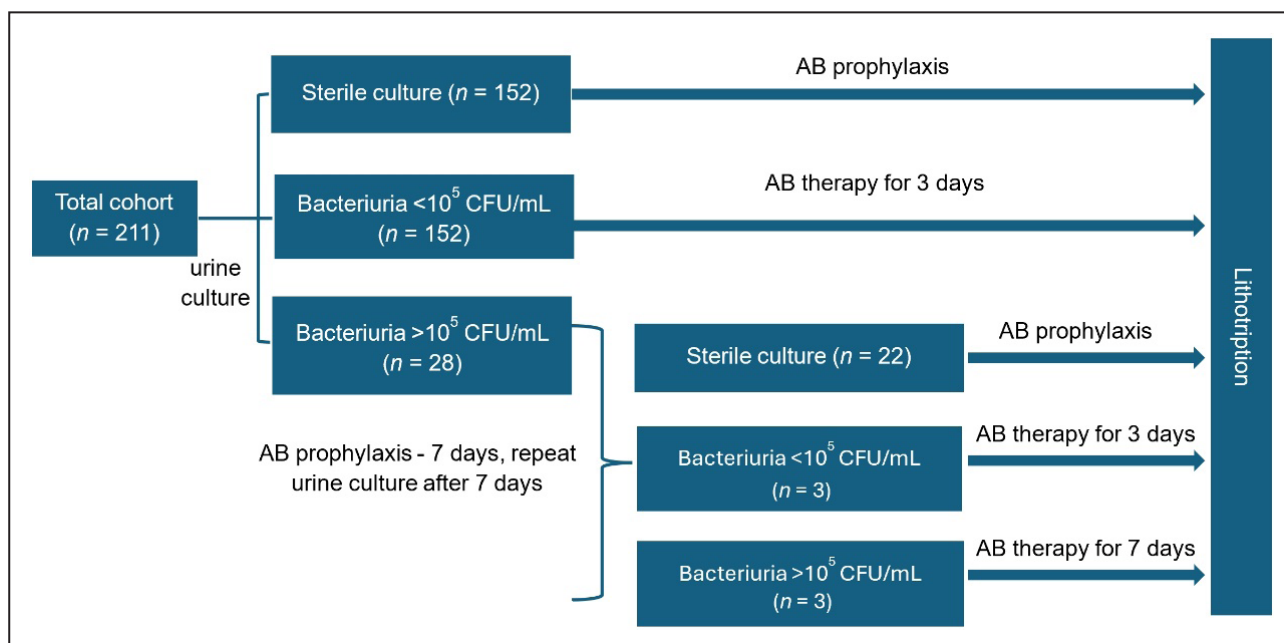


Figure 1. Study design.

surgery] (Figure 1). In cases of bacteriuria  $< 10^5$  CFU/mL, a 3-day course of antimicrobial prophylaxis was prescribed, tailored to the sensitivity of the identified pathogens. When one or more bacterial species grew in the urine greater than or equal to  $\geq 10^5$  CFU/mL, a 7-day course of antibiotic therapy was prescribed, adjusted according to the antibiotic sensitivity. After 7 days of treatment, a repeat urine culture was performed. In the absence of microbial growth, antimicrobial prophylaxis was conducted as per the standard protocol for patients with sterile urine. If pathogenic flora was detected, patients were minutely informed about the high risk of infectious complications before surgery. Patients with bacteriuria less than  $10^5$  CFU/mL were given a 3-day course of antibiotic therapy based on the antibiotic susceptibility test before surgery, while patients with bacteriuria greater than  $10^5$  CFU/mL received a 7-day course of antibiotics, also tailored to the antibiotic sensitivity test results. In the postoperative period, the incidence of infectious complications was evaluated, including episodes of fever (body temperature  $> 37.6^\circ\text{C}$ ), an elevated white blood cell count  $> 12 \times 10^9/\text{L}$ , acute purulent pyelonephritis confirmed by contrast CT, and sepsis, following the criteria of the Quick Sequential Organ Failure Assessment (qSOFA).

### Statistical analysis

Quantitative data were first tested for normal distribution using the Shapiro-Wilk test. If the data were normally distributed, the values were presented as the mean (M)  $\pm$  standard deviation (SD). For data that deviated from normal distribution, values were presented as the median (Me) and the lower and upper quartiles ([Q1; Q3]). Categorical data are presented with absolute values (n) and proportions (%). For evaluating proportions and constructing 95% confidence intervals (CIs), the binomial test was used. A multivariate logistic regression (MLR) model was employed to analyze the likelihood of hyperthermia and

leukocytosis, as well as factors influencing these probabilities. ROC analysis was performed to assess the quality of the model. Statistical analysis was performed using R version 4.1.3 ('The R Foundation for Statistical Computing', Vienna, Austria).

### Results

The patient's age was 57 [44; 66] years, with 93 patients (44.1%) being female and 118 patients (55.9%) male. The body mass index (BMI) was 28.7 [25.08; 32.4] kg/m<sup>2</sup>. The comorbid background was complicated by type 2 diabetes in 26 patients (12.3%). 144 patients were primary stone formers (68.2%), while 67 patients (31.8%) were treated due to recurrent (secondary) stones. The maximum stone size was 12 (9; 17) cm<sup>3</sup>. The stone volume was 0.44 (0.15; 1.11) cm<sup>3</sup>. The stone density was 1100 (803.5; 1337) HU (Hounsfield units). A single stone was diagnosed in 89 patients (42.2%), two stones in 48 cases (22.7%), three stones in 33 cases (15.6%), and four or more stones were treated in 41 patients (19.4%), while 122 patients had multiple stones.

Before the surgical treatment, 43 patients (20%) had drained upper urinary tract. In 31 patients (14.7%), had dwelling ureteral stent, while in 12 patients (5.7%), had nephrostomy tube.

Semiregid URS (7 Fr) was performed in 26 patients (12.3%), retrograde intrarenal surgery (RIRS) in 16 patients (7.6%), and percutaneous nephrolithotomy (PCNL) in 169 patients (80.1%).

In 149 cases (70.6%), the surgical procedure was performed under general anesthesia, in 55 cases (26.1%) under spinal anesthesia, and in 7 cases (3.3%) intravenous anesthesia was used.

A total of 155 patients (73.5%) had ASA score II, while 56 patients (26.5%) had a III ASA score. The median op-

**Table 1.** Clinical characteristics of the patients.

Parameter	n (%) or Value [95% CI]
ASA Score II	155 (73.5%)
ASA Score III	56 (26.5%)
Median operation time, min [Q1; Q3]	40 [30; 50]
Sterile urine	152 (72.0%)
Bacteriuria (total)	59 (28.0%) [22%; 34.5%]
< 10 <sup>5</sup> CFU/mL	31 (14.7%)
≥ 10 <sup>5</sup> CFU/mL	28 (13.3%) [9%; 18.6%]
With urinary drainage (stent or nephrostomy)	n = 43
Positive culture (with drainage)	15 (34.9%) [21%; 50.6%]
- Ureteral stent	4 (33%)
- Nephrostomy tube	11 (92%)
No urinary drainage	n = 168
Positive culture (without drainage)	26.2% [19.7%; 33.5%]
Most common pathogens	
<i>Enterococcus faecalis</i>	18 (8.5%)
<i>Escherichia coli</i>	15 (7.1%)
<i>Klebsiella pneumoniae</i>	8 (3.8%)

eration time was 40 (30; 50) minutes.

All patients underwent a bacteriological urine analysis prior to surgery. Primary sterile urine was diagnosed in 152 patients (72%), while 59 patients (28%) [22%; 34.5%] were found to have bacteriuria on preoperative work out. Among these, 31 patients (14.7%) had clinically insignificant less than 10<sup>5</sup> CFU/mL bacteriuria, and 28 patients (13.3%) [9%; 18.6%] had clinically significantly greater than or equal to ≥ 10<sup>5</sup> CFU/mL bacteriuria. The proportion of patients with positive urine culture among those with drained urinary tract (ureteral stent or nephrostomy drainage) was 34.9% [21%; 50.6%], compared to 26.2% [19.7%; 33.5%] in patients without any urinary tract drainage. However, this difference was not statistically significant (*p*-value of Fisher's exact test = 0.427). Dwelling ureteral stent or nephrostomic tube, Positive urine culture was found in 4 (33%) patients with a ureteral stent and in 11 (92%) patients with nephrostomy tube. The most common pathogens were *Enterococcus faecalis* in 18 (8.5%) patients, *Escherichia coli* in 15 (7.1%), and *Klebsiella pneumoniae* in 8 (3.8%) patients (Table 1).

After a course of primary antibiotic therapy in patients with significant bacteriuria (≥ 10<sup>5</sup> CFU/mL), urine sterility was achieved in 22 patients (78.6%) [59%; 91.7%]. In 6 patients (22%), bacteriuria persisted with 3 patients (11%) showing persistent significant bacterial counts, and another 3 patients (11%) showing bacterial counts reduction. Eventually, 37 patients (17.5%) [12.8%; 23.4%] with bacteriuria underwent surgery. Among them 3 patients (8%) with clinically significant bacteriuria and 34 (92%) with clinically insignificant bacteriuria.

In the postoperative period, leukocytosis greater than 12 × 10<sup>9</sup>/L was observed in 54 patients (25.6%), 17 patients (8.1%) had fever, in 11 patients (5.2%) fever was accompanied by leukocytosis. Fever 6 (16.2%) was significantly more common in patients with bacteriuria compared to 11 (6.3%) in patients with sterile urine [95% CI] 2.85 [0.8;

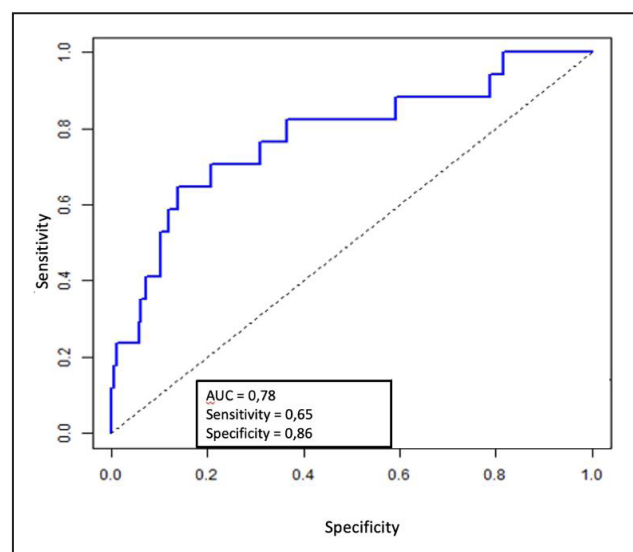
9.18], (*P*-value for Fisher's exact test = 0.087). Fever was observed only in 2 patients with clinically significant bacteriuria. No cases of purulent pyelonephritis or sepsis were registered.

According to the results of the multivariate logistic regression analysis, statistically significant associations were found between the probability of developing fever and bacteriuria before surgery (Figure 2). A positive urine culture increases the risk of fever by 4.75 times (OR = 4.75, 95% CI [1.222; 18.803], *P* = 0.023). No statistical significance was found between fever and other model parameters such as gender, age, BMI, presence of diabetes, stone volume and size, types of urinary tract drainage, and duration of the surgery (*P* > 0.05). The AUC for the ROC curve was 0.78, indicating satisfactory model quality.

There was no statistically significant association between bacteriuria and urinary tract drainage in this model (*P* = 0.427).

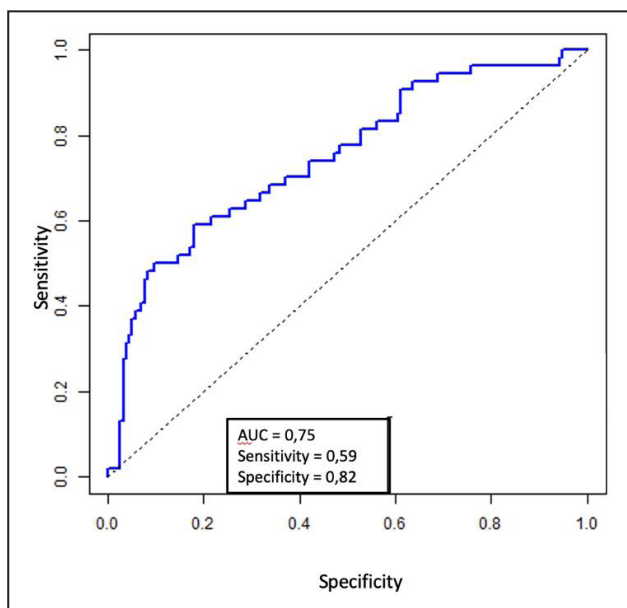
Based on the results of the multivariate logistic regression analysis, the factors statistically significantly influencing leukocytosis were stone volume (*P* = 0.008) and dwelling ureteral stent (*P* = 0.006). Ureteral stent (OR = 0.154, 95% CI [0.033; 0.512], *P* = 0.006) reduces the chance of leukocytosis, while greater stone volume increases the likelihood of leukocytosis by 1.54 times (OR = 1.543, 95% CI [1.128; 2.158], *P* = 0.008). There was no statistically significant correlation between leukocytosis and other parameters in the model, such as gender, age, BMI, diabetes, nephrostomy tube, positive urine culture, operation time, or type of operation (*P* > 0.05). The AUC for the ROC curve is 0.75, indicating an acceptable model quality (Figure 3). Additionally, the analysis revealed that the development of leukocytosis > 12 × 10<sup>9</sup>/L increases the risk of fever by 8.57 times (OR = 8.57, 95% CI [2.63; 32.85], *P* < 0.001).

## Discussion



**Figure 2.** ROC curve of multivariate logistic regression for hyperthermia.





**Figure 3.** ROC curve of multivariate logistic regression for leukocytosis.

Infectious complications remain one of the most significant problems of endourology. According to the results of a meta-analysis by R. Bapir *et al.*, incidence of infectious complications does not depend on type of endourological procedure [3]. The study demonstrated that the risk of infectious complications remains similar for various procedures, such as retrograde intrarenal surgery (RIRS), standard PCNL, mini-PCNL, and tubless PCNL. The only advantage observed was the lower odds for fever after PCNL with suctioning sheath, which is likely related to the decreased intrarenal pressure. On the other hand, several authors have identified key risk factors for infectious complications [10, 21, 22], including female gender, leukocyturia, leukocytosis, high neutrophil-to-lymphocyte ratio, ureteral stents, diabetes mellitus, stone size, multiple accesses to the kidney, operation time, residual fragments, infectious stones, positive urine culture, positive pelvic urine culture, and positive stone culture. Although bacteriuria is a well-recognized risk factor for the development of infectious complications, current data indicate that a significant portion of patients with positive urine cultures still undergo surgical treatment. In a multicenter, retrospective study by J. Gutierrez *et al.*, an analysis of 5,354 patients treated with PCNL was conducted [20]. Preoperative diagnostics revealed bacteriuria in 865 patients (16.2%), with the most common pathogen being *E. coli* — 350 patients (6.5%). In the postoperative period, hyperthermia was observed in 8.8% of patients with negative urine cultures and in 18.2% of those with positive cultures. Unfortunately, to date, no clinical guideline includes recommendations on the algorithm for the preoperative management of patients with bacteriuria; therefore, the decision regarding the possibility of performing endoscopic surgery and decision on the use of antibacterial prophylaxis regimen is left to the doctor. The current literature contains data challenging the paradigm of the sufficiency of a single dose of antibacterial medication in preventing infectious complications [23] and demonstrating higher

efficacy of extended (up to 7 days) courses of antibacterial prophylaxis in preventing systemic inflammatory response and sepsis in patients with high-risk factors.

Our study cohort, the proportion of patients with bacteriuria seeking surgical treatment was 28.0%, with clinically significant bacteriuria identified in almost half of the cases. The preliminary course of antibacterial therapy based on urine culture achieved urine sterility in 79.0% of treated patients, with 11.0% still having persistent clinically significant bacteriuria after treatment. Our study also revealed a statistically significant association between bacteriuria and the development of infectious complications. No statistically significant association was found between infectious complications and other known risk factors, nor between bacteriuria and urinary tract drainage, which was present in 35.0% of patients compared to 26.0% in patients without stents or nephrostomy tubes.

Moderate fever rates in our study, that are consistent with global averages (8.0%), along with the absence of complications such as purulent pyelonephritis, systemic inflammatory response, and sepsis, suggest that endourologic procedures can be performed safely in patients with positive urine culture provided adequate antimicrobial prophylaxis is given.

Limitations of the study include its retrospective design, as well as the non-inclusion of patients with multidrug-resistant bacteriuria, which limits the results obtained to the population of patients contaminated with non-hospital strains of bacteria.

## Conclusions

Our study highlights that a positive urine culture is a significant risk factor for infectious complications following endoscopic surgery. Prolonged antibiotic prophylaxis for patients with clinically significant ASB appears to be an effective strategy to minimize the risk of postoperative infectious complications.

## Declarations

**Authors' contribution:** V. Malkhasyan—study design development, data analysis, drafting the manuscript. N. Gadzhiev—study concept, scientific editing. S. Sukhikh—statistical data processing, drafting the manuscript. E. Maltsev—literature review; I. Kindarov—data acquisition, data analysis; D. Pushkar—supervision, study design development, critical review.

**Financial support and sponsorship:** None.

**Conflicts of interest:** Not applicable.

**Ethical approval and informed consent:** The study was designed according to the prescriptions of the Declaration of Helsinki (revised in Fortaleza, Brazil, October 2013). The study was approved by the Intercollegiate Ethics Committee (Protocol No 02-24 dated February 15, 2023).

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