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РОССИЙСКОЕ ОБЩЕСТВО УРОЛОГОВ

ФГАОУ ВО ПЕРВЫЙ МОСКОВСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ ИМЕНИ И.М. СЕЧЕНОВА МИНИСТЕРСТВА ЗДРАВООХРАНЕНИЯ РОССИЙСКОЙ ФЕДЕРАЦИИ (СЕЧЕНОВСКИЙ УНИВЕРСИТЕТ)

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CONTENTS

ORIGINAL ARTICLES

LITERATURE REVIEWS

E.V. Kulchavenya[1,2], V.V. Rafalskiy[3]

SPECTRUM OF PATHOGENS AND THEIR ANTIMICROBIAL RESISTANCE IN CYSTITIS, PYELONEPHRITIS, AND PROSTATITIS

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Introduction. Infectious and inflammatory diseases of the genitourinary tract account for approximately 42% of all outpatient urology cases, and disorders such as cystitis, pyelonephritis, and prostatitis are often characterized by a chronic, recurrent course. One of the key contributors to recurrent urinary tract infections is inappropriate therapy that does not take into account the local microbial spectrum and pathogen resistance profiles.
Aim. To determine the spectrum of uropathogens and their antimicrobial resistance patterns in patients with cystitis, pyelonephritis, and prostatitis.
Materials and methods. We analyzed the results of microbiological urine cultures from outpatient urology patients processed by the Invitro Laboratory between 2022 and 2024. In total, 4031 bacterial isolates were included: 2903 (72.0%) from patients with cystitis, 1017 (25.2%) from patients with pyelonephritis, and 111 (2.8%) from patients with chronic prostatitis.
Results. The structure of the microbial landscape differed by diagnosis. E. coli was the predominant pathogen in all groups, with a detection rate of 73.8–75.3% in cystitis and pyelonephritis, while in chronic prostatitis the rate was markedly lower at 53.1%. Klebsiella pneumoniae and Enterococcus faecalis were more frequently isolated in prostatitis (19.0% and 15.3%, respectively) compared with urinary infections, where their combined frequency ranged from 6.9% to 11.9%. Other pathogens (Proteus mirabilis, Streptococcus agalactiae, Enterobacter cloacae, Pseudomonas aeruginosa) accounted for 6.4% of isolates in cystitis, 7.6% in pyelonephritis, and 12.6% in prostatitis.
Antimicrobial resistance was assessed for E.coli isolates. Resistance to amoxicillin/clavulanate was 24.9% in cystitis, 31.0% in pyelonephritis, and 38.9% in prostatitis. Levofloxacin resistance was observed in approximately one third of isolates from cystitis and in about half of isolates from pyelonephritis, whereas all E.coli isolates from prostatitis cases were susceptible. Resistance to trimethoprim-sulfamethoxazole in prostatitis was approximately twice as high as in cystitis and pyelonephritis.
Conclusion. Urinary tract infections are predominantly caused by E.coli, while chronic prostatitis is associated with a more diverse spectrum of pathogens, with E.coli detected in only 53.1% of cases. Antimicrobial resistance profiles differ substantially between urinary infections and prostatitis, underscoring the importance of tailoring empirical therapy to local pathogen distribution and resistance patterns.

Keywords: *bacteriuria, urinary tract infections, cystitis, pyelonephritis, prostatitis, antimicrobial resistance*

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Introduction. Urinary tract infections (UTIs) are the most common bacterial infections and affect at least one million people worldwide each year [1–4]. Among nosocomial infections, UTIs rank second only to upper respiratory tract infections, which account for 24% in developing countries [5]. UTIs have been shown to adversely affect mental health and quality of life [6].

Unfortunately, UTIs are associated with a high recurrence rate [1]. Women are at higher risk of developing UTIs than men; within six months, recurrence occurs in one in five women [7–8]. Chronic UTI increases the likelihood of gestational pyelonephritis [9]. Postmenopausal women are more prone to recurrent UTIs because lower estrogen levels lead to unfavorable changes in the urogenital epithelium and the urogenital microbiome [10].

UTIs are caused by a wide range of pathogens, including Gram-negative and Gram-positive bacteria, as well as fungi. Uropathogenic E. coli (UPEC) is the principal etiological agent of UTIs, accounting for about 75% of uncomplicated UTI cases; however, less common pathogens such as Klebsiella pneumoniae (K. pneumoniae), Staphylococcus saprophyticus (S. saprophyticus), Enterococcus faecalis (E. faecalis), group B Streptococcus (GBS), Proteus mirabilis (P. mirabilis), Pseudomonas aeruginosa (P. aeruginosa), Stafphylococcus aureus (S. aureus), and other microorganisms cause opportunistic UTIs [1].

UPEC is responsible for complicated UTIs in at least half of cases [2]. The insufficient efficacy of initial antibacterial therapy for UTIs and the subsequent development of conditions favoring recurrence are largely explained by pathogen evolution, particularly the development of antimicrobial resistance.

Aim. To determine the spectrum of uropathogens and their antimicrobial resistance in cystitis, pyelonephritis, and prostatitis.

Materials and methods. The results of microbiological urine studies from urology outpatients performed by the Invitro laboratory network (https://www.invitro.ru/) over a three-year period (2022–2024) were analyzed. A total of 4031 bacterial isolates were evaluated: 2903 (72.0%) strains were obtained from patients with acute cystitis or chronic cystitis during exacerbation, 1017 strains (25.2%) from patients with acute pyelonephritis or chronic pyelonephritis during exacerbation, and 111 strains (2.8%) from patients with chronic bacterial prostatitis.

The study included patients residing in the Siberian Federal District (Altai Republic, Altai Krai, Irkutsk Region, Kemerovo Region, Krasnoyarsk Krai, Novosibirsk Region, Omsk Region, Tomsk Region, Republic of Tyva, Republic of Khakassia) during the period from January 1, 2022 to December 31, 2024. All urine samples were taken at the outpatient basis. Midstream urine samples were collected at any time of day, 2–3 hours after the previous voiding; in patients with prostatitis, urine was collected after prostatic massage. To avoid contamination, genital hygiene procedures were observed. Samples were collected in sterile plastic Uri-swab transport containers (COPAN Diagnostics Inc.) and delivered to local offices and laboratories of the commercial Invitro network within two hours after voiding at ambient temperature. When prompt delivery of urine samples to the laboratory was not possible, they were refrigerated at +5° C for no longer than 24 hours. Samples with a bacterial load $\geqslant 10^4$ CFU/mL underwent pathogen identification followed by antimicrobial susceptibility testing. Preanalytical processing of clinical samples was performed using the automated WASP processor (COPAN, Italy). E-swab tubes were processed using the WASP system (standard culture and preparation of microscopy slides with Gram staining). Standard culture was performed using the four-quadrant streak method with the WASP system on CLED agar (bioMerieux, France) or Columbia agar with 5% sheep blood (Becton Dickinson, USA). Microorganism identification was carried out by a semi-automated method using the VITEK2 system (bioMerieux, France) and MALDI Biotyper Microflex (Bruker Daltonik GmbH, Germany). Antimicrobial susceptibility was determined by an automated method using the VITEK2 analyzer (bioMerieux, France) in accordance with the manufacturer's recommendations. For quality control, internal and external quality assurance procedures were performed at least twice a year. External quality control was carried out using the procedures of the Center for External Quality Control of Clinical Laboratory Investigations (FSVOK, Russian Federation, www.fsvok.ru). As part of internal quality control, at least once a month, reference strains were used for pathogen identification and antimicrobial susceptibility testing.

The raw laboratory data were exported from the laboratory information system in CSV format and processed using proprietary software for subsequent analysis. The transformed data were stored as two-dimensional tables and analyzed by creating appropriate queries written in the Python programming language. Relevant patents were obtained for the original algorithm for data transformation and analysis, the software, and the databases containing the processed information.

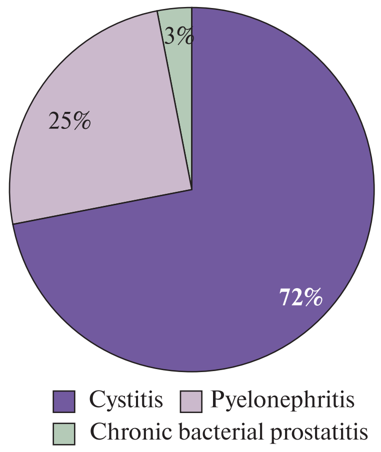

Fig. 1. Disease structure of patients included in the study

Results. The distribution of nosologies is presented in *Figure 1.* The structure of the microbial landscape differed depending on the diagnosis. E. coli was the predominant pathogen in all groups; however, while in cystitis and pyelonephritis it was detected in 73.8 and 75.3%, respectively, in patients with chronic prostatitis the detection rate of E. coli was 53.1%. The growth of Klebsiella pneumoniae and Enterococcus faecalis was more frequently observed in prostatitis, at 19.0 and 15.3%, respectively, whereas in urinary tract infections the frequency of identification of these pathogens ranged from 6.9 to 11.9%. The "other" group included Proteus mirabilis, Streptococcus agalactiae, Enterobacter cloacae, and Pseudomonas aeruginosa. Their proportion in the microbial landscape ranged from 0.7 to 6.3%; overall, "other microorganisms" were identified in 6.4% of cases of cystitis, 7.6% of pyelonephritis, and 12.6% of chronic prostatitis. The spectrum of uropathogens by nosology is presented in *Figure 2.*

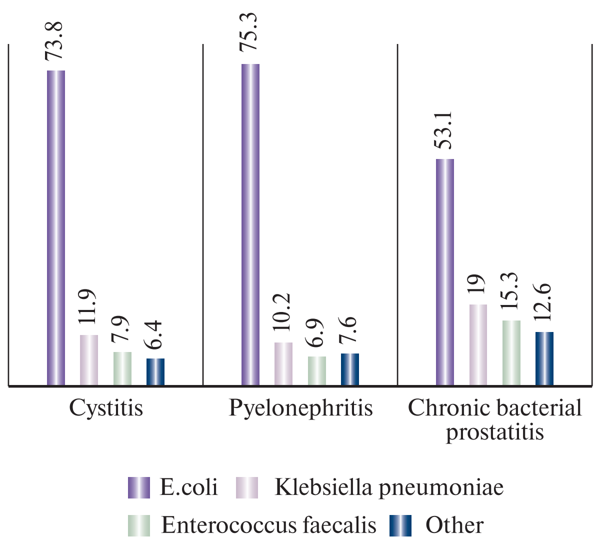

Fig. 2. Microbial spectrum structure (%)

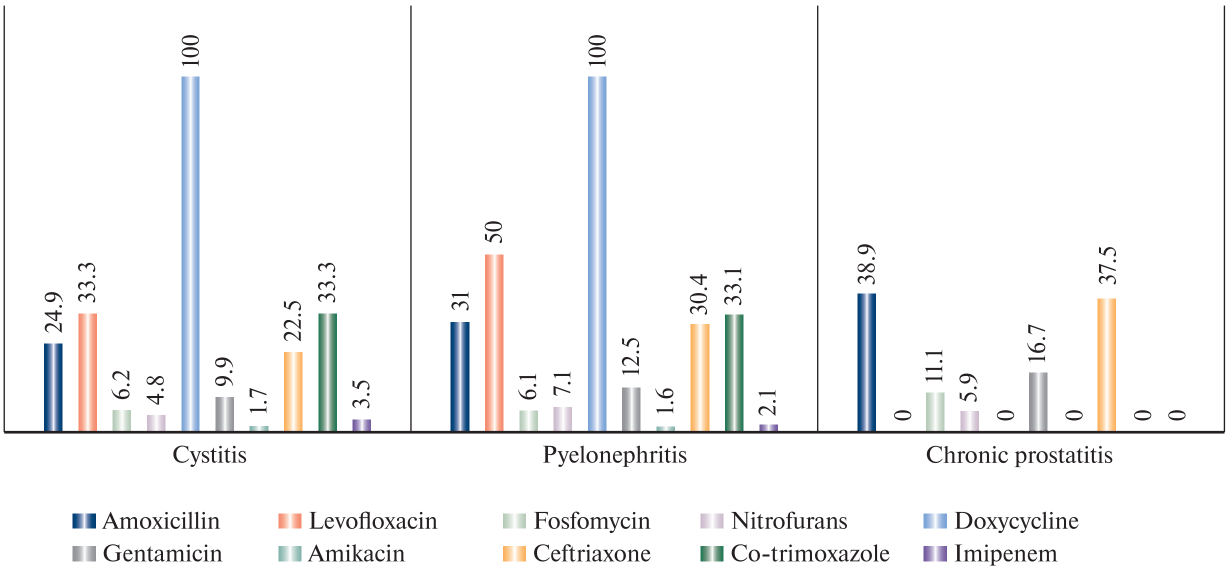

Fig. 3. Proportion of resistant uropathogens by UTI locus (%)

Resistance of the pathogenic microflora was assessed for E. coli. The proportion of E. coli strains resistant to amoxicillin/clavulanate was 24.9% in cystitis, 31.0% in pyelonephritis, and 38.9% in prostatitis. Every third E. coli strain isolated from a patient with cystitis was resistant to levofloxacin, as was every second strain in pyelonephritis; however, in prostatitis all E. coli strains were susceptible to this antibiotic. In prostatitis, E. coli resistance to co-trimoxazole was twice as high as that observed in cystitis and pyelonephritis. These results are illustrated in *Figure 3*.

Discussion. Antibiotics and antimicrobial chemotherapeutic agents have been used to treat UTIs since the introduction of sulfonamides in the 1940s, and this class of drugs remains the most commonly recommended therapeutic option for UTIs [1]. Efforts should be made to minimize the development of resistance by adhering to recommended treatment courses and dosages [11]. According to recent studies, older adults are at increased risk of UTIs caused by multidrug-resistant pathogens [12]. The use of empirical antibiotics should be limited to cases in which symptoms are pronounced and/or there is concern about a more serious infection [13]. When selecting an antibiotic, local resistance patterns of uropathogens should be taken into account [14].

There is no convincing evidence supporting the use of antibiotic prophylaxis for recurrent UTIs; on the contrary, increasing evidence supports non-antibiotic preventive regimens for recurrent UTIs [15]. The 2025 European Association of Urology guidelines state that alternative methods of prevention and treatment have reduced antibiotic use for UTIs by 63% [16]. Since excessive antibiotic use is the main driver of the emergence of multidrug-resistant bacteria, and because about 25% of all antibiotic prescriptions are issued for UTIs, antibiotic prophylaxis should be used only after all non-antibiotic treatment options have been exhausted [17]. Recent studies have demonstrated the potential of bacteriophage therapy for the treatment of urinary tract infections caused by multidrug-resistant bacteria such as E. coli and K. pneumoniae [18]. However, although the preliminary data obtained with this therapy are highly promising, substantial preclinical and clinical work is still required before bacteriophages can become an alternative to antibiotics in the future. The results of our study showed that knowledge of antimicrobial susceptibility of uropathogens in a specific region may also be insufficient; fluctuations in microbial resistance depending on the site of inflammation should also be taken into account. Antimicrobial resistance of uropathogens is continuously monitored worldwide, including in different patient categories [19–26]. In the Russian Federation, the large-scale DARMIS study is conducted regularly [27–29]; however, previous investigators examined the characteristics of uropathogens depending on the region, whereas we determined the spectrum and resistance of pathogens depending on the site of inflammation.

Conclusion. Thus, urinary tract infection is caused predominantly by E. coli, whereas in prostatitis the spectrum of pathogens is more diverse and the proportion of E. coli is 53.1%. Antimicrobial resistance of pathogens differs substantially between urinary tract infections and prostatitis, but regardless of the diagnosis, it is highest to amoxicillin/clavulanate and lowest to nitrofurans and fosfomycin.

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PREDICTORS OF DE NOVO PELVIC DYSFUNCTION AFTER RECONSTRUCTIVE PELVIC SURGERY WITH VAGINAL ACCESS: A PROSPECTIVE COHORT STUDY

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Introduction. Vaginal reconstructive surgery aims to correct pelvic dysfunctions, but some patients may experience new symptoms after the procedure. These patients may develop a negative attitude toward treatment. The available literature is ambiguous due to the use of different study samples, instruments, and insufficient follow-up periods for this patient group.
Objective. The aim of the prospective cohort study was to identify predictors of de novo pelvic dysfunction after vaginal reconstructive surgery while monitoring patients for 12 months.
Materials and methods. A prospective cohort study included 159 patients admitted for surgery for pelvic dysfunction. Prior to surgery, patients completed validated questionnaires – PISQ-12, ICIQ-SF, PFIQ-7, PFDI-20. After the surgical treatment, patients were invited for follow-up visit after 3, 6, and 12 months, during which they were asked to complete questionnaires again and undergo a gynecological exam.
Results. The prevalence of de novo pelvic dysfunction in women after vaginal urogynecological surgery was 9,7%, according to our study. In three quoistionares (ICIQ-SF, PFDI-20, and PFIQ-7), a higher ICIQ-SF score significantly increases the risk of postoperative urinary incontinence. Higher BMI also increases of postoperative urinary incontinence. The PFDI-20 preoperative questionnaire scores predict a chance of pelvic organ prolapse.
Conclusions. Modern research shows that despite the success of urogynecological operations, such as correction of pelvic prolapses and incontinence treatment, the risk of de novo pelvic dysfunction remains significant. Improving the treatment and monitoring of patients with pelvic dysfunctions creates favorable conditions for reducing the number of postoperative complications and de novo symptoms.

Keywords: *de novo pelvic dysfunctions, pelvic organ prolapse, urinary incontinence, reconstructive pelvic surgery*

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Introduction. Pelvic floor disorders are a common problem worldwide and significantly reduce patients' quality of life. According to the study by Hafidh B.A. et al. (2013), the incidence of de novo pelvic floor disorders ranges from 4 to 51% [1]. Vaginal reconstructive surgery is aimed at treating these disorders. However, in some patients, newly developed symptoms (de novo) are recorded after surgical procedures. In such cases, patients develop a negative attitude toward treatment. The literature data are contradictory, which is associated with the study of heterogeneous cohorts, the use of different assessment tools, and insufficient follow-up duration in this group of patients. There are many tools for assessing pelvic floor disorders, in particular validated questionnaires, the use of which helps medical personnel [1].

During our study, the following questions were studied: can we identify a combination of preoperative factors that accurately predicts the overall risk of developing new symptoms of pelvic floor disorders after surgery? Do preoperative assessments of symptom severity using ICIQ-SF (International Consultation on Incontinence Questionnaire Short Form), PFDI-20 (Pelvic Floor Distress Inventory), PFIQ-7 (Pelvic Floor Impact Questionnaire), and PISQ-12 (Pelvic Organ Prolapse/ Urinary Incontinence Sexual Questionnaire) allow prediction of the development of specific new symptoms of pelvic floor disorders, for example, bowel symptoms, bladder symptoms, or pelvic organ prolapse symptoms after surgery?

Further research in this area is needed for a better understanding of the causes and mechanisms of de novo pelvic floor disorders, as well as for the development of methods for their prevention and correction.

Aim. To identify predictors of de novo pelvic floor disorders after vaginal reconstructive surgery during 12 months of follow-up.

Materials and methods. A prospective cohort study involving 159 patients admitted for surgical treatment of pelvic floor disorders (pelvic organ prolapse, urinary incontinence) from March to October 2023 was carried out. Of these, three patients refused surgical treatment after completing the questionnaires. Inclusion criterion was patients with symptomatic pelvic organ prolapse and urinary incontinence in the absence of an effect from conservative therapy. Exclusion criteria were patients who refused surgery during the study and those who did not attend the follow-up visit. Non-inclusion criteria were pregnant women, neurogenic bladder dysfunction,

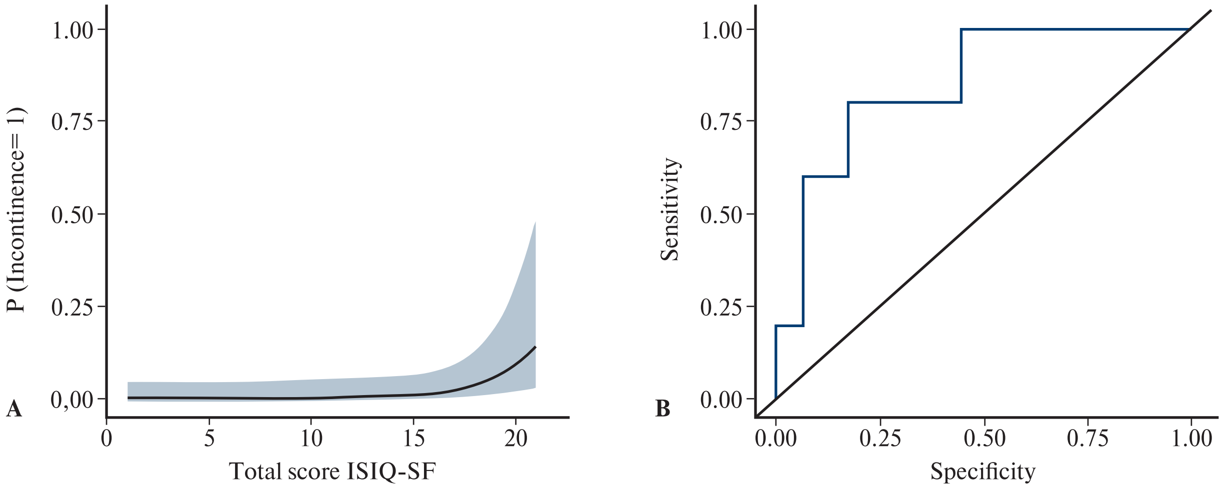

Fig. 1. ROC curve and plot of the relationship between the probability of the event (postoperative urinary incontinence) and the predictor value (total ICIQ-SF score): A — relationship plot; B — ROC curve

a history of radiotherapy, urgency urinary incontinence, and women with genital prolapse POP-Q <2 (POP-Quantification system). Before surgery, patients completed the validated questionnaires ICIQ-SF (International Consultation on Incontinence Questionnaire Short Form), PFDI-20 (Pelvic Floor Distress Inventory), PFIQ-7 (Pelvic Floor Impact Questionnaire), and PISQ-12 (Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire). After surgical correction, patients were invited for repeat visits at 3, 6, and 12 months to assess the postoperative condition by repeated completion of the questionnaire.

The study was approved by the Ethics Committee of the Russian University of Medicine (Protocol No. 04-23 dated April 13, 2023). The participants signed informed voluntary consent to participate in the study. Statistical data processing was performed using the Jamovi 1.8.3 statistical package, as well as Excel (product code: 00334-38920-77957-AA497). Logistic regression analysis was used to identify predictors of de novo pelvic floor disorders (urinary incontinence and pelvic organ prolapse). For significant predictors, an ROC curve and a plot showing the relationship between event probability and predictor value were constructed.

Results. The mean age of the patients was 56.3±12 years, and the mean body mass index (BMI) was 28.6±5.12. Stress urinary incontinence was diagnosed in 77 patients (48%), and mixed urinary incontinence in 60 patients (38%). Pelvic organ prolapse of varying severity was diagnosed in 32 of 159 patients (20%). The mean parity was 2. Perineal tears during childbirth were present in 55.9% of patients. A total of 194 surgical procedures were performed. Twenty-three patients (14%) underwent more than one surgical procedure. All surgical procedures were performed by one experienced physician. The types of procedures performed are presented in the *Table*.

After surgical treatment, the patients were invited for follow-up visits at 3, 6, and 12 months and were asked to complete the same questionnaires again. De novo stress urinary incontinence was recorded in 5 patients during follow-up, and pelvic organ prolapse of varying severity in 10 patients. According to our study, the prevalence of de novo pelvic floor disorders in women after vaginal urogynecological surgery was 9.7%. Analysis of data from three questionnaires (ICIQ-SF, PFDI-20, and PFIQ-7) showed that a higher ICIQ-SF score was a statistically significant predictor of postoperative stress urinary incontinence (p=0.045; OR 1.62; 95% CI 1.01–2.59). However, the increase in risk was moderate: at a score close to 20, the probability of urinary incontinence increased by 25% compared with patients with minimal scores (*Fig. 1*).

When risk factors such as parity, age, and BMI were analyzed, higher BMI (p=0.042; OR 1.21; 95% CI 1.01–1.46) was found to increase the likelihood of postoperative urinary incontinence (*Fig. 2*).

It should be noted that all patients with postoperative urinary incontinence had undergone procedures for urinary incontinence via the transobturator approach. At the same time, there was no significant association

Table

Groups of patients by type of surgical intervention

Group of procedures	Number of procedures (%)
Transobturator correction of urinary incontinence	86 (44.4)
Retropubic correction of urinary incontinence	39 (20.1)
Adjustment (tightening) of the Remeex adjustable sling	1 (0.5)
Correction of pelvic organ prolapse using synthetic prostheses	19 (9.8)
Mini-slings for correction of urinary incontinence	4 (2.1)
Correction of pelvic organ prolapse using native tissue	22 (11.3)
Correction of pelvic organ prolapse using anchoring systems	23 (11.8)

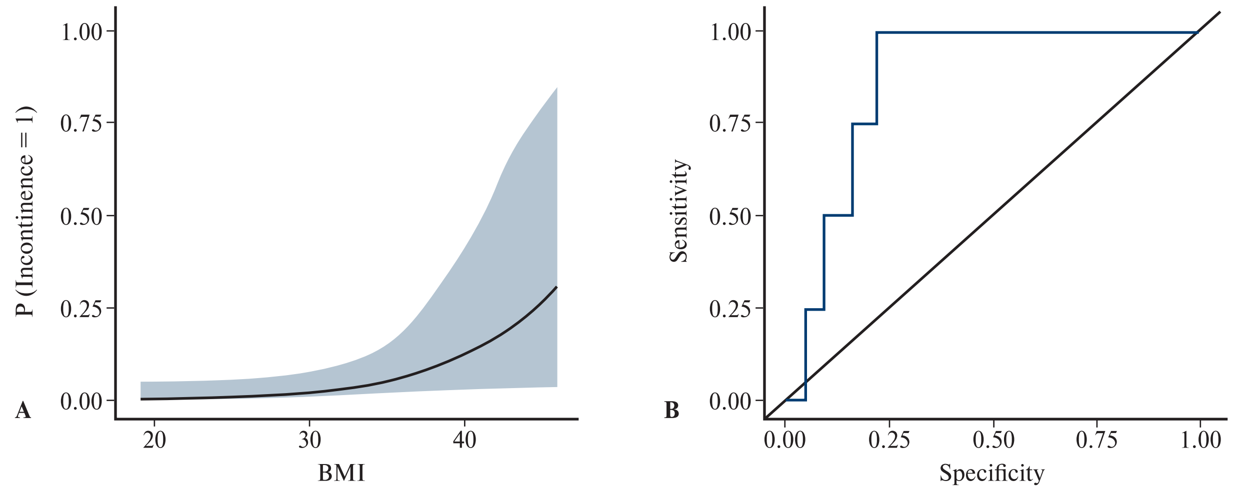

Fig. 2. ROC curve and plot of the relationship between the probability of the event (postoperative urinary incontinence) and the predictor value (BMI): A – relationship plot; B – ROC curve

between the type of surgery and the presence of postoperative urinary incontinence, which may be related to the small number of patients with postoperative urinary incontinence.

A predictor of pelvic organ prolapse was the preoperative PFDI-20 score (p=0.014; OR 0.77; 95% CI 0.62–0.95). At the same time, a significantly lower questionnaire score was associated with the development/recurrence of pelvic organ prolapse (*Fig. 3*).

Patients with postoperative pelvic organ prolapse underwent different types of procedures: native tissue repair, repair using synthetic prostheses, and repair using anchoring systems. The type of surgery was not a statistically significant factor for the occurrence of postoperative pelvic organ prolapse.

Discussion. The present study was aimed at identifying preoperative predictors of new symptoms of pelvic floor dysfunction after surgical treatment using data from the preoperative questionnaires PFDI-20, PFIQ-7, ICIQ-SF, and PISQ-12. Our results revealed several important associations, highlighting the potential of preoperative assessment to identify patients at higher risk of developing specific de novo symptoms of pelvic floor disorders in the postoperative period. These findings provide valuable information for patient counseling, surgical planning, and targeted postoperative management strategies.

The question of heterogeneity of surgical procedures in the study cohort is a legitimate one. However, combining the patients into a single group for analysis appears methodologically justified for several reasons.

First, despite differences in surgical technique, all procedures were aimed at restoring a single anatomical and functional system, the pelvic floor structures, and were performed within a unified surgical approach, namely the vaginal route. This minimizes variability associated with fundamentally different surgical approaches, such as laparoscopic or open surgery.

Second, the main objective of the study was not to compare the efficiency of specific procedures, but to identify predictors of de novo symptoms. The identified

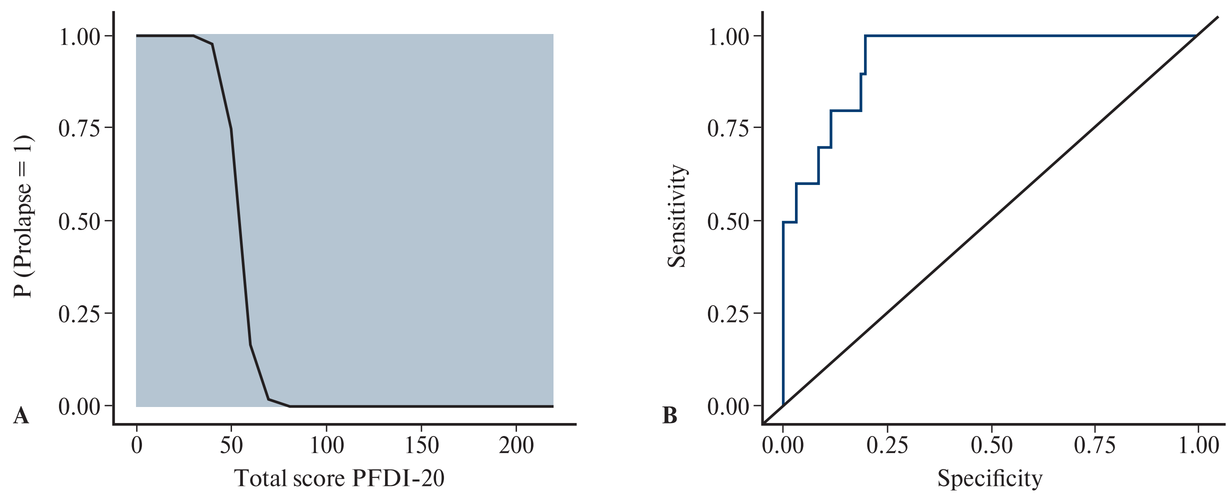

Fig. 3. ROC curve and plot of the relationship between the probability of the event (postoperative pelvic organ prolapse) and the predictor value (total PFDI-20 score): A – relationship plot; B – ROC curve

predictors are markers of initially reduced functional reserve of the pelvic floor, which creates a pathogenetic basis for the development of de novo symptoms after pelvic floor reconstructive surgery.

Thus, analysis of a unified cohort makes it possible to identify general patterns and risk factors, which increases the clinical value of the study and contributes to the development of preventive measures for patients undergoing pelvic floor reconstructive surgery.

Higher preoperative bladder symptom scores on the ICIQ-SF were associated with a higher likelihood of developing de novo urinary incontinence. These data suggest that patients with pre-existing, including subclinical, bladder dysfunction are more prone to the development of clinically significant symptoms after surgery. Nerve or muscle injury during procedure, as well as changes in pelvic floor biomechanics, may potentially unmask or aggravate pre-existing vulnerabilities.

According to the study by Simsek A. et al. (2014), a significant improvement in ICIQ-SF scores was observed after sling surgery in women with urinary incontinence. In addition, postoperative urine leakage was associated with worse questionnaire scores [2]. These observations underscore the need for thorough preoperative evaluation to identify patients with subtle but potentially clinically significant symptoms of pelvic floor disorders. Although these symptoms may not be the main reason for seeking surgical treatment, their presence may increase the risk of developing clinically significant de novo symptoms in the postoperative period. Addressing these underlying problems through preoperative interventions such as pelvic floor physiotherapy, biofeedback, or dietary modification may potentially reduce the risk of new-onset or worsening pelvic floor dysfunction symptoms after surgery.

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In our study, all patients with postoperative urinary incontinence had undergone transobturator procedures for correction of urinary incontinence. At the same time, there was no significant association between the type of surgery and the presence of postoperative urinary incontinence, which may be related to the small number of patients with postoperative urinary incontinence. Gomes C.M. et al. (2017) studied the incidence of de novo urgency symptoms after surgery for urinary incontinence and found that the incidence was 0.2–25% after retropubic urethropexy and 0–15.6% after the transobturator approach [3]. In our study, 7 patients (4.7%) with mixed urinary incontinence had persistent urgency after correction of the stress component of mixed urinary incontinence. Persistent urgency and de novo urgency urinary incontinence were analyzed for their association with the total preoperative score on all questionnaires, age, BMI, and parity. The presence of urgency symptoms was not significantly associated with any of these variables.

It is important to note that we did not find a significant association between any of the preoperative questionnaire results and the development of de novo pelvic organ prolapse symptoms after surgical treatment. This contrasts with some previous studies suggesting that certain preoperative factors, such as age and parity, may increase the risk of recurrent prolapse or de novo prolapse after pelvic floor surgery [4–6]. This may be related to differences in the study populations, surgical techniques, or the relatively short follow-up period in our study. The predictor of recurrence/development of pelvic organ prolapse was the total preoperative PFDI-20 score. At the same time, a low total score on this questionnaire was a risk factor. It is possible that when symptoms are mild and the PFDI-20 score is low, surgery may lead to de novo pelvic floor dysfunction. Thus, before proceeding with surgical treatment in patients with a low questionnaire score, conservative treatment should be preferred. Our study included patients with anatomically confirmed stage 2–4 pelvic organ prolapses according to the POP-Q classification. However, the key conclusion of this work is that indications for surgical treatment should primarily be based not on the degree of anatomical defect, but on the severity of symptoms affecting quality of life, as assessed by standardized questionnaires such as the PFDI-20. In our cohort, the predictor of an unsatisfactory outcome (recurrence or development of de novo dysfunction) was a low total score on the preoperative PFDI-20 questionnaire. This means that even in the presence of significant anatomical prolapse (POP-Q stage 3–4), a low subjective level of discomfort reported by the patient may indicate a lower appropriateness of primary surgical intervention. In such clinical situations, when objective findings (POP-Q) and subjective feeling (questionnaire results) are discordant, full patient counseling and consideration of a phase of conservative treatment appear to be the most balanced approach. This conclusion requires further investigation in a larger number of patients.

This study has several strengths, including the use of validated questionnaires to assess pelvic floor dysfunction symptoms, its prospective design, and the fact that surgical treatment was performed by a single surgeon. However, there are also several limitations that should be considered. First, our study was carried out at a single center, which may limit the generalizability of our findings to other populations and surgical settings. Second, the follow-up period was limited to 12 months, which may have been insufficient to detect all de novo pelvic floor dysfunction symptoms, especially those with delayed onset.

Future studies should include longer follow-up periods to assess the long-term impact of preoperative factors on pelvic floor dysfunction symptoms, as well as incorporate objective measures of pelvic floor function, such as urodynamic testing and assessment of pelvic floor muscle strength, to provide a more comprehensive evaluation of pelvic floor dysfunction.

The results of our study have important clinical implications. By identifying patients at higher risk of developing new pelvic floor dysfunction symptoms after surgery, clinicians may tailor their preoperative counseling and management strategies to reduce these risks.

Conclusion. Contemporary studies show that despite the success of urogynecological procedures such as correction of pelvic organ prolapse and treatment of urinary incontinence, the risk of de novo pelvic floor dysfunction remains substantial. Possible predictors of postoperative urinary incontinence include a higher total preoperative ICIQ-SF score (p=0.045; OR 1.62; 95% CI 1.01–2.59) and a higher BMI (p=0.042; OR 1.21; 95% CI 1.01–1.46). Improvement of treatment strategies and postoperative follow-up in patients with pelvic floor dysfunction may reduce the incidence of postoperative complications and de novo symptoms.

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Ethical statement. The study was designed according to the prescriptions of the Declaration of Helsinki (revised in Fortaleza, Brazil, October 2013) and approved by the Ethics Committee (Protocol No. 04-23 dated April 13, 2023).

Informed consent. All patients signed an informed consent to participate in the study and to process personal data

Authors' contribution: Ausheva B.Kh. – study design development, literature review, data acquisition, data analysis, statistical data processing, drafting the manuscript. Kasyan G.R. – study concept concept, scientific editing, critical review. Pushkar D.Y. – supervision.

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DYNAMICS OF THE RENAL PELVIS SIZE DURING NORMAL PREGNANCY

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Objective. To evaluate changes in the anteroposterior renal pelvis diameter (APD) from the first to the third trimester in healthy primigravid women.
Materials and Methods. A prospective observational study was conducted from March 2021 to July 2022, involving 30 healthy pregnant women aged 18–40 years. Inclusion criteria were: primigravida, singleton pregnancy, absence of significant medical conditions, and no history of urinary tract infections. Renal ultrasound examinations was performed in the first (10–12 weeks), second (22–24 weeks) and third (34–36 weeks) trimesters. Statistical analysis was performed using nonparametric methods (Statistica 10, StatSoft).
Results. In 10 women, APD was not detectable throughout the pregnancy. In the right kidneys, the APD increased from the first to the second trimester in 40% of women, while in the left kidneys? in increased in 33.3%. From the first to the third trimester, an increase in APD was observed in 30% of women in the right kidneys and in 53.3% in the left kidneys. Significant differences in the APD were noted only in the left kidneys between the first and second trimesters (p=0.005) and the first and third trimesters (p=0.003). In the right kidneys, the changes approached significance (p=0.072 and p=0.075, respectively). Differences between the second and third trimesters were not statistically significant.
Discussion. The study results demonstrated that dilation of the renal pelvis in pregnant women can vary: some women exhibit no dilation, while others shou an increase or decrease. Notably, an increase in APD was more frequently observed in the left kidneys, which contradicts the common belief of a predominance of right-sided hydronephrosis. It is important to note that changes in the APD do not always correlate with clinical symptoms, making it difficult to distinguish between physiological and pathological dilation. These findings highlight the need for further research to refine diagnostic criteria and understand the factors influencing the progression of maternal hydronephrosis.
Conclusion. Dilation of the renal collecting system in healthy primigravid women may be absent, increase, or decrease during pregnancy. The most significant changes in the collecting system of the kidneys occur from the first to the second trimester, particularly in the left kidneys. These findings underscore the necessity for further studies to differentiate between physiological and pathological dilation of the upper urinary tract and to clarify their clinical significance.

Keywords: maternal hydronephrosis, normal pregnancy, anteroposterior renal pelvis diameter

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Introduction. Asymptomatic "mild" hydronephrosis is considered a normal finding during pregnancy in healthy women in more than 90% of pregnancies [1, 2]. Moreover, so-called physiological hydronephrosis is more often pronounced in the right kidney than in the left [3–5] and in the second half of pregnancy [6]. Dilatation of the ureters and the pelvicalyceal system is thought to result from compression of the ureters by the gravid uterus [7] and the effects of progesterone [7, 8], whereas the predominance of right-sided upper urinary tract dilatation is explained by conflict with the iliac vessels and enlarged ovarian vessels in 40% of pregnancies [9].

At present, abdominal ultrasonography is recognized as the first-line imaging modality for the diagnosis of hydronephrosis during pregnancy [10]. However, differentiation between physiological and asymptomatic obstructive hydronephrosis by ultrasonography is problematic [11]. The generally accepted approach to determining the presence or absence of pelvic dilatation is measurement of the anteroposterior diameter (APD) on the transverse scan [11].

The absence of pelvic dilatation is defined as the inability to record its APD. Mild dilatation is defined as a renal pelvic APD <10 mm, moderate dilatation as 11–20 mm, and severe dilatation as >20 mm [11].

It should be emphasized that changes in renal volume during pregnancy have been studied in a number of investigations [12, 13]. A significant increase in renal volume from the first to the third trimester of pregnancy has been demonstrated.

At the same time, changes in renal pelvic size during normal pregnancy remain insufficiently studied.

Aim. To assess changes in the anteroposterior diameter (APD) of the renal pelvis from the first to the third trimester in healthy primigravid women.

Materials and methods. Between March 2021 and July 2022, a single-center, non-interventional, observational, prospective study with consecutive enrollment of

30 pregnant women was carried out. Inclusion criteria were women aged 18–40 years, primigravid pregnancy, singleton gestation, stable marital status, sexual activity for at least 6 months before pregnancy, no history of concomitant diseases, including diseases of vital organs, and consent to participate in the study. Exclusion criteria were as follows: any woman with a history of abortion, miscarriage, stillbirth, or neonatal death, as well as inability to understand Russian, antidepressant use, depression, and any comorbidity, including urinary tract infections. Pregnant women entered the study from the moment of laboratory and ultrasound confirmation of pregnancy. During the initial examination and subsequent follow-up, women with maternal or fetal complications were excluded. In total, 250 women were not included in the cohort.

Preparation of pregnant women for kidney and collecting system ultrasonography was performed according to the standard protocol. Real-time grayscale ultrasonography was performed using a Samsung HS 40 scanner (South Korea) with a 2–8 MHz convex transducer. Kidney dimensions, parenchymal echogenicity, and the anteroposterior diameters of the renal pelves were documented. Examinations were performed in the first trimester at 10–12 weeks, in the second trimester at 22–24 weeks, and in the third trimester at 34–36 weeks.

Statistical analysis was performed using Statistica 10 software (StatSoft Inc., USA). The data were analyzed using nonparametric methods; qualitative variables are presented as absolute and relative frequencies (percentages). Descriptive statistics for quantitative variables are presented as the median (Me) and interquartile range [lower quartile (LQ) and upper quartile (UQ)]; paired variables were compared using the Wilcoxon and Kruskal-Wallis tests. Differences were considered statistically significant at an error probability of less than 5% ($p<0.05$).

Results. The demographic and clinical characteristics of healthy study participants with singleton first pregnancies are presented in *Table 1.* In 10 cases, the APD of the renal pelvis was unmeasurable in both kidneys throughout pregnancy. The mean APD values of the right and left renal pelves during pregnancy are presented in *Table 2.*

In 12 (40%) cases, the APD of the right renal pelvis increased from the first to the second trimester, in 5 (16.7%) it decreased, and in 13 (43.3%) it remained unchanged. In the left kidneys, the APD of the renal pelvis increased from the first to the second trimester in 10 (33.3%) pregnant women, decreased in 1 (3.3%), and remained unchanged in 19 (63.3%) women.

In the right kidneys, the APD of the renal pelvis increased from the first to the third trimester in 9 (30%) pregnant women, decreased in 4 (13.3%), and remained unchanged in 17 (56.5%). In the left kidneys, the APD of the renal pelvis increased from the first to the third trimester in 16 (53.3%) cases, decreased in 2 (6.7%), and remained unchanged in 12 (40%).

The distribution of renal pelvic APD in the 20 cases in which the pelvis was visualized is presented in *Table 3.* The minimum and maximum APD of the renal pelvis were 5 and 27 mm, respectively. Significant differences in renal pelvic APD were observed only between the first and second trimesters (0.005) and between the first and third trimesters (0.003) in the left kidneys. In the right kidneys, similar differences approached significance: first and second trimesters, p=0.072; first and third trimesters, p=0.075. Differences in renal pelvic APD between the

Table 1

Demographic and clinical characteristics of pregnant women

Demographic parameters	Me [LQ; UQ] (min-max)
Maternal age, years	25.0 [21.0; 27.0] (17.0–36.0)
Husband's age, years	28.0 [25.0; 35.0] (21.0–45.0)
Age at sexual debut, years	18.0 [16.0; 19.0] (14.0–24.0)
Number of sexual partners before pregnancy	3.0 [1.0; 4.0] (1.0–8.0)
Time from sexual debut to pregnancy, years	6.0 [4.0; 10.0] (1.0–19.0)
Height, m	1.7 [1.6; 1.7] (1.5–1.8)
Baseline body weight, kg	60.0 [55.0; 70.0] (46.0–93.0)
Final body weight at delivery, kg	74.5 [67.0; 82.0] (55.0–105.0)
Body weight change during pregnancy, kg	11.5 [10.0; 14.0] (-5.0–21.0)
Body weight gain, %	16.2 [13.3; 21.1] (-6.7–26.9)
Baseline BMI, kg/cm^2	21.7 [19.4; 25.8] (16.4–30.9)
BMI at the end of pregnancy, kg/cm^2	25.9 [24.2; 28.7] (19.7–34.3)
BMI change, %	19.3 [15.4; 26.8] (-6.3–36.8)

Table 2

Median APD values of the right and left renal pelvis

Kidney, trimester	n	Median	LQ	UQ	Minimum	Maximum
Right kidney, first trimester	20	8.0	2.5	11.0	0.0	27.0
Right kidney, second trimester	20	10.0	6.5	15.5	0.0	21.0
Right kidney, third trimester	20	10.0	3.5	17.0	0.0	24.0
Left kidney, first trimester	20	8.0	5.0	13.0	0.0	18.0
Left kidney, second trimester	20	10.5	8.0	14.5	0.0	18.0
Left kidney, third trimester	20	10.0	9.0	16.0	0.0	22.0

Table 3

Anteroposterior diameter of the renal pelvis

Right kidney				Left kidney			
0 mm	<10 mm	11–20 mm	>20 mm	0 mm	<10 mm	11–20 mm	>20 mm
3	8	6	3	–	7	13	–

second and third trimesters were not significant in either kidney.

Discussion. It is generally accepted that dilatation of the upper urinary tract to some extent is present in virtually all pregnant women [5–7, 14–16], and such dilatation should be interpreted as physiological [17], since it is not accompanied by symptoms of renal pain, signs of urinary tract infection, or obstruction by a stone. However, when the above symptoms and signs of upper urinary tract obstruction appear, the dilatation is proposed to be considered pathological and termed hydronephrosis.

At the same time, a number of investigators have shown that low back pain is only weakly associated with dilatation [18–20]. Therefore, there is still no full consensus in the literature on how to define the boundary between physiological and pathological degrees of dilatation. There is no reason to believe that in more than 90% of pregnant women the observed dilatation of the renal pelvis and calyces represents pathological hydronephrosis.

In this regard, W.J. Watson and B.C. Brost [21] proposed considering renal pelvic dilatation of less than 10 mm as physiological. It is also important to understand that during pregnancy the peristalsis of the upper urinary tract and the rate of development of dilatation, as well as the factors significantly contributing to its progression in each individual pregnancy, remain insufficiently studied.

Accordingly, our study was based on the analysis of 30 pregnant women selected from 280 examined women with an "ideal" course of a singleton first pregnancy and strict adherence to the monitoring protocol.

Standardized measurements of the renal pelvis in 60 right and left kidneys revealed absence of visualization in 23 (38.3%) kidneys. Another 15 (25.0%) kidneys had an APD of less than 10 mm, and only 22 (36.7%) kidneys had a renal pelvic APD greater than 10 mm. Moreover, renal pelvic diameters >20 mm in three pregnant women were identified in the first trimester. Thus, a renal pelvic APD greater than 10 mm was observed in 9 (15.0%) right kidneys but in 13 (21.7%) left kidneys, which contradicts the common view that right-sided hydronephrosis is more frequent in pregnant women [4, 5].

Only 40% of right kidneys showed an increase in renal pelvic APD from the first to the second trimester, whereas in left kidneys similar dynamics were observed in 33.3% of cases. Changes in renal pelvic APD from the first to the third trimester showed an increase in 30% of cases on the right but in 53.3% of cases on the left, which also contradicts the published data. It is important to emphasize that changes in left renal pelvic APD were highly significant throughout pregnancy in 20 women with pelvic dilatation, whereas in the right renal pelvis similar changes only approached the level of statistical significance.

Thus, our study shows that consensus on dilatation of the renal collecting system during pregnancy, particularly in the group of healthy primigravid women, has not yet been reached. In a substantial proportion of such pregnant women, there is no dilatation at all during pregnancy; in others, a decrease in dilatation from the first to the second trimester or no change in renal pelvic APD is observed. Moreover, the differences in renal pelvic APD from the second to the third trimester are not significant on either side.

The limitations of our study include the small number of subjects examined (30), the absence of randomization in the study design, and the inability to confirm or refute ultrasound findings by other imaging modalities such as computed tomography. Nevertheless, further studies of this type are needed in both healthy and comorbid pregnant women, as well as in symptomatic hydronephrosis, to enable differentiation between functional and pathological dilatation of the upper urinary tract.

Conclusion. In healthy women with singleton first pregnancies, the renal collecting system may be nonvisualized, enlarged, or reduced during pregnancy. The increase in renal pelvic APD is more pronounced from the first to the second trimester than from the second to the third trimester. Significant changes in renal pelvic APD from the first to the third trimester were observed only in the left kidneys. Differences in renal pelvic size (mm) during pregnancy are, to some extent, arbitrary, as they are not grounded in functional parameters that may ultimately help distinguish physiological from pathological dilatation of the upper urinary tract.

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EARLY EVALUATION OF THE EFFICACY OF RADIOGUIDED SURGERY IN REDUCING THE INCIDENCE OF LYMPHOCELE AND LOWER LIMB LYMPHEDEMA AFTER ROBOT-ASSISTED PROSTATECTOMY WITH PELVIC LYMPH NODE DISSECTION

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Introduction. Robot-assisted radical prostatectomy (RARP) with pelvic lymphadenectomy (PLND) is the «gold standard» for the surgical treatment of prostate cancer with the risk of lymphatic involvement ⩾5% according to predictive nomograms. PLND is associated with the development of lymphatic complications (lymphocele, lymphedema) with a frequency up to 51%.
Aim. To evaluate the effectiveness of intraoperative navigation technique via a gamma probe and lymphotropic tracer (99mTc) during RARP with PLND to prevent the incidence of postoperative lymphatic complications.
Materials and methods. A single-center prospective study conducted between 2024 to 2025. The study included 50 patients with intermediate and high oncological risk according to the D'Amico classification. In the main group (n=23), RARP with PLND were performed with preservation of the lymphatic ducts of the lower limbs (LL). In the control group (n=27) RARP with PLND without LL lymphatic ducts preservation were performed. The frequency of the postoperative lymphatic complications was the primary endpoint, an evaluation of the intraoperative and postoperative complications was the secondary endpoint.
Results. Two patients in the main group developed lymphocele, which subsequently resolved within three months, compared with eight lymphoceles in the control group, one of which required repeat surgery. Lymphedema developed in one patient in the main group, compared with three patients in the control group. Intraoperative and postoperative parameters in the study group were comparable to those in the control group.
Conclusions. The use of radioguided surgery with lymphotropic tracer (99mTc) during RARP with PLND can reduce the risk of complications associated with the operation. The approach described above may be a promising solution to the problem of postoperative lymphatic complications.

Keywords: prostate cancer, complications of pelvic lymphadenectomy, lymphocele, lower limb lymphedema, robot-assisted radical prostatectomy, gamma-probe

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Introduction. Prostate cancer (PCa) is one of the most common malignancies in men. According to global statistics, PCa ranks second in incidence among oncourological diseases and fifth in cancer-specific mortality [1, 2]. In the Russian Federation, the past decade has been characterized by a heterogeneous pattern in PCa incidence and mortality rates. A marked decline in 2020 during the COVID-19 pandemic was associated with a temporary deterioration in the epidemiological situation and restrictive measures [3]. These measures led to reduced healthcare-seeking behavior and, consequently, to a decrease in PCa detection rates. At present, the indicators show an upward trend, driven by optimization of outpatient services, implementation of screening methods, advances in diagnostic technologies, and wider adoption of preventive measures [4]. Despite advances in early diagnosis, surgery remains the gold standard for the treatment of localized and locally advanced PCa [5].

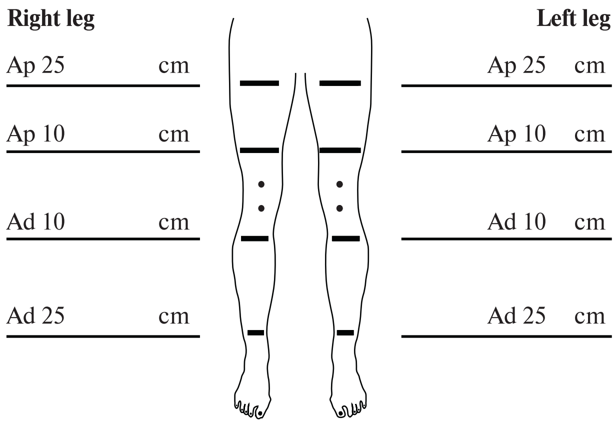
In contemporary urological practice, preference is given to endoscopic video-assisted surgical techniques, in particular robot-assisted radical prostatectomy (RARP). The advantages of RARP include a lower risk of intraoperative and postoperative complications, high therapeutic efficacy, and improved early functional outcomes [6, 7]. Extended pelvic lymph node dissection (ePLND) is often performed during the procedure. According to the Clinical Guidelines of the Ministry of Health of the Russian Federation, ePLND is indicated in patients with a risk of lymphatic invasion of ⩾5% [8]. Despite ongoing debate regarding the oncological significance of ePLND [9, 10], this procedure remains the most reliable method for assessing the status of regional lymph nodes (LNs) and plays a key role in disease staging [11], given the limited sensitivity of currently available imaging modalities, including magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography/computed tomography (PET/CT), for the detection of micrometastases [12].

The increasing incidence of PCa leads to a growing number of patients undergoing radical prostatectomy with pelvic lymph node dissection (PLND). Frequent complications of extended PLND include lymphocele formation and secondary lower limb lymphedema, which develop as a result of impaired regional lymphatic drainage [13]. In view of these possible postoperative consequences, preservation of the lower limb lymphatic collectors is an important issue as a potential strategy for preventing complications of extended PLND. During a search of the PubMed biomedical database, we identified a study aimed at developing a multispectral fluorescence imaging method for differentiating LNs draining the prostate from LNs draining the lower limbs [14]. The main limitation of that study was its preclinical nature, which did not allow reliable extrapolation of the findings to human anatomy and disease progression. An alternative approach to intraoperative guidance is radioguided surgery, based on the use of radionuclides followed by detection of their accumulation with a gamma probe. The most extensively studied and most commonly used radiopharmaceutical is ^{99m}Tc. This technique has high sensitivity for identifying sentinel LNs associated with the primary tumor [15–17]. No studies were found in the literature evaluating the possibility of using radioguided technologies for intraoperative identification of lower limb lymphatic collectors within the PLND field in order to reduce the incidence of postoperative complications.

Aim. To evaluate the efficiency of an intraoperative navigation technique using a gamma probe and a lymphotropic tracer (^{99m}Tc) during RARP and ePLND for reducing the incidence of postoperative lymphatic complications.

Materials and methods. A single-center prospective study was crried put at the Institute of Urology and Human Reproductive Health, Sechenov University, from July 2024 to May 2025. The study included 50 patients divided into two groups: the study group: RARP and ePLND with preservation of lower limb lymphatic collectors (LLLCs) (*n*=23), while in the control group RARP and ePLND without preservation of LLLCs was done (*n*=27). The study was approved by the local ethics committee (No. 30 dated September 29, 2023). Inclusion criterion: patients scheduled for RARP with ePLND with a calculated risk of regional LNs metastases of ⩾5% according to the Memorial Sloan Kettering Cancer Center (MSKCC), Briganti, and Russian Society of Oncourology nomograms. Exclusion criterion: developmental abnormalities of the lower limb lymphatic system identified on lymphoscintigraphy.

Methods for postoperative monitoring of lymphatic complications. To assess lymphocele formation, pelvic ultrasonography was performed on postoperative days 1, 7, and 90. Lower limb status was assessed by measuring circumferences at four points on each leg (*Fig. 1*). For these measurements, the patient was placed in a sitting position with the legs flexed at 90 degrees. The patella served as the anatomical landmark. Measurement of the circumference of the upper half of the lower limb was performed 10 cm above the superior border of the patella (first measurement point) and 15 cm distally from that point (second point). An analogous procedure was performed for the lower half of the lower limb, starting 10 cm below the inferior border of the patella. Leg circumference measurements were recorded in centimeters. The truncated cone formula was used to calculate the volume of the proximal and distal parts of the leg (mL). The estimated lower limb volume was calculated as the sum of these two values.



Note. Ap 25 – measurement of the circumference of the upper limb segment at a distance of 25 cm above the superior border of the patella; Ap 10 – measurement of the circumference of the upper limb segment at a distance of 10 cm above the superior border of the patella; Ad 10 – measurement of the circumference of the lower limb segment at a distance of 10 cm below the inferior border of the patella; Ad 25 – measurement of the circumference of the lower limb segment at a distance of 25 cm below the inferior border of the patella.

Fig. 1. Lower limb measurement scheme

$$V = \frac{h \times (C_1^2 + C_1 \times C_2 + C_2^2)}{12\pi}$$

V, lower limb volume, h, cone height (constant of 15 cm), C1, proximal measurement, C2, distal measurement.

Patients underwent lower limb lymphoscintigraphy with single-photon emission computed tomography/computed tomography (SPECT/CT) of the pelvic organs using a radiopharmaceutical labeled with ^{99m}Tc at a dose of 50 MBq for each leg, administered intradermally (effective dose 0.2+3.3 mSv), on the day before surgery to assess preservation of lymphatic transport function and to exclude lymphatic block and reflux. The injection site was the first interdigital space of the feet. On the day of surgery, 120 minutes before the procedure, the radiopharmaceutical was administered again.

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Surgical technique. All procedures were performed through a transperitoneal approach using the Da Vinci Xi robotic surgical system (Intuitive Surgical, United States). Radioguidance was carried out using a rigid laparoscopic gamma probe (Amplitude Research and Technology Center LLC, Russia) connected to a portable personal computer with Radikal software (Amplitude Research and Technology Center LLC, Russia). The sterile gamma probe was introduced into the abdominal cavity through a 12-mm port located above the right iliac crest. Real-time feedback on ^{99m}Tc activity measurements was provided by the portable personal computer with digital display and acoustic guidance. Background measurements on the transversus abdominis muscle served as the reference. In addition, radioactivity signals from structures located near the lower limb lymphatic collectors, including the ureters and iliac vessels, were measured to assess possible nonspecific uptake of the radioactive signal. Imaging results were considered positive if the activity of the radioactive tracer in the examined tissues exceeded the reference background value by 1.5 times. After verification of the lower limb lymphatic collectors, lymph node dissection was performed with preservation of these structures.

During ePLND, fibrofatty tissue with LNs located between the external and internal iliac vessels was removed from the level of the bifurcation of the common iliac artery to the artery encircling the pubic bone (a branch of the obturator artery). The lateral boundary of the lymph node dissection was the genitofemoral nerve, the medial boundary was the obturator nerve, and the posterior boundary was the obturator muscle. After pelvic lymph node removal, RARP was performed.

Methods of statistical data analysis. Statistical analysis was performed using Microsoft Excel 2021 and MedCalc v20.104 software. Quantitative data are presented as standard descriptive statistics, including mean and standard deviation (M±SD), standard error of the mean (SE), and the 95% confidence interval for the sample mean. Variables with non-normal distribution are presented as median and interquartile range, Me [Q25; Q75]. Qualitative variables are presented as proportions and frequencies (%). Treatment outcomes were assessed during the first three months after surgery.

Comparison of the two groups for quantitative variables was performed using the nonparametric Mann-Whitney U test. Differences between the study groups for qualitative variables were assessed using Pearson's chi-square test. The significance level for hypothesis testing was set at $p<0.005$. Control of the type I error rate in pairwise intergroup comparisons was performed using the Bonferroni correction.

Results. Patient characteristics are presented in *Table 1.* The participants belonged to the intermediate- and high-risk oncological groups according to the D'Amico classification. Clinical stages ranged from T1c to T3b. No significant differences were observed between the study groups. Preoperative measurements of lower limb parameters were statistically comparable between the two groups (*Table 2*).

During surgery, 120 minutes after administration of the radiopharmaceutical, accumulation of the lymphotropic tracer was detected in the fibrofatty tissue located in the region of the external iliac vessels. The median minimum and maximum signals recorded from LNs and lymphatic channels were 240.2 [IQR 45.0; 600.0] and 1135.5 arbitrary gamma probe signal units [IQR 955.75; 1530.25], respectively. The main areas of preservation of lymphatic collectors within the field of ePLND were as follows: the lateral chain of lymphatic channels and LNs located along the lateral surface of the external iliac artery, the medial chain of lymphatic collectors located along the medial surface of the external iliac artery, and the intermediate chain of lymphatic collectors located between the external iliac vessels (*Figs. 2–5*).

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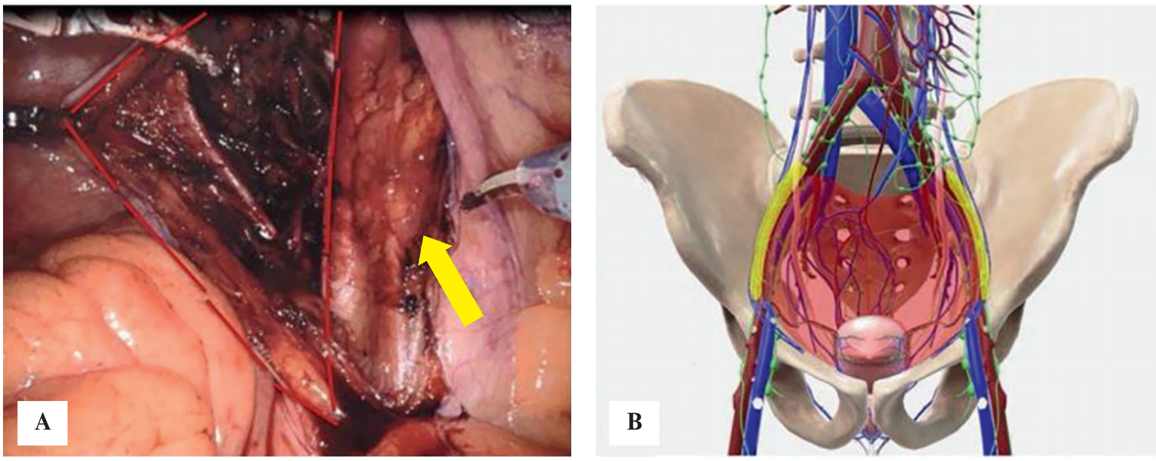
Table 1

Patient characteristics

Variable	Study group (n=23)	Control group (n=27)	*P-value*
Age (years), M [± SD]	64.74 [±8.67]	66.11 [±6.98]	0.6259
BMI, kg/m^2, M [± SD]	27.86 [±4.75]	29.94 [±5.59]	0.6127
Preoperative total PSA level, ng/mL, M [± SD]	21.13 [±28.69]	18.79 [±24.97]	0.2630
Clinical stage, n (%)			
cT1	5 (21.74%)	9 (33.33%)	
cT2	4 (17.39%)	13 (48.15%)	
cT3	14 (60.87%)	5 (18.52%)	
ISUP grade, n (%)			
ISUP 1	0 (0%)	3 (11.11%)	
ISUP 2	3 (13.04%)	9 (33.33%)	
ISUP 3	0 (0%)	5 (18.52%)	
ISUP 4	10 (43.48%)	5 (18.52%)	
ISUP 5	10 (43.48%)	5 (18.52%)	
Number of positive biopsy cores (%), M [± SD]	46.91 [±28.16]	51.30 [±0.3431]	0.3431
Prostate volume on MRI, cm^3, M [± SD]	42.19 [±17.68]	44.60 [±15.74]	0.3205

Note. M, mean; SD, standard deviation; BMI, body mass index; PSA, prostate-specific antigen; n, number of patients; ISUP, International Society of Urological Pathology.



A – intraoperative view, B – schematic representation of the preserved chain. Red marking indicates the area of lymph node dissection, yellow indicates the area of preservation of lower-limb lymphatic collectors.

Fig. 2. Preservation of the lateral chain of lymphatic vessels and lymph nodes in the region of the external iliac vessels

of the external iliac artery, and the intermediate chain of lymphatic collectors located between the external iliac vessels (*Figs. 2–5*).

The operative time was significantly shorter in the study group than in the control group, averaging 106 minutes versus 115 minutes (p=0.0145). The duration of pelvic lymphadenectomy was significantly longer in the control group, averaging 27.5 minutes versus 26 minutes in the study group (p=0.038). Mean blood loss was 100 mL [IQR 100; 150] in the study group and 150 mL [IQR 100; 200] in the control group, with no significant difference (p=0.2083). The mean number of removed LNs in the study and control groups was 9.48 [±5.60] and 10.11 [±6.49], respectively (p=0.8990). According to the pathological examination, metastases in removed LNs were detected in 5 (21.74%) patients in the study group and 3 (11.11%) patients in the control group. The time to urethral catheter removal after RARP averaged 6 days in both subgroups and did not differ statistically. In the postoperative period, lymphocele developed in 2 patients in the study group and in 8 patients in the control group (Clavien-Dindo grade I), one of which required repeat laparoscopic surgery followed by drainage (Clavien-Dindo grade IIIb).

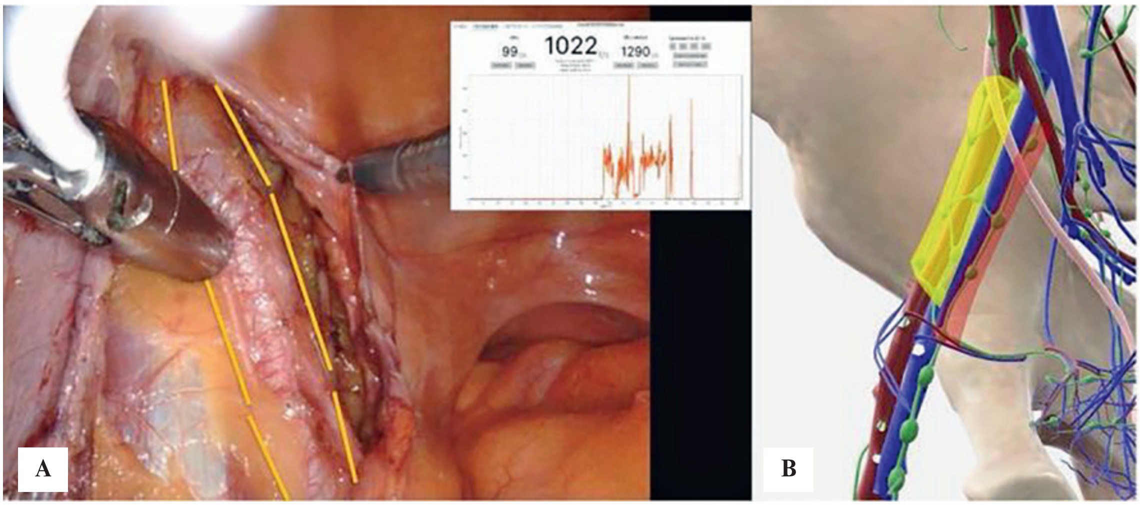
Follow-up was carried out for three months; the median total PSA level in both groups was 0.03 [IQR - 0.01; 0.08]. In addition, secondary lower limb lymphedema developed in 3 (11.1%) patients in the control group, including unilateral lymphedema in 2 patients (7.41%) and bilateral lymphedema in 1 patient (3.7%), compared with 1 patient (4.35%) in the study group. Dynamic assessment of lower limb status at 3 months after surgery demonstrated significant changes in the absolute majority of parameters in the

Table 2

Preoperative measurements of lower limb parameters

Parameter	Main group (n=23)	Control group (n=27)	P value
Circumference, Up RL 25 before surgery, cm, M [± SD]	58.09 [±5.02]	58.28 [±5.43]	0.9922
Circumference, Up LL 25 before surgery, cm, M [± SD]	57.02 [±4.91]	57.90 [±5.67]	0.6058
Circumference, Up RL 10 before surgery, cm, M [± SD]	49.92 [±4.73]	48.79 [±5.04]	0.2350
Circumference, Up LL 10 before surgery, cm, M [± SD]	49.64 [±4.33]	48.53 [±5.10]	0.2466
Circumference, Low RL 10 before surgery, cm, M [± SD]	41.17 [±2.61]	40.42 [±2.93]	0.3755
Circumference, Low LL 10 before surgery, cm, M [± SD]	40.15 [±2.80]	39.73 [±2.66]	0.7111
Circumference, Low RL 25 before surgery, cm, M [± SD]	26.25 [±1.48]	26.27 [±1.75]	0.9766
Circumference, Low LL 25 before surgery, cm, M [± SD]	26.18 [±1.44]	26.21 [±1.85]	0.9687
Upper half volume, RL before surgery, mL, M [± SD]	3513.04 [±619.41]	3461.12 [±692.88]	0.5527
Upper half volume, LL before surgery, mL, M [± SD]	3423.82 [±586.16]	3422.45 [±709.43]	0.7777
Lower half volume, RL before surgery, mL, M [± SD]	1383.10 [±152.80]	1353.27 [±178.76]	0.4895
Lower half volume, LL before surgery, mL, M [± SD]	1337.12 [±163.28]	1321.01 [±170.05]	0.7187
Total volume, RL before surgery, mL, M [± SD]	4896.13 [±757.30]	4814.39 [±842.84]	0.5658
Total volume, LL before surgery, mL, M [± SD]	4760.95 [±729.18]	4743.45 [±856.61]	0.6899

Note. Ap 25 – measurement of the circumference of the upper half of the lower limb at a distance of 25 cm above the upper edge of the patella; PNC – right lower limb; M – mean; SD – standard deviation; LNC – left lower limb; Ap 10 – measurement of the circumference of the upper half of the lower limb at a distance of 10 cm above the upper edge of the patella; Bp 10 – measurement of the circumference of the lower half of the lower limb at a distance of 10 cm below the lower edge of the patella; Bp 25 – measurement of the circumference of the lower half of the lower limb at a distance of 25 cm below the lower edge of the patella; VP – upper half; NP – lower half.



A – intraoperative view, B – schematic representation of the preserved chains. Red marking indicates the area of lymph node dissection, yellow indicates the area of preservation of lower-limb lymphatic collectors.

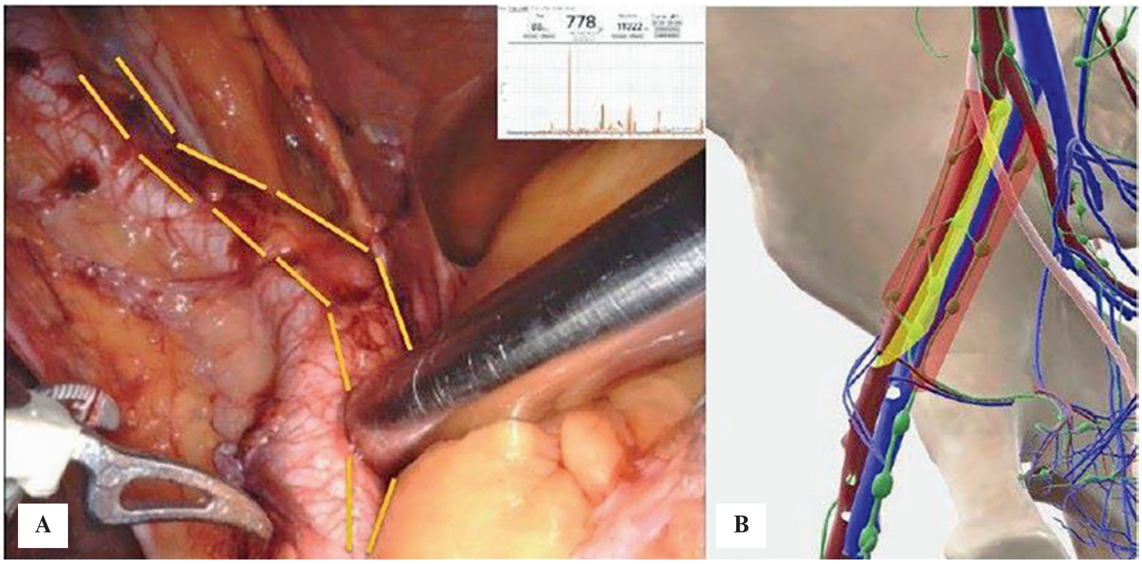
Fig. 3. Preservation of the lateral and medial chains of lymphatic vessels and lymph nodes in the region of the external iliac vessels

control group, further indicating the development of postoperative lower limb lymphostasis (*Table 3*).

Discussion. This is the first reported experience of intraoperative navigation using radioguided surgery and a lymphotropic tracer. According to the preliminary data, the technique may be considered a method for minimizing postoperative lymphatic complications of ePLND.

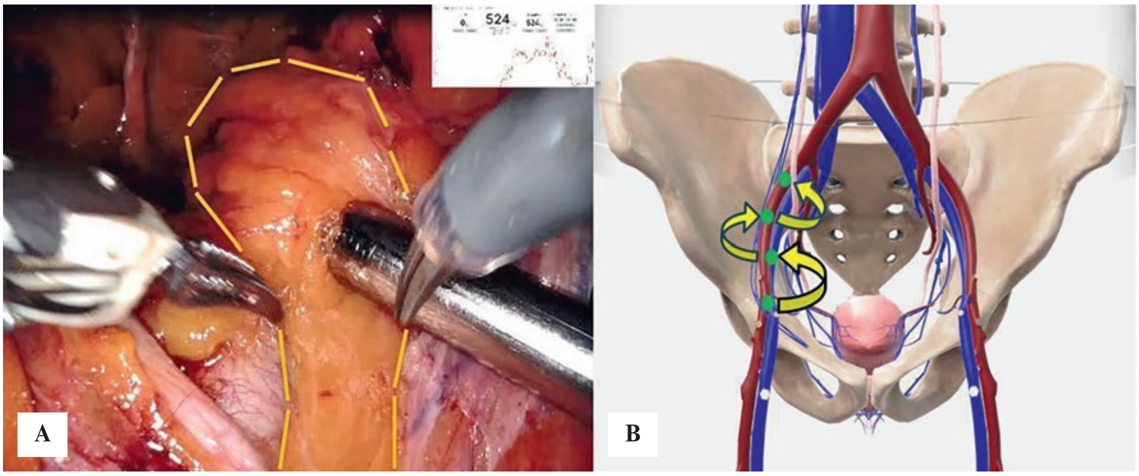
In intragroup pairwise comparisons, almost all postoperative parameters obtained from lower limb measurements differed significantly. ePLND with preservation of lower limb lymphatic collectors required less time (26.0 min [IQR 23.0; 27.0]) compared with ePLND without preservation of lower limb lymphatic collectors (27.0 min [IQR 26.0; 29.0]), which may be explained by preservation of part of the fibrofatty tissue during lymph node dissection; as a result, the surgical procedure took less time overall (106.0 min [IQR 99.0; 113.0] versus 115.0 min [IQR 109.5; 118.5]).

When analyzing the extent of PLND in the study cohort, the median number of removed LNs was 9.5 [range: 1–32]. The question of the minimum number of removed LNs required to ensure adequate control of disease progression remains controversial. In the study by Sayedin et al., the correlation between the number of LNs removed during



A – intraoperative view, B – schematic representation of the preserved chain. Red marking indicates the area of lymph node dissection, yellow indicates the area of preservation of lower-limb lymphatic collectors.

Fig. 4. Preservation of the medial chain of lymphatic vessels and lymph nodes in the region of the external iliac vessels



A – intraoperative view, B – schematic representation of the preserved chain. Red marking indicates the area of lymph node dissection, yellow indicates the area of preservation of lower-limb lymphatic collectors.

Fig. 5. Preservation of the intermediate chain of lymphatic vessels and lymph nodes in the region of the external iliac vessels (spiral variant)

Table 3

Postoperative outcomes at 3 months

	Variable	M [± SD] before surgery	M [± SD] at 3 months after surgery	Change (%) at 3 months	*P*-value
Study group (*n*=23)	Circumference Sup RLL 25	58.09 [±5.02]	58.16 [±5.14]	0.12	0.3083
	Circumference Sup LLL 25	57.02 [±4.91]	57.12 [±4.79]	0.18	0.2604
	Circumference Sup RLL 10	49.92 [±4.73]	50.10 [±4.84]	0.37	0.3229
	Circumference Sup LLL 10	49.64 [±4.33]	49.71 [±4.41]	0.14	0.1573
	Circumference Inf RLL 10	41.17 [±2.61]	41.16 [±2.74]	-0.03	0.2803
	Circumference Inf LLL 10	40.15 [±2.80]	40.32 [±2.86]	0.42	0.0355
	Circumference Inf RLL 25	26.25 [±1.48]	26.38 [±1.59]	0.50	0.1531
	Circumference Inf LLL 25	26.18 [±1.44]	26.27 [±1.52]	0.35	0.4342
	Volume Upper Half RLL	3513.04 [±619.41]	3530.75 [±635.44]	0.50	0.6482
	Volume Upper Half LLL	3423.82 [±586.16]	3434.40 [±584.68]	0.31	0.0885
	Volume Lower Half RLL	1383.10 [±152.80]	1387.95 [±164.06]	0.35	0.9515
	Volume Lower Half LLL	1337.12 [±163.28]	1347.98 [±168.37]	0.81	0.0186
	Volume RLL	4896.13 [±757.30]	4918.70 [±785.69]	0.46	0.6926
	Volume LLL	4760.95 [±729.18]	4782.39 [±735.96]	0.45	0.0285
Control group (*n*=27)	Circumference Sup RLL 25	58.28 [±5.43]	58.79 [±6.11]	0.87	0.0030
	Circumference Sup LLL 25	57.90 [±5.67]	58.50 [±6.42]	1.03	0.0004
	Circumference Sup RLL 10	48.79 [±5.04]	49.09 [±5.38]	0.61	0.1635
	Circumference Sup LLL 10	48.53 [±5.10]	49.20 [±6.28]	1.37	0.0027
	Circumference Inf RLL 10	40.42 [±2.93]	40.52 [±2.99]	0.24	0.1244
	Circumference Inf LLL 10	39.73 [±2.66]	40.08 [±3.00]	0.89	0.0092
	Circumference Inf RLL 25	26.27 [±1.75]	26.39 [±1.72]	0.42	0.0113
	Circumference Inf LLL 25	26.21 [±1.85]	26.33 [±1.90]	0.48	0.0093
	Volume Upper Half RLL	3461.12 [±692.88]	3519.66 [±775.87]	1.69	0.0053
	Volume Upper Half LLL	3422.45 [±709.43]	3515.70 [±867.48]	2.72	<0.0001
	Volume Lower Half RLL	1353.27 [±178.76]	1361.60 [±181.47]	0.62	0.0152
	Volume Lower Half LLL	1321.01 [±170.05]	1341.70 [±192.01]	1.57	0.0023
	Volume RLL	4814.39 [±842.84]	4881.26 [±927.74]	1.39	0.0010
	Volume LLL	4743.45 [±856.61]	4857.40 [± 038.31]	2.40	<0.0001

Note. Sup 25, circumference measurement of the upper half of the lower limb at a distance of 25 cm above the superior border of the patella; RLL, right lower limb; M, mean; SD, standard deviation; LLL, left lower limb; Sup 10, circumference measurement of the upper half of the lower limb at a distance of 10 cm above the superior border of the patella; Inf 10, circumference measurement of the lower half of the lower limb at a distance of 10 cm below the inferior border of the patella; Inf 25, circumference measurement of the lower half of the lower limb at a distance of 25 cm below the inferior border of the patella.

extended PLND and biochemical recurrence-free survival was assessed [18]. According to the results of that analysis, with a median number of removed LNs of 5 [range: 1–33], no correlation was established between the extent of lymph node dissection and recurrence-free survival in the intermediate- and high-risk patient cohorts. These conclusions are supported by a study that included a large-scale analysis of the CaPSURE database with assessment of 5-year recurrence-free survival [19]. In that cohort of 4693 patients, in which the median number of removed LNs was 5.8 [range: 0–71], no significant differences in survival were found either after stratification by risk groups or after dichotomization of the extent of PLND (<9 versus ⩾10 removed LNs). However, it should be taken into account that extending the boundaries of PLND is associated with an increased risk of postoperative complications, particularly lymphatic complications [20]. The results obtained in our study are consistent with this position.

For robot-assisted procedures, the main methods of intraoperative navigation are fluorescence guidance and radioguided surgery. Wawroschek et al. were the first to describe the potential use of ^{99m}Tc nanocolloid during PLND for the detection of lymphatic metastases. In that study, the authors noted limited sensitivity for detecting involved LNs because of variability in lymphatic drainage from the prostate [21]. In the study by Malkewicz et al., the possibilities of radioguidance in combination with single-photon emission computed tomography/computed tomography (SPECT/CT) were evaluated in patients with intermediate- and high-risk PCa who underwent radical prostatectomy with PLND. Of 119 LNs identified preoperatively, 118 were visualized using the gamma probe. Both methods had a sensitivity of 90%, whereas specificity was low at 6.06%. Despite these results, the use of the described methods makes it possible to assess individual lymphatic drainage patterns in the operative field [22].

In the article by Gondoputro et al., the efficiency and safety of a ^{99m}Tc-based prostate-specific membrane antigen tracer were evaluated for improving intraoperative navigation, with an increase in the number of detected involved LNs in 12 high-risk patients. According to the results of that study, sensitivity, specificity, positive predictive value, and negative predictive value were 76%, 69%, 50%, and 88%, respectively [23]. Combined use of intraoperative navigation methods, including radionuclide and fluorescence mapping, makes it possible to achieve a synergistic effect, increasing the probability of visualization of LNs and lymphatic channels and improving the precision of surgical technique [24, 25].

The main limitations of our study are the duration of follow-up and the small sample size. It is important to emphasize that our work is the first study to present results on the use of the lymphotropic tracer ^{99m}Tc for intraoperative preservation of lower limb lymphatic collectors in the field of PLND using a gamma probe. Further continuation of the study is planned with an increased sample size and longer follow-up to assess the dynamics of postoperative lymphatic complications. In addition, evaluation of the efficiency of a combined tracer (^{99m}Tc and indocyanine green) is planned, as well as analysis of oncological outcomes between the two study groups.

Conclusion. The use of robot-assisted radical prostatectomy and extended PLND with intraoperative navigation using a gamma probe and a lymphotropic tracer may reduce the likelihood of postoperative lymphatic complications. It should be noted that further studies are required to confirm the reliability of the obtained results.

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COMPARATIVE ANALYSIS OF THE RESULTS OF IMMUNOHISTOCHEMICAL STUDY OF ANDROGEN RECEPTOR EXPRESSION IN THE EPITHELIAL TISSUE OF THE PROSTATE GLAND IN PATIENTS WITH PROSTATE HYPERPLASIA WITH TESTOSTERONE DEFICIENCY AND NORMAL TESTOSTERONE LEVELS

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Introduction. Benign prostatic hyperplasia (BPH) is a disease characterized by the growth of the periurethral glandular zone of the prostate gland, leading to lower urinary tract obstruction and lower urinary tract symptoms (LUTS).
Objective. To conduct a comparative analysis of the results of an immunohistochemical study of androgen receptor expression in prostate epithelial tissue in patients with BPH with testosterone deficiency and normal testosterone levels.
Materials and methods. We analyzed the results of a morphological examination of resected prostate tissue from 188 men with BPH, divided into two groups: Group I – 71 patients with testosterone deficiency; Group II (control) – 117 patients with testosterone levels above 12.1 nmol/L.
Results. Immunohistochemical examination of prostate tissue samples from patients with Tc levels above reference values revealed a positive reaction for androgen receptors, detected both in the nuclei of glandular secretory cells and in their cytoplasm. In patients with testosterone deficiency, a weak positive reaction for androgen receptors was detected only in the nuclei of glandular secretory cells.
Conclusion. In patients with testosterone deficiency, androgen receptor expression in prostate epithelial tissue samples is reduced compared to patients with Tc levels within the reference range.

Keywords: *prostate hyperplasia, immunohistochemistry, androgen receptor expression, testosterone deficiency, hypogonadism*

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Introduction. Benign prostatic hyperplasia (BPH) is a disease characterized by proliferation of the periurethral glandular zone of the prostate and leading to lower urinary tract obstruction, accompanied by lower urinary tract symptoms (LUTS) [1, 2]. BPH is based on two components, static and dynamic. The first component is related to an increase in prostate volume, which may cause obstructive symptoms as a result of enlargement of the prostate. The dynamic component develops as a result of increased sympathetic tone and ischemia of the smooth muscle fibers of the prostatic stroma, urinary bladder, and posterior urethra, which usually cause irritative symptoms [3, 4].

With age, serum testosterone (T) levels decrease in most men, whereas the frequency and severity of LUTS increase with age [5, 6]. Therefore, age and T level are two interrelated predictors of BPH/LUTS. Testosterone in men has proven direct effects on virtually all lower urinary tract structures, including the vascular endothelium, neurothelium, muscle structures, and urothelium [6, 7]. In addition, bladder blood flow is often reduced in patients with LUTS associated with testosterone deficiency, and reduced bladder blood flow and ischemia caused by aging/testosterone deficiency lead to functional and anatomical changes [8–10]. Epithelial cells are no exception, as many of their characteristics change in testosterone deficiency. In our previous studies, we found that epithelial tissue of the prostate has reduced functional activity in hypogonadal patients [11, 12]. In addition, testosterone deficiency is associated with predominance of epithelial atrophy, which leads to involution of the receptor compartment targeted by drug therapy for BPH [9, 11].

According to Russian, European, and American clinical guidelines, α1-adrenoceptor blockers are the first-line medical therapy for patients with moderate to severe LUTS. In testosterone deficiency, the efficacy of α1-adrenoceptor blocker therapy has been shown to decrease; this may be due to reduced expression of androgen receptors in the epithelial tissue of the prostate [11].

The study of androgen receptor expression in epithelial cells in BPH in hypogonadal and eugonadal men is of particular interest, and this work is devoted to that issue.

Aim. To perform a comparative analysis of the results of immunohistochemical assessment of androgen receptor expression in the epithelial tissue of the prostate in patients with BPH and testosterone deficiency versus those with normal testosterone levels.

Materials and methods. The results of immunohistochemical examination of prostatic tissue from 188 men with BPH who underwent transurethral resection were analyzed. The patients were divided into two groups: group 1 included 71 patients with testosterone deficiency, and group 2 (control group) included 117 patients with testosterone levels above 12.1 nmol/L.

Immunohistochemical analysis was performed on paraffin sections using the Ventana BenchMark XT immunostainer. Rabbit monoclonal antibodies against androgen receptors (clone SP107, Cell Marque, USA) were used as primary antibodies. The ultraView Universal DAB Detection Kit (Ventana, USA) was used as the detection system. The areas of prostatic glands and interstitial tissue were measured using the VideoTest 4.0 Morphology software (St. Petersburg); the area of each field of view at a microscope magnification of ×400 (objective ×40, eyepiece ×10) was 96,238 μm2.

The results of immunohistochemical analysis for nuclear expression of the studied antigens were assessed by calculating the histoscore using the formula $Hs=\sum P \times I$, where I is staining intensity and P is the percentage of stained cells. For cytoplasmic and membranous antigen expression, morphometric analysis of immunohistochemical slides was performed using the medical microvisor digital image analysis system μVizo-103.

For subsequent statistical analysis, the obtained results were categorized by expression level as follows: 1 for weak, 2 for moderate, and 3 for strong expression. The study results were processed using Microsoft Excel spreadsheets from the Microsoft Office 2007 software package. Statistical data processing was performed using the STATISTICA 6.1 statistical software package (StatSoft Inc., USA).

The study was carried out within the framework of the dissertation project ("Characteristics of benign prostatic hyperplasia and its treatment in testosterone deficiency"), approved by the Local Independent Ethics Committee of Rostov State Medical University, Ministry of Health of Russia, No. 16/21 dated October 21, 2021. The study received no sponsorship support.

Results. In patients with testosterone deficiency, morphological examination of resected prostatic tissue showed that prostatic hyperplasia had a diffuse stromal pattern combined with cystic deformation of the acini, with flattened, non-secretory epithelium against a background of basal cell hyperplasia. In patients with normal testosterone levels, the pattern of hyperplasia was glandular (epithelial) in all patients, and the acinar epithelial cells were tall columnar cells with signs of active secretion.

Immunohistochemical assessment of androgen receptor expression in prostatic tissue samples from patients with testosterone deficiency showed weak, focal receptor expression, predominantly with an apical cytoplasmic and membranous pattern (*Fig. 1*).

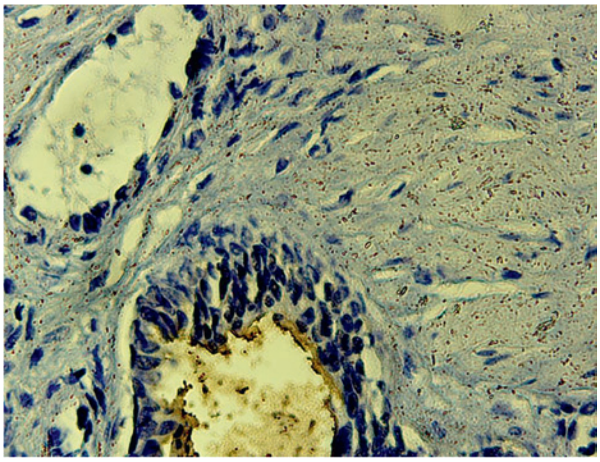

Fig. 1. Immunohistochemical assessment of androgen receptor expression in Group I patients. Markedly reduced expression

Quantitative immunohistochemical analysis of epithelial tissue samples from the prostate in patients of group 1 demonstrated a weak positive reaction for androgen receptors in the nuclei of glandular secretory cells, and the mean number of stained nuclei was significantly reduced and amounted to 22.7±3.7% (p<0.01). In group 2, expression was diffuse, strong, and involved both nuclear and cytoplasmic patterns (*Fig. 2*).

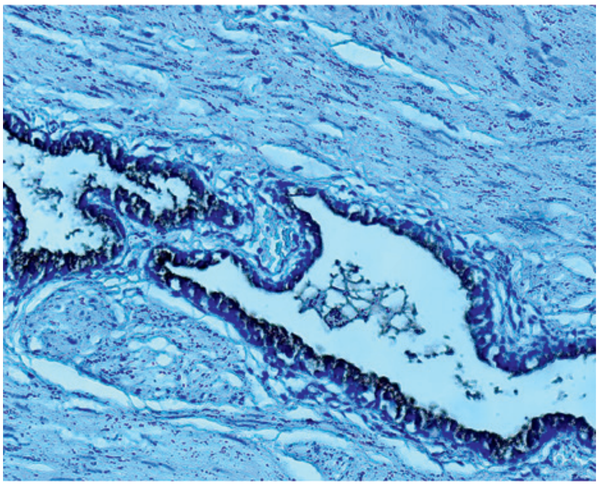

Fig. 2. Immunohistochemical assessment of androgen receptor expression in Group II patients. Moderate expression

Quantitative immunohistochemical analysis of samples from patients in group 2 demonstrated a strong positive reaction for androgen receptors in the nuclei of glandular secretory cells, and the mean number of stained nuclei was significantly higher than that in the immunohistochemical samples from patients in group 1, amounting to 84.7±5.7% (p<0.01) (*Fig. 3*).

Discussion. Testosterone deficiency is a condition that substantially aggravates the clinical course of LUTS/BPH by affecting the morphometric parameters of all prostatic structures [13]. To date, extensive scientific and clinical experience has been accumulated, and fundamental studies have confirmed that correlations exist between testosterone deficiency and LUTS/BPH. It has been demonstrated that hypogonadal men have more severe and pronounced LUTS compared with eugonadal patients [14].

In our study, morphological examination of prostatic tissue samples from patients with testosterone deficiency revealed a diffuse stromal pattern of prostatic hyperplasia combined with cystic deformation of the acini, flattened non-secretory epithelium, and a background of basal cell

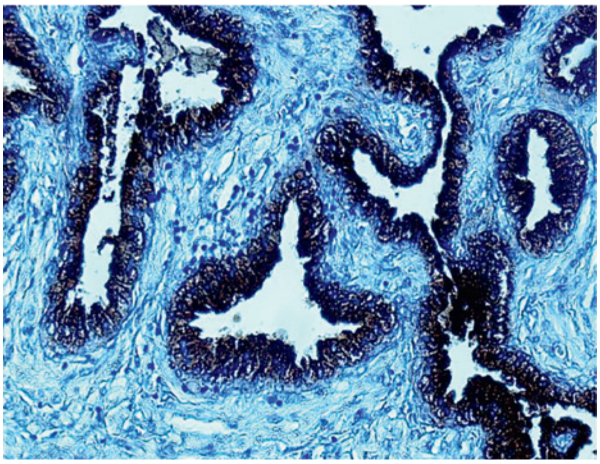

Fig. 3. Immunohistochemical assessment of androgen receptor expression in Group II patients. Marked expression

hyperplasia. In patients with normal testosterone levels, morphological examination of resected prostatic tissue samples showed a glandular (epithelial) pattern of hyperplasia in all cases, and the acinar epithelial cells were tall columnar cells with signs of active secretion.

Immunohistochemical examination of prostatic tissue samples from patients with testosterone levels above the reference range demonstrated a positive reaction for androgen receptors, detected both in the nuclei of glandular secretory cells and in the cytoplasm, whereas in patients with testosterone deficiency a weak positive reaction for androgen receptors was observed, detected only in the nuclei of glandular secretory cells.

A decrease in androgen receptor expression in the epithelial tissue of the prostate is one of the leading causes of reduced efficacy of α1-adrenoceptor blockers in patients with BPH associated with testosterone deficiency.

Conclusion. Thus, in patients with testosterone deficiency, androgen receptor expression in epithelial tissue samples of the prostate is reduced compared with patients whose testosterone levels are within the normal reference range.

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RESULTS OF THE FIRST MULTICENTER STUDY ASSESSING THE EFFICIENCY OF A TISSUE SENSOR DURING THULIUM FIBER LASER LITHOTRIPSY

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Introduction. Currently, the main surgical approach for urinary stone removal is minimally invasive endoscopic procedures. Various laser systems compatible with most modern instruments are used for stone disintegration. Due to high efficacy and minimal fragment retropulsion during fragmentation, the domestic thulium fiber laser has become a serious alternative to the conventional holmium laser. At the same time, the safety profile of thulium fiber lithotripsy remains debatable because of the potential risk of irrigation fluid heating and damage to surrounding tissues during fragmentation. Implementation of a "Tissue Sensor" (TS) capable of differentiating stone from mucosa during lithotripsy allows automatic cessation of laser emission to prevent injury to the organ wall.

Aim. To assess efficiency and improve the safety of lithotripsy using a new-generation thulium fiber laser with the tissue sensor function activated.

Materials and methods. The study included 70 patients from three medical centers aged 25 to 73 years with 101 ureteral and renal stones. Ureteroscopy with laser lithotripsy was performed in 23 patients, retrograde intrarenal surgery in 30, and percutaneous nephrolithotomy in 17. Mean stone volume was 0,7±0,4 cm3; stone density was 1080±370 HU. Various thulium fiber laser (TFL) settings were used for stone disintegration (dusting, fragmentation, popcorning). In addition to the standard rectangular pulse (Standard), different types of pulse modulation were used: minimal retropulsion modes (MRP); fine dusting (FinePulse); and fragmentation as a "packet" of pulses (UltraPulse). Energy and frequency ranges were 0,2–1,5 J and 5–40 Hz, respectively, for Standard, MRP, and FinePulse. For UltraPulse energies of 3–30 J and frequencies of 1–4 Hz were used. In all patients, laser lithotripsy was performed with the "Tissue Sensor" function enabled. Safety, based on the nature of mucosal impact in the organ where fragmentation was performed, was assessed using the Traxer–Sierra scale from 0 to 5. Early postoperative complications were recorded and graded using the modified Clavien–Dindo classification.

Results. The mean operative time was 48±28 minutes; laser time 16±13 minutes; pedal time 7 ± 6 minutes; laser emission time 5±4 minutes. The TS efficiency coefficient, defined as the ratio of emission time to pedal time, was 65%, reflecting frequent sensor activation to prevent injury to surrounding tissues. The complete stone clearance rate was 98%. In the vast majority of cases (96%), no complications were observed. According to questionnaires, operating urologists reported that TS function did not affect procedure duration while helping avoid soft-tissue injury in most cases. No severe thermal injuries on the Traxer–Sierra scale were recorded (no injury in 46% of cases; grade I injury in 47%).

Conclusion. A tissue type recognition system (Tissue Sensor) improves the safety of lithotripsy by reducing unintended mucosal injury and preventing an increase in irrigation fluid temperature while maintaining high stone disintegration efficacy.

Keywords: *thulium fiber laser, laser lithotripsy, tissue sensor*

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Introduction. Minimally invasive endoscopic surgery remains the main method for removing urinary tract stones. Among the various methods of intracorporeal lithotripsy, laser lithotripsy has become established as the "gold standard" because of its compatibility with different types of miniaturized instruments, including rigid, semirigid, and flexible endoscopes, which allows the procedure to be adapted to minimally invasive access [1].

In recent years, the thulium fiber laser (TFL, Tm:Fiber) has emerged as a promising alternative to the conventional holmium laser (Ho:YAG, holmium:yttrium-aluminum-garnet). The high water absorption coefficient of TFL radiation provides effective stone fragmentation, whereas minimal retropulsion reduces the risk of stone migration during surgery [1-4].

Despite numerous studies demonstrating the safety of TFL use [5, 6], scientific debate continues regarding fluid heating during stone fragmentation, which may hypothetically lead to hyperthermia of the surrounding tissues. In addition, during lithotripsy there is a potential risk of accidental injury to the mucosa of the urinary tract due, for example, to stone migration, perforation through the stone, or poor endoscopic visibility [7, 8]. Thermal injury is particularly undesirable during ureteral stone fragmentation, as it increases the risk of stricture formation or perforation, especially when high-energy settings are used [7, 9]. These risks are further aggravated when procedures are performed by urologists with limited experience: novice operators demonstrate a higher complication rate during complex retrograde intrarenal procedures [10, 11].

To address these problems, real-time tissue recognition systems integrated into laser platforms are being actively developed. Such systems would make it possible to automatically differentiate between stone material and mucosal tissue during laser emission and thereby control energy delivery, particularly when the beam is directed toward the mucosa or other soft tissue [12, 13]. At present, systems with automatic detection of urinary stones in front of the laser fiber tip based on collection of fluorescence signals from the stone are under development [12-14]. However, no commercially available implementations of these systems currently exist.

A significant achievement of the new-generation отечественных TFL systems manufactured by VPG Laserone (Urolase+, Urolase+ Premium, Urolase Max) is the “tissue sensor” function. This system analyzes the optical signal reflected from the target and transmitted through the laser fiber to determine whether the laser is directed at a stone or at soft tissue. If no stone is detected, the Tissue Sensor automatically interrupts laser emission, thereby reducing the risk of thermal injury and limiting heating of the irrigation fluid.

Aim. To evaluate the efficiency of lithotripsy and improve its safety using a new-generation TFL with the Tissue Sensor function activated.

Materials and methods. This prospective clinical study, approved by the Ethics Committee, was carried out at three medical centers starting in February 2024. The study included 70 patients aged 25 to 73 years who were diagnosed with a total of 101 ureteral and renal stones. Twenty-three patients underwent retrograde ureteroscopy, 30 underwent retrograde intrarenal surgery, and 17 underwent percutaneous nephrolithotomy.

All study participants underwent comprehensive clinical and laboratory evaluation, including contrast-enhanced multislice computed tomography to determine stone size and density. Stone volume was calculated from linear dimensions using the ellipsoid volume formula: $4/3 \times \pi \times$ (radius length)/2 × (radius width)/2 × (radius depth)/2. The results of the analysis of demographic data and stone characteristics are presented in Table 1.

The inclusion criterion was the presence of symptomatic renal or ureteral stones in patients who were candidates for percutaneous or retrograde endoscopic surgery. Exclusion criteria included systemic diseases that could impair wound healing or represent a contraindication to surgery, as well as concomitant inflammatory changes in the genitourinary organs.

All procedures were performed by urologists with more than two years of lithotripsy experience. Ureteral stones were treated by ureteroscopy using semirigid ureteroscopes (Olympus, Karl Storz, Richard Wolf) with a diameter of 7-9 F. Laser energy was delivered through laser fibers with core diameters of 200 and 365 μm. Renal stones were treated by either percutaneous nephrolithotomy (PNL) or retrograde intrarenal surgery. PNL was performed using rigid mini-nephroscopes, 7.5-19.5 F, from Karl Storz and Olympus. Fibers with diameters of 365 or 550 μm were used. Retrograde intrarenal surgery was performed using single-use flexible ureterorenoscopes, 8.7-9.2 F, from Innovex, Karl Storz, Pusen, and Boston Scientific, and 150/200 μm fibers were used to deliver laser energy to the stones. The choice of procedure depended on stone size, stone location, and the risk of infectious-inflammatory complications or bleeding risk.

Within the study, different TFL settings and stone treatment techniques, dusting, fragmentation, and popcorning, were used depending on the clinical situation and the surgeon’s preference. In addition to the standard rectangular pulse (Standard) typical of TFL, the latest-generation Urolase+ Premium and Urolase Max systems allow selection of a modulated pulse shape, minimal retropulsion modes (MRP and FinePulse), or a “burst train” (UltraPulse) for fragmentation lithotripsy. Energy and frequency ranges were 0.2-1.5 J and 5-40 Hz, respectively, for the Standard, MRP, and FinePulse pulse modes. UltraPulse was characterized by energy settings of 3-30 J and a frequency of 1-4 Hz. In this mode, the high energy setting reflects not a single pulse, but the sum of all subpulses within the pulse train [15, 16]. In all procedures, the

Table 1.

Preoperative patient characteristics: demographic data and stone characteristics

Parameter	Value
Total number of patients	70
Men, n (%)	49 (70%)
Women, n (%)	21 (30%)
Age, years	53±13 (25–73)
Stone volume, cm³	0.7±0.4 (0.06-5.6)
Stone density, Hounsfield units	1080±370 (400–1800)

"high" peak power setting was selected where peak power adjustment was available for the chosen pulse mode.

All patients underwent laser lithotripsy using the Urolase+ Premium thulium fiber laser (VPG Laserone, Russia) with the active innovative Tissue Sensor function. It allows to "recognize" the object in front of the fiber tip, tissue or stone, and to control laser energy delivery: when the fiber is directed toward soft mucosal tissue, laser emission is automatically interrupted. Before stone fragmentation, Tissue Sensor must be calibrated by collecting optical signals from soft tissue, the mucosa of the target organ, and from the stone.

A key feature of the emission control system is the ability to adapt sensitivity parameters depending on the stage and type of lithotripsy. For the main stone fragmentation stage, the default setting is Medium mode. This mode clearly differentiates tissue from stone and is considered optimal for lithotripsy under conditions of normal visibility and adequate irrigation outflow. When non-contact lithotripsy is used, standard sensitivity settings may reduce efficiency because of frequent interruptions of laser emission. In such cases, Hard mode is recommended: it increases sensitivity and minimizes the frequency of shutoffs, thereby improving stone ablation efficiency. Under conditions of limited endoscopic visibility and poor irrigation outflow, Soft mode is recommended; in contrast, this mode reduces system sensitivity. This makes it possible to maintain a balance between safety and efficacy while minimizing intraoperative risk in challenging anatomical conditions.

The following parameters were recorded during surgery: total duration, calculated from the beginning of the endoscopic procedure, excluding anesthesia induction, to its completion, including the time required for drainage by ureteral catheter, external drainage, or stent placement; and laser procedure time, defined from insertion of the fiber instrument to its removal from the body. In addition, because Tissue Sensor blocks laser pulses when the fiber is not directed at a stone, the time of laser emission actually directed at stone fragmentation and the pedal press time were assessed separately. The most informative parameter for evaluation of the Tissue Sensor is the efficiency coefficient, defined as the ratio of emission time to pedal press time. This coefficient shows the percentage of instances in which Tissue Sensor generated a permissive signal for laser emission; the remaining percentage reflects inhibition by the sensor and, consequently, absence of laser emission. Mean laser power, total laser energy delivered, and ablation efficiency, that is, the energy required to ablate a unit volume of stone material, were also assessed. At follow-up examination performed 1-8 weeks after lithotripsy, the stone-free rate (SFR) was determined.

Based on several questionnaires, the operating urologist assessed the effect of the Tissue Sensor on the efficiency of laser lithotripsy using a 4-point scale: 1, the system reduces operative time; 2, the Tissue Sensor has no effect on operative time; 3, the Tissue Sensor slightly increases operative time; 4, the system substantially increases operative time. The degree of safety improvement achieved by using the object recognition system during lithotripsy was also assessed on a 4-point scale: 1, the system prevents all soft tissue injuries; 2, the Tissue Sensor helps avoid soft tissue injury in most cases; 3, the Tissue Sensor prevents injury in some cases; 4, the system does not prevent injury.

According to the nature of the impact on the ureteral mucosa, safety was assessed using the Traxer-Sierra scale from 0 to 5: grade 0 corresponded to the absence of any injury, grade 1 to fewer than five minor mucosal injuries, grade 2 to fewer than five major injuries, grade 3 to more than five minor injuries, grade 4 to more than five major injuries, and grade 5 to extensive major injury involving the entire mucosal surface [17]. Early postoperative complications were recorded and graded according to the modified Clavien-Dindo classification [18].

Automated statistical analysis of the obtained data was performed using Statistica® and the Microsoft Excel® software package.

Results. During laser lithotripsy, stones were either completely disintegrated, resulting in spontaneous passage of sand-like fragments through the urinary tract, or fragmented to a size allowing extraction with a basket or stone extractor, or washed out through a percutaneous or ureteral access sheath.

The study results and intraoperative and postoperative complications are presented in Table 2. During the main phase of stone fragmentation in the kidney and bladder, the Medium Tissue Sensor mode was used predominantly. In the kidney, during the popcorning stage, when the fiber instrument was positioned at a distance and the stones were not in contact with the fiber tip, the Hard mode was activated. In ureteral stone surgery, the Soft mode was used predominantly, particularly for impacted stones and in cases of poor endoscopic visibility associated with inadequate outflow.

The safety of procedures performed with the Tissue Sensor was analyzed on the basis of several indicators. Laser-induced injury to the mucosal wall was assessed using the Traxer-Sierra scale [17]; examples of thermal injuries observed during the study are shown in Figures 1 and 2. No visible injury was observed in 46% of cases (n=32), whereas grade 1 injury was recorded in 47% (n=33) (Table 2, *Fig. 1*), and grade 2 injury was identified in 7% of cases (n=5) (*Fig. 2*). Subjective assessment by the urologists, expressed as the safety score according to the operating urologist, confirmed improved safety with the use of the Tissue Sensor system: in 46% of cases (n=32), there was no visible mucosal injury, corresponding to score 1 on the questionnaire; in 51% (n=36), minor injuries were recorded, corresponding to score 2; and in 3% (n=2), score 3 was assigned.

Complications analyzed according to the Clavien-Dindo classification [18] were relatively infrequent: grade I and II complications occurred in two cases (3%), and one grade IIIa complication (1%) was identified. However, this event is unlikely to have been related to the function of the Tissue Sensor, since only minor thermal injury in the form of small coagulation spots was observed during that procedure. In the remaining 67 cases (96%), no complications were recorded.

According to the urologists, use of the Tissue Sensor had no significant effect on lithotripsy duration in 61% of cases (n=43). An increase in operative time was noted in 30% (n=21), whereas a reduction was reported in 9% (n=6).

Discussion. The findings of this study confirm the relevance and clinical utility of the Tissue Sensor system, which identifies the type of object in front of the distal tip of the fiber instrument during laser lithotripsy and controls the delivery of laser pulses.

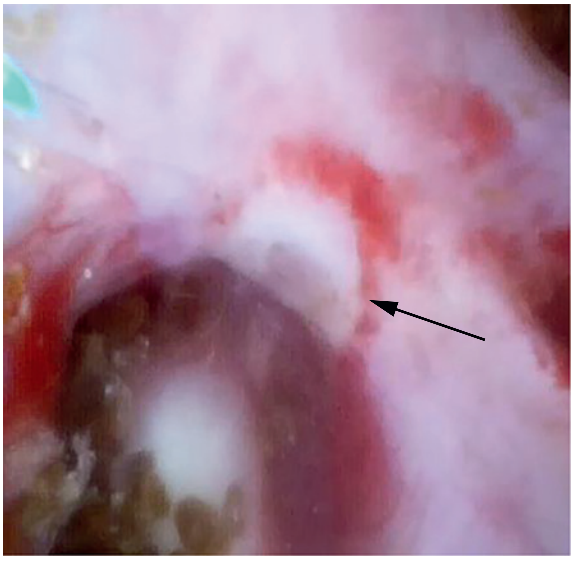

Fig. 1. Endoscopic view of grade 1 thermal urothelial injury according to the Traxer-Sierra scale.

Fig. 2. Endoscopic view of grade 2 thermal urothelial injury according to the Traxer-Sierra scale.

It should be noted that the concept of creating systems capable of differentiating biological tissues during surgical manipulation has existed for quite a long time [19]. The use of laser platforms has made such ideas feasible because of the possibility of applying optical methods for tissue identification, including absorption spectroscopy, diffuse reflectance spectroscopy, fluorescence, and related techniques [12-14, 20, 21]. The advantage of the Tissue Sensor lies in its ability to function in real time, while requiring no additional instruments or devices, since the optical signal is collected through the surgical fiber itself and no additional wavelength source is required.

In modern endourology, laser lithotripsy has become the "gold standard" for minimally invasive stone removal

Table 2

Research results, intra- and postoperative complications

Parameter		Value
Laser emission time, min		5±4 (0.1-30)
Total laser energy delivered, kJ		8.3±4.7 (0.03-58)
Pedal press time, min		7±6 (0.1-33)
Laser procedure time, min		16±13 (2-63)
Total duration of procedure, min		48±28 (10-120)
SFR, %		98
Tissue Sensor efficiency coefficient, %		65
Ablation efficiency, J/mm³		18±15 (0.23-118)
Mean laser power, W		16±8 (4-40)
Early postoperative complications according to the Clavien-Dindo classification	No complications	67 (96%)
	Grade I-II	2 (3%)
	Grade IIIa	1 (1%)
	Grade >IIIa	0 (0%)
Efficiency assessment according to the operating urologist	Grade 1	6 (9%)
	Grade 2	43 (61%)
	Grade 3	21 (30%)
	Grade 4	0 (0%)
Safety assessment according to the operating urologist	Grade 1	32 (46%)
	Grade 2	36 (51%)
	Grade 3	2 (3%)
	Grade 4	0 (0%)
Assessment of thermal injury according to the Traxer-Sierra scale	Grade 0	32 (46%)
	Grade 1	33 (47%)
	Grade 2	5 (7%)
	Grade >2	0 (0%)

because of its efficiency. Laser systems currently used in urology differ in laser type (Ho:YAG, Tm:YAG, Tm:Fiber), maximum average and pulse power, number of dedicated pulse modes, and other characteristics. Recent advances in laser technology in endourology have been characterized by increased energy and power parameters compared with previous-generation systems [22, 23]. A recent breakthrough has been achieved through the introduction of intelligent tissue differentiation technology into TFL systems. The incorporation of this functionality into laser platforms makes it possible to perform lithotripsy more effectively by enabling the use of higher power and pulse energy settings while reducing the risk of serious thermal injury and perforation.

The Tissue Sensor function may be of particular interest for less experienced and novice urologists, as it may allow them to perform laser stone surgery with lower risk [24]. Moreover, this clinical study demonstrated that the Tissue Sensor provides tangible advantages during lithotripsy in complex anatomical situations. For example, in cases of narrow or tortuous ureters with impaired irrigation outflow, which often results in poor endoscopic visibility and makes accurate laser targeting more difficult, urologists in routine practice often interrupt laser emission in order to irrigate the operative field and are forced to proceed with increased caution to avoid tissue injury. However, with the Tissue Sensor activated, operators were able to achieve effective stone fragmentation and dusting even under conditions of poor visibility, while leaving the mucosa intact or causing only minimal collateral damage, such as isolated grade 1 mucosal injuries.

The study findings indicate that the Tissue Sensor is of greatest interest during ureteral procedures or in anatomically vulnerable areas. A small number of minor injuries, in the form of coagulation spots, were recorded. This can be explained by the use of non-contact ablation, popcorning, for which the Hard mode was activated. However, these injuries were not clinically significant, as they were not associated with severe complications.

In the present study, laser procedure time was shorter than that reported in generally accepted standards of lithotripsy using previous-generation thulium fiber lasers [25-27] and Ho:YAG lasers [28-30]. Comparison of the ablation efficiency for ureteral and renal stones in the present study with published data showed that ablation efficiency with the Tissue Sensor was higher than the corresponding values reported for previous-generation thulium fiber lasers and for Ho:YAG lasers [22, 28, 29]. However, no superiority in stone ablation efficiency was observed compared with data for new-generation thulium fiber lasers without the Tissue Sensor [15, 27], which is most likely explained by the higher power characteristics of the latest thulium fiber laser platforms compared with other laser systems.

Of particular interest is the use of the Tissue Sensor during retrograde intrarenal surgery, a procedure that requires a high level of technical skill and substantial experience on the part of the urologist [10]. An additional challenge is the unpredictable movement of the fiber instrument within the renal collecting system caused by the patient's respiration. When the tissue recognition system was activated, laser emission was automatically interrupted whenever the fiber tip deviated from the stone toward adjacent tissue. This safety function allowed continuous pedal activation without interruption, thereby enabling effective stone treatment while minimizing thermal injury to the renal mucosa and shortening the procedure.

It is important to emphasize that although the system prevents most tissue injuries, it does not eliminate them completely. Residual mucosal injury usually occurs because of tangential laser impacts near the stone edge, where there is partial overlap between the laser pulse and the tissue, or when the sensor is used in the increased-sensitivity Hard mode. It should also be emphasized that this is not comparable to the extent of injury that may be observed during conventional lithotripsy [17]. In the present study, the efficiency of the tissue differentiation function did not depend on laser settings, because its algorithm controls each pulse, or pulse train, according to the target at which the fiber is directed. In addition, by interrupting "non-productive" pulses, for example those not directed at the stone, the system reduces the total delivered energy. As a result, heating of the irrigation fluid is also reduced, which further contributes to minimization of thermal risk during prolonged laser activation.

Conclusion. This clinical study demonstrates that the tissue recognition system, Tissue Sensor, improves the safety of lithotripsy by reducing unintended mucosal injury and preventing excessive heating of the irrigation fluid. This is achieved through automatic deactivation of laser emission in situations where: 1) the laser fiber passes through the stone during ablation, 2) irrigation conditions are suboptimal and endoscopic visibility is poor, 3) retrograde intrarenal surgery is performed in the presence of respiratory motion, or 4) stone fragments split during fragmentation. By stopping non-target laser activation, that is, activation not directed at the stone, the system prevents accidental thermal injury without requiring intervention by the urologist.

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EFFECTIVENESS OF URETHROPLASTY IN STRICTURES AND DISTRACTION DEFECTS OF THE MEMBRANOUS URETHRA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective. To evaluate the outcomes of urethroplasty for strictures and distraction defects of the membranous urethra through a systematic review and meta-analysis, and to supplement these findings with a neural network analysis to identify key predictors of success.
Materials and methods. Ten original studies (totaling 930 patients) meeting criteria were included. The primary outcome was defined as the absence of restenosis, confirmed by urethrography/cystoscopy. Proportions were meta-analyzed using logit transformation and a random-effects model (for I^2 >50%). Kaplan–Meier survival analysis was performed for overall and subgroup (traumatic vs. radiation-induced strictures) recurrence-free survival. An experimental neural network model (three hidden layers with ReLU activation) was developed using inputs such as stricture length, etiology, and history of prior interventions to predict success probability.
Results. The overall success rate was 88.3% (95% CI 85–91%). Subgroup analysis revealed that traumatic strictures achieved success rates of 90–95%, while radiation-induced strictures had lower rates (70–80%, p=0.03). Kaplan–Meier curves showed 5-year recurrence-free survival of 87% for traumatic and 70% for radiation-induced cases. The neural network confirmed that stricture length and previous interventions are the most critical predictors of failure, with age and comorbidities playing a secondary role.
Conclusions. Anastomotic urethroplasty is a highly effective treatment for membranous urethral strictures, particularly in traumatic cases. In radiation-induced strictures, the risk of restenosis and complications is higher, necessitating specialized management and close follow-up during the first 1–2 years post-surgery. Neural network analysis provides valuable personalized outcome predictions that can help optimize treatment strategies.

Keywords: urethral stricture, membranous urethra, pelvic fracture urethral distraction defect, urethroplasty, anastomotic urethroplasty, systematic review, meta-analysis

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Introduction. Strictures of the posterior (membranous) urethra in men are a severe condition that often develops as a result of pelvic trauma, the so-called pelvic fracture urethral distraction defects, or after radiation therapy to the pelvic organs [1]. These lesions are characterized by cicatricial narrowing or complete disruption of the urethra in the membranous segment, leading to urethral obstruction, chronic urinary retention, and a marked reduction in patients' quality of life. Treatment of such strictures is particularly challenging because of their proximal location, close to the sphincter and prostate, impaired tissue vascularization, especially after irradiation, and associated injuries [2, 3].

The "gold standard" for the treatment of such urethral strictures is open urethroplasty, that is, surgical restoration of the urethral lumen by excision of the scarred segment and approximation of the healthy ends, anastomosis, or with the use of reconstructive materials, such as a bladder flap, buccal mucosa, and others [4]. According to data from specialized centers, primary anastomotic urethroplasty achieves success rates of up to 90-95% [4]. Nevertheless, outcomes may vary depending on stricture length, etiology, and technical aspects of the procedure. Thus, in radiation-induced strictures, urethral tissues are affected by fibrosis, which reduces the likelihood of satisfactory anastomotic healing and increases the risk of urinary incontinence [3]. In extensive defects greater than 3-4 cm, a simple end-to-end anastomosis may be impossible without excessive tension; in such cases, more complex approaches are required, including combined approaches, Webster maneuvers with partial pubectomy [1, 5], or the use of buccal mucosal grafts [6, 7].

Numerous case series have been published describing the outcomes of different urethroplasty techniques for posterior urethral strictures, but their results are inconsistent. Some investigators report success rates of 73-86% [8, 9], whereas others report success rates of 95-99% for urethroplasty [10, 11], which may be related to differences in patient populations, for example the proportion of radiation-induced strictures, and in the techniques used. Previous reviews indicate that anastomotic urethroplasty provides consistently good outcomes in most cases [1, 5];

however, there is still no unified meta-analytic estimate of success that reflects contemporary experience over the last 10-15 years, including newer approaches. In addition, it remains unclear to what extent the use of alternative methods, such as one-stage flap reconstruction or staged reconstructions, is justified and how their outcomes compare.

Aim. To perform a systematic review and meta-analysis of the effectiveness of urethroplasty for strictures and distraction defects of the membranous urethra and to supplement the results with neural network analysis to identify key predictors of success.

Materials and Methods. Review protocol and eligibility criteria. The systematic review and meta-analysis were performed in accordance with PRISMA 2020 [12].

Inclusion and exclusion criteria (PICO):

- Population (P): men with stricture or complete disruption, distraction defect, of the membranous urethra.
- Intervention (I): open urethroplasty, any technique.
- Comparison (C): none, as the included studies were predominantly single-arm.
- Outcomes (O): absence of restenosis/reintervention, complications, and functional outcomes.

Inclusion criteria were as follows: at least 10 patients; separately reported data for membranous/posterior strictures; a clear definition of success, namely absence of restenosis according to urethrography/cystoscopy or absence of repeat intervention; and follow-up of at least 6 months. Single case reports, series with fewer than 10 patients, abstracts and incomplete texts, as well as publications without separate analysis of the membranous segment or with overlapping cohorts, were excluded.

Literature search. The search was carried out in Medline (PubMed), Embase, Scopus, RSCI, and the Cochrane Library from 1990 through December 2024 using combinations of the following terms: posterior urethral stricture, membranous urethra, pelvic fracture urethral distraction, urethroplasty, anastomotic urethroplasty, and urethral reconstruction. In addition, a manual search of the reference lists of key articles and Google Scholar was performed. Study selection and data extraction were conducted independently by two authors.

The initial search identified 312 unique publications. After title and abstract screening, 45 articles were selected for full-text review; 35 studies were excluded because of a non-target urethral lesion level, absence of a clear definition of "success," small case series, incomplete text, or overlapping cohorts. Ten original studies published between 1997 and 2023 were included in the quantitative synthesis, meta-analysis, in accordance with PRISMA 2020 [12].

To minimize the effect of duplicate data, potential cohort overlap was assessed separately, for example in publications from the same center across different years. When overlap of patient populations was suspected, preference was given to the article with the larger sample size and/or longer follow-up, whereas alternative publications were used only as a source of additional descriptive data. This approach reduces the risk of artificially inflating the contribution of an individual center to the pooled effect and is consistent with recommendations for conducting systematic reviews [12].

Data collection and quality assessment. Two authors independently extracted the study design and sample size, patient characteristics, including age, etiology, and stricture length, urethroplasty technique, success criteria, follow-up duration, and the rates of recurrence and complications, including urinary incontinence, erectile dysfunction, and others.

Disagreements in data extraction and quality assessment were resolved by consensus; when necessary, a third author was involved. In mixed series, only subgroups of membranous/bulbomembranous strictures were considered, provided that the results were reported separately and allowed inclusion in the calculation of proportions.

Study quality and risk of bias were assessed using the Newcastle-Ottawa Scale, NOS, taking into account the single-arm design of most case series.

The NOS was adapted for the predominantly single-arm observational series: the key domains were considered to be population representativeness, completeness of follow-up, clarity of outcome definition, and sufficient follow-up duration. Overall, the included studies had acceptable methodological quality; however, limitations typical of retrospective series remained, including patient selection, differences in follow-up criteria, and incomplete functional questionnaire data.

Data analysis. For each study, the success proportion, defined as the absence of restenosis, was calculated. Meta-analysis of proportions was performed using a random-effects model, DerSimonian-Laird, with logit transformation; heterogeneity was assessed using I^2. Subgroup analyses were planned according to etiology, post-traumatic and post-radiation, as well as technique, anastomotic and substitution/augmentation when data were available. Recurrence-free survival was evaluated using the Kaplan-Meier method with the log-rank test.

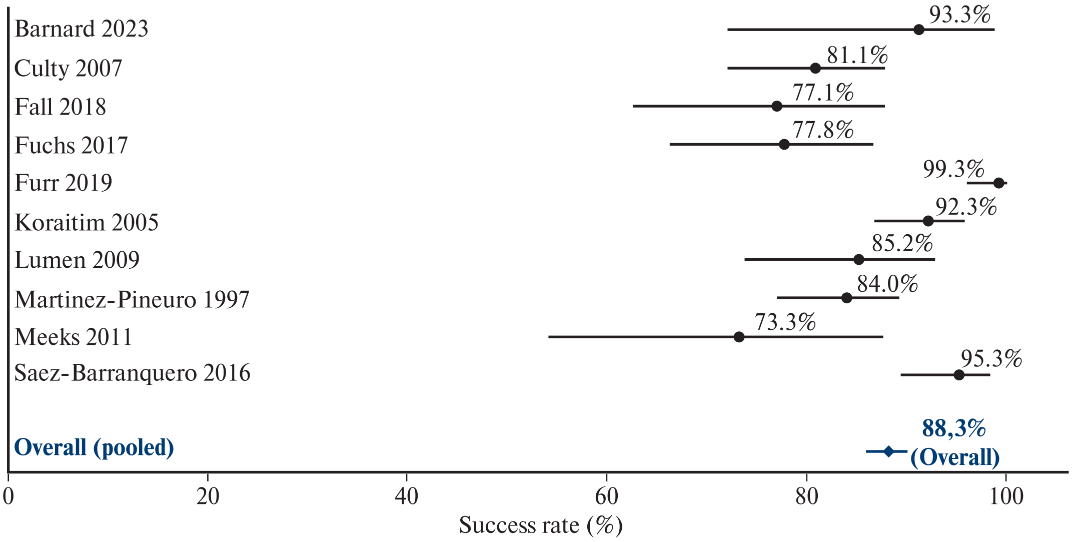
For calculation of 95% confidence intervals for individual proportions, the exact or approximate Wilson method was used; for pooling, logit transformation of proportions was applied to stabilize variance. Heterogeneity was interpreted as moderate at I^2 30-60% and high at I^2 >60%. In addition to subgroup analyses by etiology and technique, a leave-one-out sensitivity analysis was performed by sequentially excluding individual studies to assess the influence of large series on the overall estimate of success. Differences between subgroups were assessed using the z test for the difference between proportions, and statistical significance was set at $p<0.05$.

Outcome definition. "Success" was defined as the absence of clinically significant restenosis at the last follow-up. Priority was given to objective criteria, including urethrography/cystoscopy and calibration; however, in their absence, the lack of repeat interventions in the setting of satisfactory uroflowmetry and clinical symptoms was also considered. If several definitions of success were presented in a given study, the longest follow-up period and/or the strictest criterion was selected for meta-analysis. Missing values were not imputed, and study authors were not contacted; this could have resulted in underestimation of some complications or functional outcomes.

Publication bias was assessed visually using a funnel plot. Given the small number of included studies (n=10), formal tests for funnel plot asymmetry, such as the Egger and Begg tests, were not performed, since their results are unreliable with such a sample size; the assessment was therefore descriptive, based on the distribution of points relative to the overall effect.

Statistical analysis was performed using RevMan 5.4 and R 4.2 (meta, metafor); the neural network analysis was done in Python (TensorFlow).

Fig. 1. Forest plot of surgical success.



The plot shows the proportions of successful outcomes (absence of restenosis) with 95% confidence intervals for each included study and the pooled estimate. Marked heterogeneity across studies was observed (I^2=97%).

Neural network model (exploratory analysis). To additionally assess predictors of success, a simple multilayer perceptron model was constructed with input parameters including etiology, stricture length, and prior interventions, and a binary outcome, success/recurrence, on the pooled cohort (*n*=930). This analysis was exploratory in nature and did not replace the conventional meta-analysis.

For the neural network analysis, categorical variables, such as etiology, were binary encoded, whereas numerical variables, such as stricture length, were normalized. The model was trained using a split into training and validation sets, approximately 80/20, with the Adam optimizer and binary cross-entropy loss function; early stopping was applied to control overfitting. Discriminative performance was assessed by ROC AUC on the validation set, with AUC exceeding 0.8 in most runs, and feature contribution was evaluated using sensitivity/permutation methods. It should be emphasized that this component was exploratory and intended for hypothesis generation rather than for clinical decision-making without external validation.

The network architecture included three hidden layers with ReLU activation and an output layer with a sigmoid function to generate the probability of success. Because of the relatively small number of predictors and the limitations of the source data, several repeated training runs were performed using different initializations and train-validation splits, while monitoring the stability of factor ranking. For interpretation of the results, permutation importance analysis and patient visualization in reduced dimensional space using t-SNE with subsequent clustering were applied to identify typical clinical risk profiles. This approach makes it possible to move from "average" meta-analytic estimates to individualized predictions, but it requires richer prospective data and standardized outcomes.

Results

General characteristics of the studies and patients

A total of 930 patients who underwent urethroplasty for membranous stricture/distraction defect were analyzed. The main etiological groups were post-traumatic ruptures, distraction defects, accounting for 34.5%, post-radiation strictures after treatment for prostate cancer, 13.4%, and other causes, including idiopathic, iatrogenic, inflammatory, and others, 52.1%. Follow-up across the included studies ranged from approximately 21 to ⩾67 months [13, 14].

In studies devoted to post-radiation strictures, patients were older and had a higher baseline risk of functional impairment due to previous treatment for prostate cancer. By contrast, post-traumatic distraction defects were more commonly observed in younger men after pelvic fracture. In all included studies, the main reconstructive method remained one-stage anastomotic urethroplasty, excision and primary anastomosis, whereas substitution/augmentation procedures, skin flap or buccal graft, were used in a limited number of patients with longer or technically more complex strictures [8, 10, 11].

As shown in the table, the studies differed substantially in design and patient structure. Three studies mainly addressed post-radiation strictures, three focused on post-traumatic distraction defects, and the remainder represented mixed cohorts with separable subgroups. The proportion of anastomotic urethroplasty exceeded 80-90% in most series, whereas the use of buccal grafts/flaps was limited to selected subgroups with longer or recurrent strictures. Follow-up generally ranged from 2 to 5 years, allowing assessment not only of early but also of some late recurrences.

According to the included studies, the primary success rate of urethroplasty ranged from 73% to 99%; heterogeneity was high (I^2=97%, p<0.001). Such high heterogeneity is expected in a meta-analysis of case series, since the studies differed substantially in patient structure, traumatic and radiation etiology, defect length, the proportion of primary/repeat interventions, and follow-up criteria, including urethrography, cystoscopy, and clinical criteria. Sensitivity analysis showed that exclusion of any single study did not change the conclusion regarding the high overall effectiveness, with

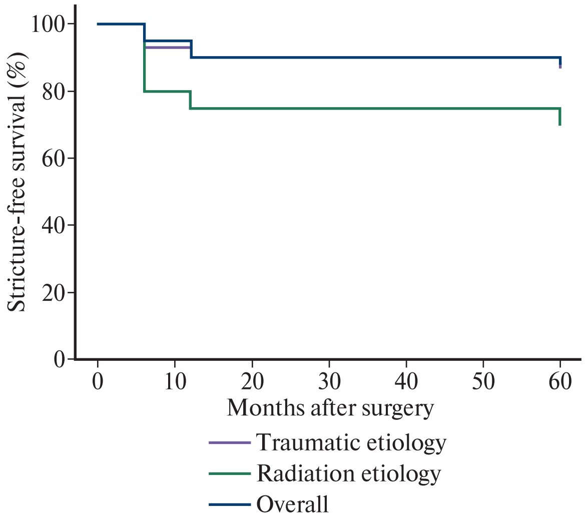
Table

Characteristics of the studies included in the meta-analysis

Author (year)	Sample size	Stricture etiology	Mean age	Stricture length	Urethroplasty method	Mean follow-up	Definition of success	Success rate	Complication rate
Barnard et al., 2023 [15]	23	Radiation-induced (stenosis after radiation therapy for prostate cancer)	69.9 years	2 cm	Primary anastomotic urethroplasty	73.1 months	Absence of restenosis at long-term follow-up	91.3%	Stress urinary incontinence – 34.8%, erectile dysfunction – 43.5%, anejaculation – 70%
Culty et al., 2007 [9]	105	Traumatic (79% pelvic fracture, 21% perineal trauma)	30 years	Not specified (usually a short defect)	54 anastomoses, 39 staged urethroplasties, 6 augmentation procedures	4.5 years (median)	Absence of restenosis (long-term "good" outcome)	81% (5-year, anastomotic); 53% (staged)	14.5% incontinence; 75% erectile dysfunction
Fall et al., 2018 [13]	48	Post-infectious – 56.3%; other (trauma, idiopathic) – 43.7%	53.5 years	1.23 ± 0.62 cm	Anastomotic urethroplasty	21.1 ± 12.6 months	No need for repeat urethrotomy or urethroplasty (criterion of failure)	77.1%	No cases of incontinence or impotence reported; 4.2% penile curvature
Fuchs et al., 2017 [16]	72	Radiation-induced (strictures after radiotherapy for prostate cancer)	71.1 years	2.0 cm vs 3.0 cm	Anastomotic urethroplasty	50 months and 22 months for different cohorts	Absence of restenosis (no need for repeat intervention)	86% (2013-2015 cohort) and 70% (2007-2012 cohort)	Urinary incontinence 34.7%
Furr et al., 2019 [10]	179 (139 + 40)	Mixed (bulbar strictures; lichen sclerosus and hypospadias excluded)	40-42 years	1.7 cm for anastomotic and 3.98 cm for buccal graft repairs	End-to-end anastomosis (139), one-stage buccal graft urethroplasty (40)	63.3 months vs 51.4 months (anastomotic vs graft)	Absence of restenosis (widely patent urethra at 4 months + no long-term recurrence)	99.3% (anastomotic) and 95% (graft)	Post-void dribbling – 8.3% (anastomotic) and 28.1% (graft); sensation of penile shortening/ tightness with erection – 23.4% (anastomotic) and 3.1%; erectile dysfunction 20-25%
Koraitim, 2005 [1]	155	Traumatic (99% due to pelvic fracture)	21 years (range 3-58)	⩽2.5 cm (73%); >2.5 cm (27%)	Primary anastomosis (perineal approach – 113; transpubic – 40)	1-22 years (range)	Absence of restenosis (durable patency without recurrence up to 22 years)	90% (perineal) and 98% (transpubic)	No incontinence developed; 2% erectile dysfunction
Lumen et al., 2009 [14]	61	Traumatic (after pelvic fracture)	33-36 years	3.5 cm	Primary anastomosis (perineal approach)	67 months (mean)	Absence of restenosis (absence of stricture recurrence)	85.2% (recurrence-free)	Post-traumatic erectile dysfunction is 32.8% (pre-existing); mild stress urinary incontinence is 1.6% (1 patient); rectal injury occurred
Martínez-Piñeiro et al., 1997 [17]	150	Mixed: trauma 42.6%, inflammatory 28%, iatrogenic 17.3%, congenital 6%, unspecified 6%	35.7 years	1-3 cm (60.6%); <1 cm (28%); >3 cm (10.6%)	Anastomotic urethroplasty (perineal – 138; abdominoperineal – 12)	44.4 months (mean; range 6-168)	Outcome assessment: "good" is complete absence of restenosis, "fair" is minor narrowing without repeat surgery, "poor" is recurrence requiring repeat surgery	84% (primary success); 93.3% (final, after repeat surgery)	Early complications: wound infection – 1.3% (2 cases), hematomas – 1.3% (2 cases); late: chordee – 0.7% (1 case), incontinence – 1.3% (2 cases), new erectile dysfunction – 4.7% (7 cases)
Meeks et al., 2011 [8]	30	Radiation-induced (stricture after treatment for prostate cancer: 50% external beam radiation therapy, 24% brachytherapy, 26% combined)	67 years	2.9 cm (mean; range 1.5-7 cm)	Anastomosis (80%), skin flap (13%), buccal graft (7%)	21 months	Absence of restenosis (lumen ⩾16 Fr on follow-up cystoscopy)	73%	Urinary incontinence: transient 10%, persistent 40% (13% underwent sphincter implantation); erectile dysfunction 50% (unchanged from preoperative level)
Sáez-Barranquero et al., 2016 [11]	107	Iatrogenic membranous urethra 11.2% (n=12); post-traumatic membranous urethra 4.7% (n=5)	42 years	1-2 cm	Primary anastomosis	59 months	Absence of need for repeat intervention (new surgery or urethrotomy)	95.3%	Recurrence 4.7% (required repeat surgery); other complications not reported

Note. The definitions of success varied across studies; the table presents the results at the last follow-up. Key complications included urinary incontinence, erectile dysfunction, as well as other postoperative events, according to the authors.

Fig. 2. Recurrence-free survival curves (Kaplan-Meier) for the overall cohort and subgroups (post-traumatic and post-radiation strictures).



the pooled proportion remaining within the range of 85-90%.

Surgical Success and Stricture Recurrence

The pooled success rate was 88.3% (821/930; 95% CI 85-91%), and the mean recurrence rate was 11.7% (Fig. 1). In most cases, restenosis developed within the first 6-12 months. Postoperative outcomes depended on etiology: success was higher for post-traumatic strictures (90-95%) than for post-radiation strictures (70-80%; p=0.03). Large series of post-traumatic defects have reported long-term patency rates of 90-98% [1, 14], whereas outcomes for post-radiation strictures are more variable, ranging from 73% in [8] to 91% with strict selection in [15] and 78% in [16].

When etiological subgroups were compared, the pooled estimate indicated a statistically significant advantage for post-traumatic anastomotic reconstruction, with an odds ratio for success of OR=1.79 (95% CI 1.04-3.08; p=0.03). In practical terms, this corresponds to an absolute difference of approximately 10-15% in the probability of a favorable outcome. Most restenoses were diagnosed early and, according to individual series, were amenable to repeat treatment or endoscopic procedures if detected in a timely manner.

Technical aspects of reconstruction may also partly explain differences in outcomes between centers. In post-traumatic distraction defects, stepwise mobilization of the bulbar urethra and adjunctive maneuvers, Webster maneuvers, namely separation of the crura of the corpora cavernosa and partial resection of the inferior pubic margin/inferior pubectomy, are often used to achieve a tension-free anastomosis. These maneuvers make it possible to gain length and perform one-stage reconstruction even in relatively extensive defects, but they require high surgical expertise and correct intraoperative assessment of tension. In the series reported in [14], the use of extended maneuvers was associated with high patency rates and an acceptable complication profile.

Recurrence-free survival, Kaplan-Meier, demonstrates that most recurrences occur within the first year: at 12 months, recurrence-free survival was 90% for post-traumatic and 75% for post-radiation strictures. After 2 years, the curves reached a plateau; the 5-year RFS rates were 87% and 70%, respectively (log-rank p=0.03; *Fig. 2*).

According to the included studies, the median time to recurrence detection was 5-8 months, which is consistent with clinical observation: if the anastomosis remains intact during the first year, the probability of late restenosis is extremely low. This supports more intensive follow-up during the first 12-24 months, followed by less frequent control visits in the setting of stable uroflowmetry. If restenosis does not develop within the first year, the subsequent risk of recurrence is minimal [1].

Predictors of Success

In addition to etiology, the reconstructive technique may also influence the outcome. Direct comparison is limited by patient selection; however, in the comparative study [10], anastomotic urethroplasty showed a success rate of 99.3%, whereas urethroplasty with a buccal graft showed 95% (p=0.06), with comparable patient satisfaction. In the substitution technique group, dribbling and a subjective sensation of penile shortening were reported more often.

It is important to note that functional outcomes are not limited to urethral patency. In some studies, lower urinary tract symptoms and quality of life were assessed, but the set of scales and the methodology of their use were heterogeneous. Thus, in the comparative analysis [10], differences in satisfaction and overall perception of the outcome between anastomotic and substitution urethroplasty were minimal, despite a tendency toward a higher frequency of dribbling in the graft group. This underscores the need for standardized assessment of patient-oriented outcomes, lower urinary tract symptoms, sexual function, and continence, in future multicenter studies.

In the remaining series, substitution/augmentation techniques were used in a small number of patients; therefore, the conclusions are limited. In study [8], when a skin flap or buccal graft was used, success was maintained in most patients; however, the statistical power was insufficient for a reliable comparison of methods.

Taken together, the data indicate that the key clinical risk factors for failure remain the length of the scarred segment and the “complexity” of reconstruction, including prior urethrotomies/urethroplasties and marked periurethral fibrosis. In short defects, generally up to 2-3 cm, achieving a tension-free anastomosis provides the best results, whereas with greater defect lengths the need for augmentation or substitution urethroplasty increases [1, 10].

Complications of Urethroplasty

The key functional complications are urinary incontinence and severe de novo erectile dysfunction. In the pooled cohort, clinically significant incontinence was observed in 4.5%, and marked deterioration of erectile function in 3.3% of patients. In post-radiation strictures, the risk of incontinence is substantially higher, 34-40% in [8, 15], compared with traumatic series, 0-1% in [1, 9, 14].

Such a low overall rate of incontinence in the pooled cohort is explained by the fact that most included patients had traumatic or mixed, non-radiation, etiology. Post-radiation strictures are characterized by sphincter damage and pronounced ischemic tissue changes; therefore, even after technically successful reconstruction, subsequent correction of incontinence, such as sling procedures or implantation of an artificial urinary sphincter, is often required. In the multicenter series [8], severe incontinence persisted in 40% of patients, and some of them required sphincter implantation; similar rates were also reported in [15].

De novo severe erectile dysfunction after urethroplasty was relatively uncommon and was more often determined by the underlying pathology. In traumatic series, new cases of erectile dysfunction accounted for 0-2% [1, 14]. After radiation therapy, the rates were more variable: in study [15], worsening of erectile function was reported in 43.5% of patients, which may reflect patient selection and the extent of reconstruction.

It is important to take into account that in post-traumatic cohorts, a substantial proportion of erectile dysfunction is already present before urethroplasty and is attributable to injury of the neurovascular structures associated with pelvic fracture. Therefore, when interpreting sexual outcomes, it is more appropriate to distinguish specifically de novo dysfunction and, whenever possible, to use validated questionnaires. In post-radiation series, worsening of erectile function may reflect both progression of radiation-induced injury and the extent of tissue resection or mobilization performed, which makes direct comparison between studies difficult [8, 15].

Other complications included infectious events (<5%), rare rectal injuries in high disruptions, two cases in [14] and one in [17], and scrotal hematomas, four cases in [17].

Life-threatening complications and fatal outcomes were not reported in the analyzed studies. Overall, the safety profile of urethroplasty for membranous lesions is acceptable; however, the procedure requires an experienced reconstructive urologist, since the operative field is in close proximity to the sphincter and prostate, and in post-traumatic disruptions pronounced scarring and distortion of anatomical landmarks may be present.

The funnel plot (*Fig. 3*) did not reveal marked publication bias; the greatest contribution to the visual asymmetry was made by the large series [10].

It should be taken into account that visual assessment of the funnel plot in the presence of substantial clinical heterogeneity reflects not only publication bias, but also real differences in patient populations, for example traumatic and post-radiation strictures. Therefore, the absence of obvious asymmetry does not exclude possible effects of patient selection in individual centers.

Results of the neural network analysis

According to the neural network analysis, the most important predictors of outcome were stricture length, prior interventions, and etiology (*Fig. 4*). Age and comorbidity made a smaller contribution.

In the validation set, the model demonstrated stable discrimination (ROC AUC usually >0.8), which indirectly confirms the presence of nonlinear relationships between clinical factors and outcome. At the same time, the contribution of the variables to the prediction was consistent with clinical logic: increasing stricture length and the presence of prior interventions reduced the probability of success more strongly than age or comorbidity, which had a secondary effect.

The model demonstrated a wide range of predictions: in a short post-traumatic stricture without prior interventions, the probability of success approached 90%, whereas in long and/or post-radiation strictures after several unsuccessful interventions it could decrease to 20-50% (*Fig. 5*).

Fig. 3. Funnel plot of treatment success. The x-axis shows log odds (the logarithm of the odds of success), and the y-axis shows the standard error. The dashed lines indicate the 95% confidence limits.

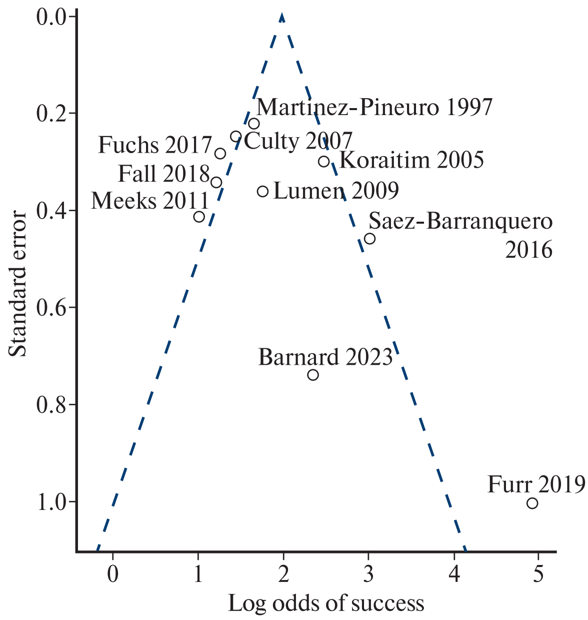
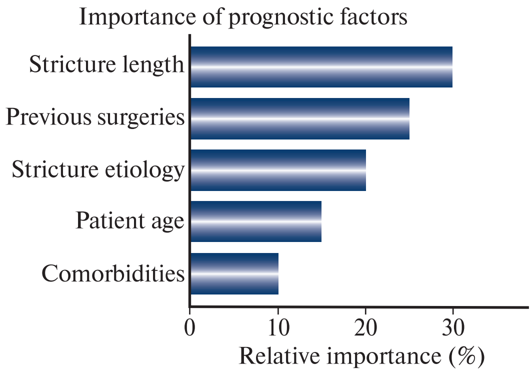


Fig. 4. Importance of the main clinical factors for predicting successful membranous urethroplasty according to the neural network analysis.



Clustering with t-SNE made it possible to identify three groups of observations with different risk profiles (*Fig. 6*): low risk, short post-traumatic strictures; intermediate risk; and high risk, long and/or post-radiation strictures after repeated interventions.

Within the identified clusters, the expected gradient of outcomes was observed: in the “low-risk” group, short post-traumatic strictures without prior interventions, the success rate approached 90-95%; in the intermediate-risk profile, it was approximately 70-80%; and in the “high-risk” group, long and/or post-radiation strictures after repeated interventions, it decreased to approximately 30-50%. These findings may be useful for risk stratification when planning follow-up, but they require confirmation in independent datasets.

Fig. 5. Model-predicted probability of a favorable outcome (absence of stricture recurrence) under different hypothetical scenarios (described in the text).

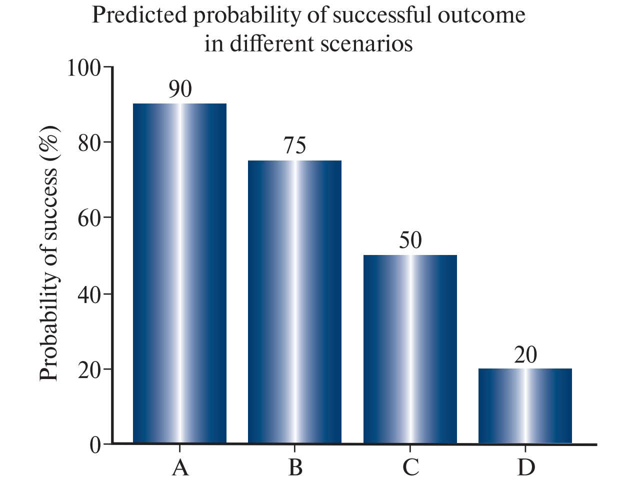
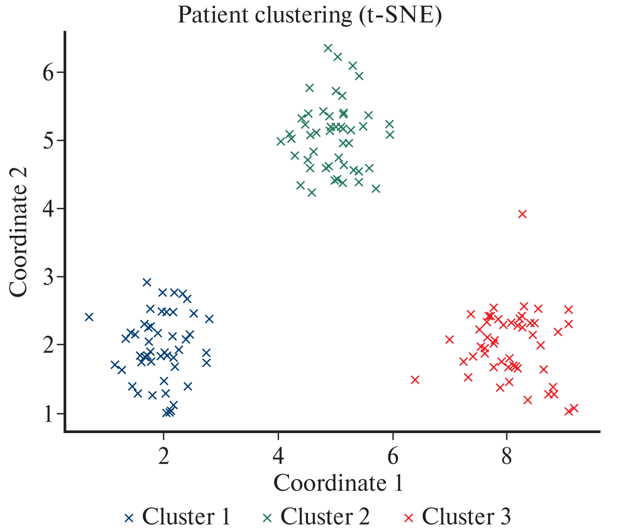


Fig. 6. t-SNE clustering of patients after urethroplasty, identifying three groups with different combinations of characteristics (described in the text).



It should be emphasized that t-SNE is used primarily as a visualization method and is sensitive to the choice of hyperparameters; therefore, the identified clusters should not be interpreted as strict diagnostic categories. Their purpose is to illustrate the possible hidden structure of the data and to generate hypotheses for further prospective studies.

Discussion. Our meta-analysis confirms the high efficiency of urethroplasty for membranous strictures/distraction defects, with an 88% success rate. Outcomes depend substantially on etiology: results are better in post-traumatic strictures, whereas in post-radiation strictures they are poorer and accompanied by a higher frequency of functional complications [1, 8, 15, 16]. Clinical reviews also emphasize the influence of stricture length and radiation etiology on prognosis [18]. Most recurrences develop within the first 6-12 months, after which the risk decreases sharply.

Unlike reviews that combine strictures of different urethral segments, the present study focuses on the membranous region, where the balance between achieving patency and preserving continence is particularly critical. Our estimates of success are consistent with data from large series of posterior urethral reconstruction and contemporary reviews, in which radiation etiology, defect length, and prior interventions are regarded as the main risk factors for recurrence [2, 18]. This confirms that with proper patient selection and adherence to reconstructive principles, urethroplasty provides predictably high success rates.

Post-radiation strictures remain the most challenging category. Radiation therapy leads to severe fibrosis, hypovascularization, and reduced tissue regenerative potential; therefore, the risk of restenosis and functional complications is predictably higher [3]. In addition, some patients have pre-existing damage to the sphincter apparatus and/or bladder neck, which explains the frequent occurrence of postoperative incontinence. From a practical perspective, such patients should be counseled in advance regarding the possibility of subsequent correction of incontinence and the advisability of treatment in centers experienced in both urethral reconstruction and artificial urinary sphincter implantation [8, 15, 16].

The most reproducible results have been obtained in post-traumatic distraction defects, when complete scar excision and formation of a tension-free anastomosis are feasible. The classical technical principles include careful mobilization of the urethral stump, adequate dissection of spongiofibrosis, and creation of a watertight, well-vascularized anastomosis. When these conditions are met, success rates of ⩾90% are achievable in specialized centers [1].

In short defects, anastomotic urethroplasty remains the method of choice, since it allows excision of the scar-altered segment and restoration of the urethral lumen with a single anastomosis. In long strictures, generally >3-4 cm, marked periurethral fibrosis, or after unsuccessful prior interventions, tension-free anastomosis may be impossible; in such situations, the use of augmentation/substitution techniques with a buccal graft or skin flap is justified [6, 7, 10]. It should be taken into account that comparison of techniques based on case series is limited by selection bias: substitution techniques are more often used in patients who are initially more complex.

For membranous strictures, repeated dilations and internal urethrotomy generally have limited effectiveness and may increase the severity of spongiofibrosis, thereby complicating subsequent reconstruction. Therefore, endoscopic methods should be considered only as a temporary measure or in carefully selected patients, whereas timely reconstructive surgery is preferable in confirmed long and/or recurrent strictures [4]. In extremely severe post-radiation lesions with concomitant incontinence, a staged approach may be considered, with primary urethral reconstruction followed by continence correction, or, in selected cases, alternative urinary diversion options.

Given that most recurrences occur within the first 6-12 months, emphasis on early follow-up appears optimal, including uroflowmetry and symptom assessment, with urethrography/cystoscopy in the event of decreased maximum flow rate, every 3-6 months during the first year and then every 6-12 months up to 2 years [4, 16]. After 24 months, with stable findings, the risk of late restenosis is low; however, in patients after radiation therapy, more vigilant long-term follow-up remains advisable because of progressive radiation-induced changes [3, 18].

Limitations. The included studies were mainly retrospective case series without control groups and with high heterogeneity, including differences in populations, techniques, definitions of "success," and follow-up duration. The available data are insufficient for direct comparison of techniques and for evaluation of rare complications. An additional source of variability is the heterogeneity in the definition of "success": some studies used strict endoscopic criteria, for example a lumen ⩾16 Fr, whereas others used the clinical outcome of no repeat intervention. In addition, patient-reported measures, such as IPSS, SHIM, and quality-of-life assessment, were not systematically recorded in all series; therefore, functional outcomes may have been underestimated. Finally, the proportion of patients with prior interventions and the duration of follow-up varied across studies, which limits direct comparison of absolute complication rates between centers.

The exploratory neural network analysis was hypothesis-generating in nature and confirmed the clinically expected predictors, namely stricture length, prior interventions, and etiology. The potential of artificial intelligence methods for outcome prediction and risk stratification is being actively discussed in the contemporary literature [19, 20]; however, external validation of these models in independent cohorts is still required.

From a methodological perspective, it is important that the neural network model was trained on aggregated data from published studies rather than on a single prospective database; therefore, "noisy" outcome labels and center-related differences may have influenced the results. Nevertheless, the concordance between predictor ranking and clinical logic, as well as published machine learning studies in urethroplasty [19, 20], supports the promise of this approach. In the future, the most rational strategy would be to create multicenter registries with a unified definition of outcomes and functional scales, which would make it possible to perform external validation and develop practical risk calculators.

Although the main outcome measure in most series is formulated as "urethral patency without restenosis," continence, sexual function, and overall quality of life are no less important to the patient. Our results show that in traumatic distraction defects, after successful reconstruction, the risk of de novo incontinence is usually minimal, 0-1% in large series, whereas in post-radiation etiology incontinence becomes one of the major limiting factors and may reach 30-40% [8, 15, 16]. This reflects not only the complexity of reconstruction, but also preexisting damage to the sphincter apparatus and pelvic tissues after radiation exposure. In practical terms, this means that continence should be assessed preoperatively, including history, pad test when needed, and cystoscopy/urodynamics when indicated, and that the likelihood of staged correction, ranging from conservative treatment to implantation of an artificial urinary sphincter, should be discussed.

Erectile function also requires careful interpretation. In post-traumatic cohorts, significant erectile dysfunction is often present before reconstruction because of neurovascular injury associated with pelvic fracture; therefore, overall postoperative rates may overestimate the contribution of urethroplasty itself. In post-radiation series, sexual dysfunction may progress independently of surgery, and the degree of deterioration is largely determined by the extent of scarring and prior treatment for prostate cancer [8, 15]. Some studies also reported subjective symptoms, such as dribbling and a sensation of penile shortening, which are rarely recorded as formal "complications," but may reduce patient satisfaction [10].

Importantly, even with a relatively high incidence of functional disorders, many patients report high satisfaction provided that durable urinary patency and predictable symptom control are achieved, which underscores the importance of appropriate counseling and alignment of expectations. In long-term follow-up, adverse effects on outcomes are associated with increasing stricture length, radiation etiology, and other factors reflecting disease "complexity"; therefore, risk stratification and early referral of patients to specialized centers may improve both anatomical and functional outcomes [21].

In short post-traumatic defects, anastomotic urethroplasty provides the highest likelihood of success; in post-radiation strictures, the increased risk of restenosis and incontinence should be discussed in advance, and treatment in specialized centers with the possibility of subsequent correction, including an artificial urinary sphincter, should be considered [4, 18, 21].

From a practical standpoint, the results of the review make it possible to refine and improve the principles of patient counseling.

1) In post-traumatic defects, after the stage of urinary diversion, cystostomy, anastomotic urethroplasty provides a high likelihood of durable success and an extremely low risk of de novo incontinence.
2) In post-radiation strictures, the probability of incontinence and the possible need for subsequent implantation of an artificial urinary sphincter should be discussed in advance. For this reason, referral to a specialized center is preferable,
3) In long strictures and/or after repeated interventions, it is advisable to plan augmentation or substitution urethroplasty in advance in order to avoid an anastomosis under tension and reduce the risk of early recurrence.
4) Follow-up should be most intensive during the first 12-24 months (see above); if early restenosis is suspected, timely endoscopic correction may reduce the need for repeat reconstruction [4, 16, 18, 21].

Future research. To further increase the level of evidence, multicenter prospective registries are needed in which the criteria for "success," both endoscopic and clinical, the timing of follow-up visits, and the set of functional scales, continence, lower urinary tract symptoms, sexual function, and quality of life, are standardized. Of particular interest is comparison of one-stage anastomotic and substitution techniques in patients with comparable disease complexity, as well as evaluation of staged strategies in severe post-radiation lesions. The availability of standardized data will make it possible to validate artificial intelligence models in independent cohorts and potentially implement decision-support tools for risk stratification and selection of the optimal treatment strategy.

Conclusion. Urethroplasty of the membranous urethra is characterized by high effectiveness, with 88% remaining recurrence-free. The best results are achieved in post-traumatic strictures, ⩾90%, whereas in post-radiation strictures the probability of cure is lower, 70-80%, and the risk of complications is higher. The exploratory neural network analysis confirms the prognostic significance of stricture length, etiology, and prior interventions.

From a practical perspective, a differentiated approach is essential, since in traumatic etiology a strategy of primary reconstruction is justified with an expectation of a high probability of cure, whereas in post-radiation strictures expanded patient counseling, assessment of the risk of incontinence, and readiness for staged correction of functional disorders are required. Most recurrences develop early; therefore, systematic follow-up during the first one to two years after surgery is of decisive importance. A promising direction remains the development of predictive models based on machine learning, provided that external validation and outcome standardization are achieved in multicenter registries.

Given the retrospective nature of most included series and the high clinical heterogeneity, the obtained quantitative estimates should be regarded as guidance for practice rather than as absolute values for a particular patient. Nevertheless, even with these limitations, the pooled data convincingly confirm that open reconstructive procedures on the posterior urethra provide more durable results than repeated endoscopic interventions and should be regarded as the preferred strategy for recurrent and/or long membranous strictures. The key directions for improving outcomes are early referral of complex patients, standardization of success and complication criteria, and integration of patient-oriented measures into routine postoperative follow-up.

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LITERATURE REVIEWS

D.L. Polishchuk[1], Z.M. Kulieva[1], N.A. Amosov[2], M.V. Amosova[1], V.V. Fadeev[1], A.V. Amosov[1], A.A. Tsymbal[1]

ANDROGEN DEFICIENCY AFTER RADICAL PROSTATECTOMY: A PHENOMENON OVERLOOKED IN UROLOGICAL PRACTICE?

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Androgen deficiency following radical prostatectomy (RP) is a clinically uncharacterised and conceptually undefined phenomenon. Meanwhile, millions of men undergo RP annually, and if persistent hypogonadism truly developed in at least a subset of them, series of observations, cohort studies, and clinical guidelines would already exist. The absence of such evidence may reflect either a real problem, concealed at the intersection of urology and endocrinology, or the inherent untenability of the idea itself. To clarify this issue, a critical reappraisal of the hypothesis of persistent androgen deficiency as a potential consequence of RP is required. The focus of analysis is not on isolated findings but on the logic of their interpretation – ranging from alterations in endocrine profiles to proposed pathophysiological mechanisms, from diagnostic criteria to the rationale for replacement therapy and follow-up strategies. In each section, the emphasis shifts from simple fact-gathering to reconstruction of argumentation. The question is not merely what data exist, but whether they allow one to speak of a distinct clinical category. The objective of this article is not to refute the hypothesis, but to assess its validity as a scientific model aspiring to diagnostic and therapeutic significance.

Keywords: *postoperative complications, endocrine disorders, androgen deficiency, hypogonadism, testosterone, radical prostatectomy, testosterone replacement therapy*

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Radical prostatectomy (RP) is one of the key treatment options for prostate cancer (PCa), and its consequences are discussed mainly in the context of functional and oncological outcomes [1]. RP is not usually regarded as an intervention capable of causing endocrine disturbances. It is generally assumed that, in the absence of androgen-deprivation therapy (ADT), the hypothalamic–pituitary–gonadal axis remains intact, making further discussion seem unnecessary [2]. However, this assumption overlooks the fact that one of the key androgen-sensitive organs is removed, potentially involved in neuroendocrine and metabolic regulation.

In the literature addressing RP sequelae, discussion of hormonal status is typically confined to ADT or sexual function [3], whereas targeted studies of androgen dynamics outside the context of ADT remain extremely limited, despite the availability of studies on the prognostic role of testosterone in PCa [4]. Several studies have tracked postoperative testosterone dynamics [5–8], and some have documented a transient decrease in the early period after RP [7, 8].

At the same time, some authors emphasize the central role of free testosterone rather than total testosterone as the most sensitive marker of clinically meaningful deviations within the concept of late-onset hypogonadism (LOH) [9, 10]. Even with normal total testosterone, a decrease in its free testosterone may be accompanied by characteristic symptoms and metabolic changes. However, the LOH concept itself remains heterogeneous: threshold values for total testosterone vary, diagnostic criteria differ across guidelines, and the role of the free testosterone is assessed inconsistently [10].

In parallel, interest is growing in testosterone replacement therapy (TRT) in men who have undergone treatment for PCa, despite persistent concerns about its potential oncogenic effect. Emerging data have gradually softened these views and led to a more personalized assessment of TRT safety [11]. Epidemiological data show increasing use of TRT among men with a history of PCa [12]. This creates a paradox: what was long considered contraindicated is gradually becoming a subject of discussion, while the question of hypogonadism after RP remains largely outside the discourse.

The question we pose is not whether androgen deficiency exists after RP, but why this hypothesis has received so little attention. Why does the contemporary literature on quality of life, sexual function, and metabolism after RP rarely analyze changes in hormonal regulation in patients not receiving ADT? The endocrine and metabolic effects of ADT are well described [13], but an important element is missing in this equation, namely RP. Its role in triggering endocrine adaptations remains in the background, perhaps unjustifiably.

ENDOCRINE PROFILE OF PATIENTS AFTER RP

Surgical stress as a model of the endocrine response

One of the earliest reports of transient changes in the androgen profile after surgery was the study by Ghanadian et al. (1981) [14], performed in a cohort of 28 men aged 67–80 years with benign prostatic hyperplasia (BPH) who underwent retropubic RP. Testosterone and dihydrotestosterone (DHT) levels were followed from baseline to two months after the intervention. A marked decrease in both parameters was observed as early as postoperative day 2. By day 7, partial recovery was noted, although values remained significantly below preoperative levels. After one month, testosterone had almost returned to baseline, whereas DHT remained reduced. Full recovery of both parameters was documented only after two months.

The dynamics of androgen level observed in this study indicate a transient suppression of secretion, which the authors attributed to surgical stress. A plausible mechanism may be activation of the hypothalamic–pituitary–adrenal axis with concomitant temporary suppression of hypothalamic–pituitary–gonadal regulation. The sharp decline in testosterone and DHT within the first 48 hours cannot be explained by age-related secretory features, metabolic disturbances, or potential neurovascular injury, as these factors typically lead to slower and more persistent changes. The slower recovery of DHT is likely related to its dependence not only on testosterone production but also on tissue conversion via 5α-reductase, the activity of which decreases with age. It should be noted that the study was conducted in a small cohort of older men with BPH, limiting extrapolation to younger patients or those with PCa. Nevertheless, the restoration of testosterone and DHT to baseline within two months supports the transient nature of these changes.

Early dynamics of androgen level

Following the initial observations of an acute testosterone decrease in response to surgical stress [14], subsequent studies sought to determine whether this short-term phenomenon evolves into a persistent disturbance. Particularly informative in this regard were the studies by Miller et al. (1998) [5] and Madersbacher et al. (2002) [2], which assessed dynamics of androgen level from one month to one year after surgery.

In the prospective study by Miller et al. (n=63), radical RP was shown to be associated with sustained changes in the androgen profile. One year after surgery, significant increases were observed in total and free testosterone, estradiol, luteinizing hormone (LH), and follicle-stimulating hormone (FSH). In contrast, DHT decreased significantly by approximately 15% (p<0,05), while sex hormone-binding globulin (SHBG) and prolactin concentrations remained stable. The authors concluded that sexual dysfunction after RP cannot be explained by androgen deficiency and suggested that the prostate may secrete factors involved in negative feedback regulation of the hypothalamic–pituitary–gonadal axis.

Similar results were reported by Madersbacher et al. [2] in a larger cohort (n=146), where patients after radical retropubic RP (n=49) were compared with men after transurethral resection of the prostate (TURP) (n=51) and an observational control group (n=46). On average, testosterone levels after RP remained stable, and similar dynamics were observed in the TURP and control groups. However, in patients with low baseline testosterone (⩽3 ng/mL), its concentration more than doubled one year after RP (from 1,5 to 3,8 ng/mL; p<0,05). An increase in testosterone was also noted in patients with high Gleason score (⩾7) (from 2,2 to 5,2 ng/mL; p<0,05). In addition, the RP group demonstrated significant increases in LH (+75%) and FSH (+59%), whereas no significant changes were observed after TURP or in the control group. SHBG levels remained stable.

An important observation from these studies was the absence of a universal endocrine pattern specifically linked to RP: androgen status varied, and no single trend applicable to all patients was identified. At the same time, hormone levels remained stable after TURP and in the control group, underscoring the specificity of changes to RP. Of particular interest is the phenomenon of paradoxical testosterone increase in patients with low baseline levels or aggressive tumors [2]. These findings challenge the view of the prostate as an exclusively passive organ in the endocrine context. Rather, they suggest that the tumor itself or prostatic tissue may contribute to lower testosterone, and that removal of this tissue may facilitate normalization of the androgen profile.

Tumor stage and the endocrine profile

In addition to analyzing postoperative changes, an important line of research has been the effect of tumor stage on the endocrine profile before RP. In the study by Heracek et al. (2007) [15], which included 250 men, patients with localized cancer (pT2, n=128) were compared with those with locally advanced PCa (pT3–pT4/N1, n=122). Most hormonal parameters, including total and free testosterone, SHBG, LH, estradiol, and cortisol, did not differ between groups. The only significant difference was a higher FSH level in patients with locally advanced disease.

These findings indicate that a more aggressive tumor stage is not necessarily accompanied by obligatory changes in androgen status. Although some reports suggest that baseline testosterone may be lower in patients with more aggressive PCa, no between-group differences were observed in this cohort for total or free testosterone, SHBG, or LH. The only parameter showing a statistically significant difference was FSH, which was higher in the locally advanced group, reflecting features of gonadotropin regulation rather than direct suppression of androgen production. Overall, this suggests no direct relationship between testosterone level and tumor aggressiveness and highlights the multifactorial interplay between the hypothalamic–pituitary–gonadal and adrenal systems and the tumor microenvironment.

Heterogeneity of the endocrine response

Later studies also support the lack of a universal endocrine pattern after RP. In the study by Olsson et al. (2010) [6], androgen profiles were assessed in 55 men with localized PCa before surgery and 90 days afterward. Total testosterone remained stable, and free testosterone also did not change. At the same time, DHT decreased, accompanied by an increase in gonadotropins: LH rose by 53% (p<0,0001) and FSH by 21% (p<0,0001). When stratified by Gleason score (5–6 vs 7–10), no differences in androgen dynamics were identified.

In a larger prospective study by Gacci et al. (2013) [7] including 100 men with localized PCa, testosterone and gonadotropin dynamics were analyzed. Blood samples were collected in the morning (08:00–11:00) 7–14 days before surgery, and again at 1 and 3 months postoperatively. A decrease in testosterone was observed at 1 month, returning to baseline by 3 months. LH and FSH increased significantly from the first month of follow-up. The preoperative correlation between LH and testosterone was strong but disappeared at 1 month; by 3 months, it was largely restored.

Whereas the study reporting a transient testosterone decline with normalization by 3 months [7] focused on early postoperative months, the study by Lumbiganon et al. (2019) [8] addressed the earliest changes. By postoperative day 14, in 63 patients, total testosterone decreased from 14,2±4,8 to 12,5±4,3 nmol/L (p=0,001); a similar trend was observed for free testosterone, while SHBG remained stable. Multiple regression analysis showed that a more pronounced decrease was associated exclusively with high Gleason grade (⩾4+3), whereas age, BMI, and preoperative prostate-specific antigen (PSA) level did not play a significant role.

Taken together, these studies suggest that changes in the androgen profile after RP are heterogeneous and predominantly transient. Different follow-up windows capture different phases of the endocrine response from an early decline in testosterone to subsequent recovery, with a persistent increase in gonadotropins. The clinical relevance of these fluctuations remains uncertain, as they more likely reflect surgical stress dynamics, adaptation of the hypothalamic–pituitary–testicular axis, and tumor biology than the development of a persistent post-RP androgen deficiency syndrome (*Table*).

POTENTIAL PATHOGENETIC MECHANISMS OF ANDROGEN DECLINE

Surgical stress as a transient factor

Transient testosterone decline in the early postoperative period after RP has been confirmed in several studies [6, 8, 14], but in itself it does not indicate the development of persistent hypogonadism. The acute stress response that

Table

Characteristics of clinical studies evaluating androgen profile dynamics in men after urological surgery

Study	Population/N	Type of surgery	Time points	Hormones measured	Results
Ghanadian et al. (1981) [14]†	BPH; n=28; age 67–80 years	RRP	Baseline, day 2, day 7, 1 month, 2 months (10:00–12:00)	T (nmol/L)	Baseline T 16,7±1,0; day 2: T 4,95±0,54 (−70%, p<0,001); day 7: T 8,19±1,11 (p<0,001); 1 month: T 13,97±1,59 (n.s.); 2 months: T 17,0±1,65 (n.s.)
Miller et al. (1998) [5]†	Localized PCa; n=63; age 43–67 years	RRP	Baseline, 12 months (both before 11:00)	T (ng/mL), FT (ng/dL, calculated), LH, FSH (mIU/mL)	T 3,5 → 4,4 (+28%, p<0,0001); FT 7.4 → 9,6 (+34%, p<0,0001); LH 2,5 → 3,1 (p=0,0004); FSH 3,8 → 4,8 (p=0,0001)
Madersbacher et al. (2002) [2]§	PCa (RP, n=49), BPH (TURP, n=51), observation n=46	RP; TURP; observation	Baseline, 12 months (7:00–10:00)	T (ng/mL), LH, FSH (mIU/mL)	RP: T 3,9 → 4,4 (+13%, p=0,18, n.s.); LH 5,2 → 8,9 (+71%, p=0,0004); FSH 5,7 → 9,3 (+63%, p=0,0003). TURP and observation: no significant changes in T/LH/FSH
Heracek et al. (2007) [15]‡	PCa pT2 (n=128), pT3–T4/N1 (n=122)	RRP	Preoperative (7:00–8:00)	T (nmol/L), FT (pmol/L, calculated), FSH (U/L)	FSH: pT2 5,63±0,31 vs pT3–T4/N1 7,07±0,65 (p=0,045 compared with baseline value); T: 16,00±0,69 vs 15,68±0,69 (n.s.)
Olsson et al. (2010) [6]†	Localized PCa; n=55	RP	Baseline, 3 months (8:00–12:00)	T (nmol/L), FT (nmol/L, calculated), LH, FSH (mIU/mL)	LH 3,24 → 4,97 (+53%, p<0,0001); FSH 6,62 → 8,04 (+21%, p<0,0001); T 13,7 → 12,7 (n.s.); FT 0,28 → 0,26 (n.s.)
Gacci et al. (2013) [7]‡,‖	Localized PCa; n=100 (92 with complete data)	RRP	Baseline, 1 month, 3 months (8:00–11:00)	T (nmol/L)‡, LH‖, FSH‖	T: 15,3 → 13,8 nmol/L at 1 month (p=0,021); by 3 months 14,4 (p=0,372 compared with baseline value). LH: 0,54 → 0,68 (1 month, p<0,0001); 0,54 → 0,65 (3 months, p<0,0001). FSH: 0,74 → 0,80 (1 month, p<0,0001); 0,74 → 0,82 (3 months, p<0,0001)
Lumbiganon et al. (2019) [8]‡	Localized/locally advanced PCa; n=85 (postoperative analysis n=65)	RP	Baseline, 2 weeks (7:00–10:00)	T (ng/dL), albumin, SHBG → BT (calculated)	T: 424,95±125,09 → 371,94±130,25 (−12,5%, p<0,001); BT: 154,57±5,57 → 123,20±4,93 (p<0,001)

Note. Values are presented as mean±SEM†, mean (95% CI)§, mean±SD‡, or median (Q1–Q3)‖ according to the original publication; p values are given relative to preoperative values; measurement units are presented as in the original publications.
RRP – retropubic prostatectomy; RP – radical prostatectomy; TURP – transurethral resection of the prostate; BPH – benign prostatic hyperplasia; PCa – prostate cancer; T – testosterone; FT – free testosterone; BT – bioavailable testosterone; LH – luteinizing hormone; FSH – follicle-stimulating hormone; SHBG – sex hormone-binding globulin; n.s. – differences not significant.

inevitably accompanies major surgery activates the hypothalamic–pituitary–adrenal axis, increasing stress hormones and mediators, including cortisol, epinephrine, norepinephrine, and pro-inflammatory cytokines, which predictably suppress gonadotropin-releasing hormone secretion and, consequently, testosterone production. This mechanism has been reproduced across different models and represents a universal physiological response rather than a marker of organic endocrine failure.

The observed dynamics are not specific to the oncological nature of the disease, because testosterone decline in the first days has been documented after a wide range of surgical procedures. In the study by Ghanadian et al. [14], in patients with BPH, the drop on postoperative days 2–3 was followed by recovery by weeks 4–6, similar to what is observed in malignant disease. Fendereski et al. [16] describe comparable patterns after nephrectomy, cholecystectomy, and other interventions. Such reversibility argues against a persistent androgen deficiency scenario, and the absence of a compensatory LH rise points not to true testicular failure but to temporary suppression of central regulation.

Nevertheless, if a universal stress response underlies most observed cases, one question remains: why is testosterone decline more pronounced and longer-lasting in some patients? This suggests that more localized mechanisms should be considered.

Neurovascular disturbances

The hypothesis that androgen decline after RP is driven by injury to neurovascular structures may appear plausible: the procedure affects the pelvic nerve plexuses and alters blood flow in periprostatic tissues. It has been suggested that denervation and local ischemia disrupt signaling cascades regulating testosterone secretion, including mechanisms related to venous outflow and local hormone transport [16]. However, in a study comparing hormonal profiles before and after RP and TURP, no substantial postoperative changes in testosterone levels were found [2]. If local injury were the leading factor, a clear relationship between the extent of damage and the severity of androgen deficiency would be expected, yet such a pattern is not observed.

The observations by Alyamani et al. (2023) [17] further complicate interpretation: higher testosterone levels in periprostatic veins compared with peripheral blood demonstrate the presence of local androgen gradients, but do not prove that loss of these gradients necessarily results in systemic hypofunction. Rather, this supports the concept of a complex and partially autonomous microphysiology of the region, whose function is only partly dependent on the integrity of the neurovascular bundle.

Data from Gacci et al. [7], describing a reversible testosterone decline with subsequent recovery without targeted correction, also argue against a model of persistent damage to regulatory pathways. If anatomical injury played a key role, spontaneous normalization would be unlikely. Instead, what is observed is a variable, transient phenomenon suggesting the involvement of factors beyond a simplified morphological explanation.

As a result, the neurovascular hypothesis of androgen deficiency appears more like a retrospective interpretation of laboratory findings than a rigorously confirmed concept. Its inability to explain why similar surgical extent is followed by testosterone decline in some patients but not in others suggests that anatomical injury, at most, is one of multiple secondary contributing factors.

Metabolic determinants

Obesity and associated metabolic disturbances are linked to lower testosterone levels [9, 18], and postoperative body weight changes are sometimes considered a potential driver of endocrine shifts. In this framework, testosterone decline after RP could be attributed either to accelerated loss of lean mass with an increase in visceral fat, or to altered tissue sensitivity to androgens as part of postoperative metabolic remodeling. Duarte et al. (2019) [18] showed that baseline obesity is already associated with reduced testosterone, and that postoperative metabolic deterioration is driven mainly by preoperative risk factors, lifestyle, and physical inactivity.

However, this model does not adequately explain early testosterone declines observed within the first days or weeks after RP [2, 5, 8, 17], when meaningful changes in body composition are unlikely to have occurred. In such cases, metabolic markers reflect a chronic background state rather than an acute trigger. Huhtaniemi and Forti (2011) [9] note that obesity and insulin resistance influence the hypothalamic–pituitary–gonadal axis slowly and progressively and cannot account for the reversible nature of postoperative changes.

Long-term follow-up demonstrates testosterone recovery without targeted metabolic correction, which contradicts a model in which body weight or waist circumference are central determinants [7]. These factors may modify the amplitude of the hormonal response, but are unlikely to determine whether it occurs at all. Reducing transient testosterone decline to a function of BMI or waist circumference is therefore an oversimplified model with multiple assumptions. In this context, it is reasonable to consider a hypothesis in which the prostate itself plays a key role as a local endocrine organ capable of autonomous regulation.

The prostate as an autonomous endocrine organ

Beyond systemic and metabolic factors, local androgen metabolism is considered a potential modifier of the endocrine profile before RP. Unlike circulating levels, local androgen concentrations may be determined by partly independent mechanisms, such as tumor metabolic activity, features of regional blood flow, and local expression of steroidogenic enzymes [17, 19]. These mechanisms may account for tumor heterogeneity, but they do not explain a decrease in testosterone after RP.

Clinical and experimental studies have documented a discordance between systemic and local androgen concentrations. Even with normal or reduced serum testosterone levels, intraprostatic and, likely, periprostatic androgen activity may remain high or even increase [17, 19]. It should be noted that these data pertain specifically to preoperative observations.

The most convincing support for this hypothesis is presented in the study by Alyamani et al. [17]. The authors were the first to demonstrate that, in a subset of patients with PCa, locally elevated testosterone in the periprostatic vein compared with peripheral blood was associated with an unfavorable prognosis, including a higher risk of recurrence and a more aggressive tumor course. Importantly, this is a prognostic association observed before surgery, rather than a mechanism of postoperative decline in serum testosterone. The proposed mechanisms maintaining locally increased androgen activity may theoretically include: (1) local synthesis of testosterone and its metabolites via steroidogenic enzyme activity in tumor tissue or the surrounding stroma; (2) altered venous architecture facilitating local androgen accumulation; (3) impaired venous outflow due to tumor infiltration or vascular compression.

The findings of Deb et al. (2021) [19] confirmed the presence of androgen steroidogenesis in both the transitional and peripheral zones of the prostate, including expression of key enzymes (CYP17A1, 3β-HSD, and SRD5A, presumably the second isoform typical of the prostate). This is consistent with the hypothesis that prostatic tissue may function as an autonomous endocrine organ, particularly under malignant transformation, when local androgen activity becomes pathophysiologically relevant. Nevertheless, these data characterize properties of the prostate itself and do not explain a decline in testosterone after its removal, indicating the need to consider the phenomenon of interindividual hormonal variability.

Interindividual hormonal variability

The endocrine response after RP lacks a single baseline pattern. Even before RP, testosterone levels differ by several-fold, so any “universal” trajectory of change becomes, in essence, a statistical average [6, 8, 15].

In the early postoperative period, testosterone decline often resembles a stress response to surgery, but the magnitude and duration of the decrease vary substantially both between patients and across studies [6, 8, 14, 18]. Acute postoperative androgen suppression is consistently observed, but its interpretation is highly method-dependent, as sampling conditions, diurnal variation, time since awakening, and other preanalytical factors may influence values to a clinically meaningful extent.

When individual data are examined, three typical endocrine trajectories can be distinguished: return to baseline, overshoot above baseline, or a modest but more prolonged decrease. The distribution of these trajectories depends on multiple factors, including the timing of measurement: a single determination several weeks or months after surgery can create the illusion of either persistent dysfunction or premature recovery [6, 8, 15].

A major source of discrepancy is the type of testosterone assessed, because marked discordance exists between total and free testosterone. Their dynamics often diverge due to fluctuations in SHBG related to age, obesity, insulin resistance, liver function, or drug effects [8, 16, 18]. With high SHBG, a biological deficit may be masked by normal total testosterone; with low SHBG, it may remain unrecognized. This is particularly relevant in later periods after RP, when metabolic factors begin to substantially influence SHBG levels and may produce a clinical picture resembling hypogonadism.

Technical issues also contribute to variability, since immunoassays and liquid chromatography–mass spectrometry (LC–MS), as well as the bioanalyzers used, yield different results, and parallel measurements in serum and urine may not match either in absolute levels or in dynamics [6, 8, 9].

Finally, systemic and local androgen status do not necessarily coincide: testosterone levels in prostatic tissue and periprostatic veins may differ markedly from level in peripheral blood [17, 19]. Attempts to explain this phenomenon via alternative mechanisms, such as an inhibin-mediated suppression hypothesis, have been unconvincing: in the corresponding study, it was tested and not confirmed [20]. This logically returns the focus to the combined role of central, peripheral, and methodological factors.

CLINICAL RELEVANCE OF METABOLIC CHANGES

The question of the clinical relevance of metabolic changes after RP is directly linked to uncertainty regarding patients’ androgen status. Data on postoperative testosterone dynamics are heterogeneous: some patients exhibit a transient decrease in the early postoperative period, whereas in others levels remain stable or even increase [5–8, 15]. Therefore, interpreting postoperative metabolic changes in the context of androgen deficiency becomes methodologically vulnerable. Additional complexity arises because, in older men, the diagnosis of LOH remains debated and lacks uniform criteria [9, 10, 21, 22].

Studies evaluating metabolic consequences of RP also do not provide a consistent picture. Neuzillet et al. (2021) [3] described a combination of metabolic syndrome features and erectile dysfunction one year after surgery, but found no association with testosterone levels. Kelkar et al. (2021) [23] showed that the risk of type 2 diabetes mellitus (T2DM) and adverse outcomes is determined primarily by obesity rather than by the fact of surgery itself. Teishima et al. (2021) [24] noted that changes in LOH symptoms after robot-assisted RP mainly reflected subjective complaints and comorbidity status, while no biochemical signs of androgen deficiency were detected.

The contrast with ADT is particularly illustrative. Meta-analyses show that pharmacological suppression of testosterone leads to a characteristic spectrum of adverse effects, including metabolic syndrome, cardiovascular complications, and disturbances in carbohydrate and lipid metabolism [13, 25, 26]. As a result, the causal relationship is evident and reproducible across different cohort studies. After RP, in contrast, such a consistent pattern is not observed, since neither metabolic syndrome risk nor cardiometabolic outcomes demonstrate a stable deterioration.

The absence of sustained changes comparable to ADT effects after RP underscores that most patients initially belong to an age group with a high risk and prevalence of obesity, T2DM, cardiovascular disease (CVD), psychoemotional disorders, and other modifying factors that can influence metabolic outcomes [3, 23]. It is possible that the combined impact of these factors prevents identification of a clear association between RP and metabolic disturbances. In this context, analysis of a younger and relatively healthy cohort, for whom RP is the first major intervention, is of particular interest: such a group could help assess the contribution of the surgery itself to changes in the metabolic profile.

DIAGNOSIS OF ANDROGEN DEFICIENCY IN THE POSTOPERATIVE PERIOD

Lack of diagnostic standards

Despite active discussion of hypogonadism in middle-aged and older men, there are no unified diagnostic standards for patients after RP. Major clinical guidelines on male hypogonadism, including the Endocrine Society (2018) [27], the American Urological Association (2018) [28], and the European Association of Urology (2025) [29], do not identify post-RP hypogonadism as a separate entity, and this issue is likewise not addressed in dedicated LOH guidelines [10].

The clinical manifestations after RP largely overlap with symptoms of LOH: decreased libido, fatigue, depression, cognitive impairment, and sleep disturbances [9, 21, 22]. At the same time, these overlap with specific consequences of surgery, including erectile dysfunction, urinary incontinence, and psychoemotional disorders. As a result, the same symptoms may be interpreted either as manifestations of hypogonadism or as consequences of surgery. Under these conditions, laboratory diagnostics become critically important, but they too face substantial methodological and conceptual limitations.

Laboratory methods for assessing androgen status

The most accurate method for assessing androgen status is liquid chromatography–mass spectrometry, recommended as the standard in international guidelines [27, 29]. However, this method is difficult to access in routine clinical practice and was not used in most studies of patients after RP. Earlier studies used radioimmunoassay [5, 15], whereas later investigations relied on enzyme immunoassays or chemiluminescent methods [7, 8].

Additional uncertainty is introduced by the circadian rhythm of testosterone secretion: for correct interpretation, blood sampling should be performed in the morning, in the fasting state, and at least twice [27, 29]. In most studies, this requirement was taken into account, and blood was collected in the morning hours (Table). Nevertheless, differences in the acceptable time window (from 7:00 to 12:00) and in the number of repeat measurements may limit reproducibility and comparability, especially when moderate postoperative testosterone fluctuations are being assessed.

Particular importance in diagnosis is attributed to free testosterone, traditionally regarded as a more sensitive marker of androgen status. In clinical practice, it is more often calculated from total testosterone, SHBG, and albumin concentrations, but such models rely on several assumptions and may produce substantial discrepancies when binding protein levels change [27, 29]. This is particularly relevant for RP, given the possible metabolic changes in this cohort. More accurate results may be obtained when free testosterone is measured after physical separation from total testosterone by equilibrium dialysis or ultrafiltration followed by quantitative analysis [30]. However, such approaches remain labor-intensive and poorly available in routine settings. Theoretically, free testosterone could prove to be a more informative indicator in this population, but at present there are no data confirming its superiority after RP. Therefore, its use should currently be regarded more as a promising direction for future research than as an established clinical tool.

Testosterone threshold values after RP

The use of universal testosterone threshold values is particularly problematic in the context of RP. Current hypogonadism guidelines recommend relying on a lower limit for total testosterone in the range of 8-12 nmol/L, confirmed by at least two morning measurements [27, 29]. LOH guidelines cite similar values (300 ng/dL or 12,1 nmol/L) [10, 28]. However, these criteria were developed in populations of otherwise healthy men and were not validated in cohorts of patients after RP.

In the study by Lumbiganon et al. (2019) [8], postoperative testosterone values in some patients fell into a gray zone, indicating the limitations of universal threshold values for assessing androgen status in the postoperative period. In contrast, Gacci et al. (2013) [7] documented a transient decrease in total testosterone at one month with recovery by the third month, but the applicability of standard diagnostic cutoffs in the postoperative setting was not discussed by the authors. Heracek et al. (2007) [15] showed that differences between localized and locally advanced PCa concerned mainly FSH levels, whereas total testosterone values remained comparable. Although the authors did not specifically aim to diagnose androgen deficiency, their data suggest that using a fixed total testosterone threshold (<12 nmol/L) would have obscured the observed differences. This further supports the view that universal threshold values are not always adequate for assessing androgen status in patients with PCa.

Questionnaires as a clinical tool after RP

In middle-aged and older men, questionnaires such as the Aging Males' Symptoms scale (AMS) and the Androgen Deficiency in the Aging Male questionnaire (ADAM) are widely used for hypogonadism screening and for evaluating symptoms of testosterone deficiency [21]. These instruments were originally developed for the general population and have not been validated in the postoperative setting. Even in the general population, they are regarded only as auxiliary tools for structuring complaints and do not have independent diagnostic value, since their results are subject to considerable fluctuation over time [21]. In patients after RP, their usefulness is even more limited: the key symptoms captured by these questionnaires, including erectile dysfunction, reduced libido, and fatigue, are nearly universal in this cohort and reflect not so much androgen deficiency as the consequences of surgery and the influence of accompanying factors [24]. As a result, the use of questionnaires in this group is clinically uninformative and cannot serve as a basis for diagnosing hypogonadism.

TESTOSTERONE REPLACEMENT THERAPY AFTER RP

Origins of the discussion on TRT after RP

Historically, attitudes toward TRT after PCa were shaped by the concept of a direct dependence of tumor growth on androgen levels [31]. As a result, the very possibility of prescribing testosterone after surgery was long not considered, since such therapy was viewed as fundamentally contraindicated.

The situation changed with the emergence of the "saturation model" proposed by Morgentaler and Traish (2009) [32]. According to this concept, prostatic tissue is sensitive to androgens only up to a certain receptor saturation threshold, and further increases in testosterone concentration do not enhance the proliferative effect. This model made it possible to reconsider the safety of TRT in patients after RP.

The first clinical observations were presented in the study by Pastuszak et al. (2013) [33], where, in carefully selected patients after RP, TRT was not associated with an increased rate of biochemical recurrence. Subsequently, analytical reviews appeared emphasizing the possibility of prescribing testosterone to such patients with careful selection and discussing the potential safety of this approach [11, 34]. In this context, the study by Ahlering et al. (2020) [35], which reported a paradoxical trend toward a reduced risk of recurrence during TRT, is of particular interest.

However, the original context of these observations should be taken into account. Most studies were not aimed at developing a new management strategy for patients after RP, but rather at solving a practical problem: how to manage men who already had hypogonadism before surgery or who might require TRT in the future for reasons unrelated to the prostate. In fact, the discussion of exogenous testosterone after RP emerged not as recognition of hypogonadism as a consequence of surgery, but as debate over whether therapy may be prescribed to patients treated for PCa when other indications are present [11, 12, 34].

Lack of an evidence base

The main limitation in discussing TRT after RP is the absence of randomized controlled trials. To date, the only identified project directly addressing this issue is the ENFORCE study (2025) [36], which is currently ongoing and is designed to assess the impact of perioperative testosterone levels on functional and oncological outcomes after RP.

Observational studies evaluating the safety of TRT after RP are limited by retrospective design, lack of randomization, risk of selection bias, and in some cases an insufficient number of patients, and therefore do not allow reliable clinical conclusions to be drawn [33, 35]. These data only allow formulation of a hypothesis and cannot serve as a basis for changes in clinical practice.

This uncertainty is also reflected in current clinical guidelines, which do not include indications for TRT in patients after RP [27–29]. The lack of data is not accidental and indicates the absence of convincing evidence for either the benefit or the safety of this intervention.

A key issue remains the questionable nature of the concept of post-RP hypogonadism itself. Most studies document only transient testosterone fluctuations in the early postoperative period without the development of persistent androgen deficiency [5, 7, 8]. In this situation, discussion of TRT after RP risks becoming an attempt to treat an unproven phenomenon, resembling overdiagnosis, where treatment justifies its own existence rather than addressing the patient's actual needs [37].

SURVEILLANCE STRATEGIES AND RISK STRATIFICATION

Oncological outcomes and androgen status

If one assumes that decreased serum testosterone after RP is persistent in some patients, its most important consequence could be an effect on oncological outcomes. Theoretically, low androgen levels might slow tumor growth, but in clinical practice the consequences are much less straightforward. In such a model, testosterone could be regarded as a surrogate marker of tumor aggressiveness or a predictor of adverse disease course, which equally opens possibilities for more precise risk stratification and for diagnostic errors.

Systematic reviews and meta-analyses show that lower baseline testosterone levels in patients with localized PCa are associated with a higher risk of tumors with unfavorable morphological features and with upgrading of the Gleason score when biopsy material is compared with postoperative specimens [4, 38]. However, such upgrading is multifactorial in nature: it is influenced by the initial clinicopathological characteristics of the tumor and its biology, biopsy technique, and the representativeness of the sampled tissue [39]. In this context, testosterone is only one of many factors.

Moreover, the local androgen milieu may be more important than the systemic testosterone level. Elevated testosterone concentrations in periprostatic veins are associated with a higher risk of biochemical recurrence after RP [17], indicating that the tumor microenvironment may override the impact of systemic testosterone changes. Even if postoperative androgen decline is observed, its prognostic role remains uncertain, since baseline testosterone levels and local venous mechanisms appear to be more relevant to disease course than post-RP hypogonadism as an independent clinical category.

Testosterone and metabolic risk

If RP can indeed lead to a decrease in testosterone levels, the most likely clinical consequence would be an effect on the risk of metabolic syndrome and associated CVD. Such a hypothesis appears logical, given that hypogonadism in men is associated with disturbances in carbohydrate and lipid metabolism, increased visceral fat mass, and greater cardiovascular risk.

Observational studies support an association between hormonal changes and metabolic disturbances in patients treated for PCa. In men with metabolic syndrome, signs of androgen deficiency are detected more frequently, and the severity of these disturbances is associated with worse quality of life and erectile function after RP [3, 26]. These observations allow testosterone changes to be considered as one possible link in the pathogenesis of postoperative metabolic disturbances.

However, metabolic syndrome and CVD in men with PCa develop under the influence of many factors, including age, lifestyle, comorbidities, and treatment received [40]. The presence of T2DM and obesity in itself significantly worsens prognosis after RP, increasing the risk of recurrence and mortality regardless of hormonal status [23]. Therefore, the influence of the surgery itself and of possible postoperative hormonal changes is difficult to isolate. Moreover, contemporary meta-analyses have shown that the pronounced metabolic and cardiovascular risks are characteristic primarily of ADT rather than of surgery [25]. This suggests that postoperative endocrine changes may be associated with metabolic disturbances, but there is no evidence of a direct causal relationship between them. Most likely, they reflect interaction with pre-existing risk factors rather than being their primary source.

Functional outcomes after RP

If RP is indeed accompanied by a decrease in testosterone, it would be logical to expect changes in sexual health, general well-being, and quality of life. Some studies support an association between low testosterone and unfavorable functional outcomes, including more pronounced erectile dysfunction and lower quality-of-life scores one year after RP [3], as well as worse sexual health in cohort studies of men treated for PCa [41].

However, these findings require cautious interpretation. Most functional impairments after RP are directly related to injury of neurovascular structures and to other mechanical consequences of surgery rather than to endocrine changes. Many symptoms traditionally attributed to hypogonadism are nonspecific: they may be determined by age, comorbidities, or psychological factors, and in the postoperative period their specificity is even lower [24]. Although the hypothesis that androgen deficiency affects quality of life and functional outcomes after RP appears plausible, it has not been convincingly confirmed by clinical data: the local consequences of RP remain the dominant factor.

Conclusion

At present, the hypothesis of post-RP hypogonadism remains not a clinical reality but a research model. A decline in testosterone after RP does occur, but its pattern is transient, variable, and methodologically vulnerable. Unlike ADT, where the consequences are reproducible and predictable, after RP there are no convincing signs of persistent androgen deficiency or of related clinical outcomes. Associations with oncological outcomes, metabolic syndrome, and quality of life remain contradictory and lack prognostic value.

A weak point of this hypothesis is also laboratory diagnosis. Universal testosterone threshold values are not adapted to this population, laboratory methods are heterogeneous, and clinical questionnaires are uninformative in the postoperative setting. This is important, but not decisive: in clinical practice, the patient's actual condition remains paramount. Under these circumstances, even discussion of TRT risks turning into treatment of an unproven phenomenon "just in case."

Nevertheless, this does not make the hypothesis useless. Rather, it draws attention to the interplay between surgical stress and endocrine regulation, the local physiology of the prostate, and interindividual hormonal variability, shifting the discussion from defining a new nosological entity to re-examining the boundary between physiological variation and disease. Future studies should focus on prospective evaluation of younger and relatively healthy patients undergoing RP, using highly accurate methods for assessing androgen status. Stratification by baseline characteristics, analysis of local androgen mechanisms, and assessment of the clinical relevance of identified changes through their relationship with oncological, metabolic, and functional outcomes are needed. Only such a strategy will bring us closer to answering the main question: is androgen deficiency after RP a phenomenon being overlooked in clinical practice?

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IATROGENIC INJURY TO THE URETERS AS A COMPLICATION OF SURGICAL INTERVENTIONS ON THE PELVIC ORGANS

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With the progressive development of video endoscopic and laparoscopic operations, a direct relationship is formed with an increase in the number of patients with iatrogenic ureteral injury (hereinafter referred to as IUI). In the postoperative period, it is sometimes difficult to identify this type of ureter injury, and complications that occur in the long term after surgery can significantly worsen the patient's quality of life, and even lead to death.
The literature review was conducted in order to study the mechanisms of the most common iatrogenic ureteral injuries, as well as methods of prevention and treatment of this complication.
Scientific articles were critically reviewed by searching the main electronic databases – Medscape, PubMed, Scopus, as well as scientific electronic libraries «CyberLeninka», RSCI and eLibrary.ru. The following search words were used: iatrogenic ureteral injury, ureteral damage, complications of endovideosurgery in urology, obstetrics and gynecology, emergency urology. 42 publications of domestic and foreign authors have been selected for this scientific article.
The literature review highlights the authors' current understanding of the aspects of IUI in various types of pathologies and surgical interventions, as well as methods of prevention and treatment of this type of complications.
IUI is an important, complex and urgent problem of modern urology. The literature review is aimed at highlighting such an urgent problem in order to reduce the risk of injury to the ureters during surgical procedures not only by urologists, but also by related specialists – obstetricians and gynecologists, proctologists, surgeons and traumatologists.

Key words: *iatrogenic injury of the ureter, damage to the ureter, complication of video e ndoscopy in urology and gynecology, emergency urology*

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The study of the causes and mechanisms of ureteral injury resulting from surgical interventions remains an important issue in operative urology, obstetrics and gynecology, and abdominal surgery. Iatrogenic ureteral injury represents a major diagnostic challenge and poses a substantial risk to the patient, as it may lead to severe, life-threatening complications such as retroperitoneal phlegmon, urinary peritonitis, and urosepsis. In the late period after iatrogenic ureteral injury, the development of pyelonephritis with subsequent nephrosclerosis, as well as the formation of ureterovaginal fistulas, may seriously impair the patient's quality of life [1].

It should be emphasized that, despite advances in surgical technique, the development of endoscopic and video-assisted surgery with improved visualization of the operative field, and the refinement of instruments and materials, ureteral injury remains a clinically significant problem that should not be overlooked or underestimated. The active expansion of laparoscopic surgery and the widespread implementation of videoendoscopic procedures in hospitals are directly associated with an increasing number of patients with iatrogenic ureteral injury [2, 3]. Thus, iatrogenic ureteral injury is a relevant problem not only for urologists, but also for general surgeons, gynecologists, colorectal surgeons, and even traumatologists, which underscores the need for effective prevention and for improving the quality and diagnostic accuracy of methods used to detect this type of injury.

This literature review was undertaken to examine the mechanisms of the most common iatrogenic ureteral injuries, as well as methods for the prevention and treatment of this complication.

The literature search was carried out using the major contemporary electronic databases, including Medscape, PubMed, and Scopus, as well as the electronic library databases CyberLeninka, RSCI, and eLibrary.ru. The following search terms were used: iatrogenic ureteral injury, ureteral injury, complications of endoscopic and video-assisted surgery in urology and obstetrics and gynecology, and emergency urology. For the present publication, 42 articles were selected and critically appraised.

This review summarizes the current perspectives of Russian and international authors on the problem of iatrogenic ureteral injury with the aim of reducing the risk of ureteral trauma during surgical procedures performed not only by urologists, but also by related specialists, including gynecologists, colorectal surgeons, general surgeons, and traumatologists.

Prevalence of Iatrogenic Ureteral Injury

The ureter is located in the retroperitoneal space. It is mobile and protected by the surrounding muscles, bones, and soft tissues, which minimizes the risk of injury from external trauma. In contrast, iatrogenic ureteral injury iatrogenic ureteral injury is a more common and clinically significant complication resulting from direct damage to the ureter, including complete or partial transection, crushing, suturing or ligation, and thermal injury [4-6].

According to both international and Russian authors, the proportion of iatrogenic ureteral injuries among intraoperative complications ranges from 1.5% to 40%, and these figures appear to be increasing [4, 7-10]. According to data from colleagues in the United Arab Emirates (UAE) at Khalifa University of Science and Technology, the overall rate of iatrogenic ureteral injury as of 2002 was 11.8%, with urological, obstetric and gynecological, and general surgical procedures being the main causes [11].

It is well known that ureteral injury is most commonly encountered in obstetric and gynecological practice: 73% of cases occur during surgery on the female reproductive organs, whereas in urological and abdominal surgery this complication is observed much less frequently, at approximately 14% [8]. It should also be noted that the incidence of ureteral injury during surgical procedures for benign neoplasms of the female reproductive system, such as uterine fibroids, ranges from 1% to 5%, whereas in malignant disease this rate rises to 30% [4].

According to the 2024 clinical guidelines of the European Association of Urology (EAU), iatrogenic ureteral injury is most frequently reported during laparoscopic hysterectomy (0.2-6.0%), urogynecological procedures for urinary incontinence or pelvic organ prolapse (1.7-3.0%), vaginal hysterectomy (0.02-0.5%), abdominal hysterectomy (0.03-2.0%), and emergency cesarean section (0.01-0.06%). The ureter may also be injured during colorectal surgery, especially during abdominoperineal resection and low anterior resection of the rectum (0.15-10%) [6]. Complications may also occur during ureteroscopy, including ureteral perforation (0.2-2.0%), submucosal passage below the ureteral orifice, and ureteral avulsion (0.3%). According to individual studies, ureteral avulsion was observed in 0.1% of patients after 9,555 ureteroscopic procedures [12, 13].

During radical prostatectomy, the reported incidence of ureteral injury is as follows: 0.05-1.6% in open retropubic radical prostatectomy and 0.05-0.4% in robot-assisted radical prostatectomy [6].

Topographically, injury to the lower third of the ureter is diagnosed most often, accounting for 74% of cases; injury to the middle third occurs in 13%, and injury to the upper third in another 13% [8]. This distribution is explained by anatomical features: the pelvic portion of the ureter lies close to organs that frequently undergo surgical intervention, and in this region the ureter has a thin wall, a narrow lumen, and specific vascular characteristics [14].

Ureteral injury cannot always be recognized intraoperatively: according to published data, only 10% to 25% of injuries are identified during surgery [15]. In most cases, signs of iatrogenic ureteral injury become apparent several days after the procedure, when symptoms of peritonitis, intoxication, and/or upper urinary tract obstruction develop [6]. Difficulties in intraoperative diagnosis are most often associated with massive bleeding and the absence of pathognomonic clinical signs of iatrogenic ureteral injury. Another reason for delayed diagnosis is that urine leakage does not always occur intraoperatively in cases of iatrogenic ureteral injury, and even when it does, it may be obscured by heavy bleeding, which, as noted above, may accompany pelvic surgery [2, 16].

Iatrogenic Ureteral Injury During Obstetric and Gynecological Surgery

As noted above, ureteral injury remains one of the most frequent complications in obstetric and gynecological practice. This is primarily attributable to the close anatomical and functional relationship between the female reproductive and urinary systems [17]. Several factors contribute to the high risk of ureteral injury.

First, the widespread adoption of laparoscopic procedures in gynecology has played an important role. Over time, these interventions have become more extensive, technically demanding, and multistage, which has been accompanied by an increase in the number of patients with iatrogenic ureteral injury [8, 17, 18].

Second, ureteral injuries often occur at characteristic anatomical sites, including the crossing with the iliac vessels, the point where the ureter crosses the uterine artery, the ovarian fossa, where the ureter is crossed by the ovarian vessels within the suspensory ligament of the ovary, the vesicovaginal space, where the distal ureter lies close to the cervix, the base of the rectovaginal septum, and the lateral aspect of the uterosacral ligament [19].

Third, certain obstetric procedures and individual stages of obstetric care may also be associated with ureteral injury.

Prolonged labor may predispose to ureteral injury when premature rupture of the membranes is followed by abrupt uterine contraction, resulting in tight compression of the fetal head against the pelvic organs and potentially causing necrosis of the distal ureter with subsequent formation of a ureterovaginal fistula.

In some cases, the use of bullet forceps may also endanger the ureters, since their pointed edge may perforate the vaginal wall and come into close proximity to the urinary tract. Ureteral injury has also been described during the application of Baksheev forceps and Henkel-Tikanadze parametrial compression for control of postpartum hemorrhage [17].

According to the clinical studies of Yu.V. Tsvelyov and S.B. Petrov (2006) and D.V. Kan (1986), transverse incision of the cervix, including during cesarean section, especially when operating in the lower uterine segment, increases the risk of ureteral injury [7, 17].

However, the main cause of IUI in gynecology is hysterectomy, including procedures performed for benign and/or malignant neoplasms of the female reproductive system [17]. This is related to alterations in the topographic anatomy of the pelvic organs as the neoplasm enlarges. Tumor growth leads to displacement of the major uterine vessels and the ureters, which substantially increases the risk of ureteral injury during hysterectomy, since the ureter may inadvertently be included in the suture during ligation of the suspensory ligament of the ovary. According to Yu.V. Tsvelyov and S.B. Petrov (2006), among 18 women with iatrogenic ureteral injury during gynecological surgery, 86% of injuries occurred during hysterectomy with adnexectomy [17].

Accidental ureteral injury is further facilitated by massive bleeding, which is not uncommon during hysterectomy. During attempts to achieve hemostasis with electrocautery, clamps, or hemostatic ligatures, the ureter may be burned, compressed, or ligated together with adjacent vessels, and this complication cannot always be recognized in a timely manner [4].

Another predictor of iatrogenic ureteral injury is the presence of interligamentous masses, such as tumors or fibroids located between the leaves of the broad ligament of the uterus. These lesions may become adherent to the ureters and alter their position within the pelvis, making identification of the ureters more difficult [17].

The risk of ureteral injury also increases in the presence of severe adhesions, particularly after previous pelvic surgery, in endometriosis, inflammatory disease, or distortion of pelvic anatomy following trauma [20].

Iatrogenic Ureteral Injury During Coloproctological Surgery

Ureteral injuries are encountered relatively frequently during surgical treatment of colorectal cancer, with reported rates ranging from 0.7% to 15%. Colorectal cancer is a serious oncological disease, and its surgical treatment is associated with a high risk of complications involving the urinary tract [21]. According to studies from the Russian Scientific Center of Roentgenoradiology, ureteral injury during surgical treatment of colorectal malignancies was identified in 7.4% of cases [21].

According to the published data, the lower third of the ureter is affected most often, accounting for 91% of all cases. This is related to the close anatomical relationship between the ureter and the distal colon and rectum [22]. These complications are highly dangerous for patients. It has been reported that mortality may be associated not only with the malignancy itself but also with complications involving the urinary tract, which may be iatrogenic in nature and may be detected only postoperatively [23].

One of the coloproctological procedures associated with a high risk of ureteral injury, reported by the EAU 2024 guidelines as 0.15-10%, is abdominoperineal resection of the rectum for cancer. According to observations reported by several authors, the following iatrogenic ureteral injuries and their late sequelae were observed during this procedure: ureteral stricture in 19% (A.A. Dovlatyan, 2012), coagulation necrosis of the ureteral wall in 0.3% (V.G. Savinkov et al., 2011), ureteral strictures with or without hydronephrosis in 2.6% (V.G. Savinkov et al., 2011; S.M. Demidov et al., 2016), and ureterovaginal fistulas in 2.6% (S.M. Demidov et al., 2016) [4, 24, 25].

Other surgical procedures used in the treatment of malignant rectal tumors and their associated complications should also be considered. There are reports indicating that anterior resection of the rectum has resulted in transection of the lower third of the ureter, long-segment ureteral fibrosis during its separation from the tumor without disruption of its integrity, and formation of a urinoma causing ureteral compression and scarring complicated by hydronephrosis, with one such case diagnosed 3 years after surgery [24, 25].

The causes of ureteral injury during abdominoperineal resection of the rectum, and during coloproctological surgery in general, include insufficient preoperative information about the condition of the urinary tract in oncological patients, altered anatomy and displacement of the ureters by the tumor, tumor invasion into the ureter, shared blood supply and innervation of the bowel and ureter, and removal of pelvic tissue followed by sclerosis in the operative field involving the ureters, even without direct ureteral injury, but with secondary changes due to scarring. Involvement of the posterior layer of the peritoneum in the tumor process, accompanied by reactive edema, also affects the adjacent ureter, which in such situations may be displaced toward the spine [21, 26].

The risk of ureteral injury also increases during ligation of the inferior mesenteric artery, dissection of the rectosigmoid colon, and mobilization of the lateral ligaments of the rectum [22, 27].

Iatrogenic Ureteral Injury During Urological Surgery

Gynecological and coloproctological procedures remain the leading causes of iatrogenic ureteral injury; however, ureteral injury may also occur during urological procedures. During ureteroscopy, such injuries most commonly occur at the junction of the upper and middle thirds of the ureter and 3-4 cm below the ureteropelvic junction, where large calculi are more likely to become impacted. Forceful extraction of these stones may lead to ureteral avulsion or perforation.

Ureteral avulsion is a serious injury that may occur as a complication of retrograde endoscopic procedures, particularly ureteroscopic lithotripsy. This injury may result from forceful extraction of a large stone from the ureteral lumen or from impaction of the ureteroscope within the juxtavesical or another narrowed segment of the ureter. Risk factors include long-standing impacted ureteral stones and a history of prior urinary tract surgery [12, 28, 29].

Ureteral perforation may occur during guidewire placement, traumatic instrument manipulation, stone fragmentation, or stone extraction. The likelihood of this complication depends on the surgeon's experience and the energy source used for lithotripsy [30].

According to the study by S.Kh. Al-Shukri et al. (2014), among 128 radical prostatectomies, intraoperative ureteral injury was diagnosed in only one patient. The authors did not specify the nature of the injury [31]. Urologic oncologists should strictly adhere to the principles of safe pelvic lymph node dissection. During radical prostatectomy, pelvic lymph node dissection is performed in close proximity to the ureters and involves extensive tissue dissection, which increases the risk of iatrogenic ureteral injury. Ureteral injury may also occur during bladder neck dissection and at the point where the ureter crosses the iliac vessels.

According to the literature and clinical cases, robot-assisted radical prostatectomy or simple prostatectomy may result in injury to the distal ureter in the presence of an enlarged median prostatic lobe. This risk is especially increased when the ureteral orifices are closely adjacent to the median lobe, which creates technical difficulties during resection and subsequent bladder neck reconstruction. It is important to remember that extensive bladder neck resection is hazardous for the ureters because of their close proximity to the resection margin. Dissection in this area requires particular attention, and maximum caution is necessary during anastomosis formation in order to minimize the possibility of ureteral obstruction during suturing [32, 33].

Transurethral surgery of the prostate and bladder should also not be overlooked, as iatrogenic ureteral injury may likewise be quite likely in such procedures, especially in the presence of large bladder tumors, atypical anatomy of the prostate, and insufficient surgeon experience.

Prevention of Iatrogenic Ureteral Injury

The main principle of any surgical intervention is the prevention of complications and intraoperative injury to adjacent organs. In pelvic procedures, this issue is especially relevant because of the intimate anatomical proximity of organs belonging to different systems in this region.

Given the severe complications that may result from ureteral injury, surgeons have developed and continue to develop methods for the prevention of iatrogenic ureteral injury. Some of these methods have, over time, fallen out of favor and are no longer recommended in clinical practice, whereas others remain the subject of discussion and scientific debate.

One of the most obvious methods of preventing ureteral injury is direct intraoperative identification of the ureter. Typical danger points may serve as landmarks for the surgeon, for example the iliac vessels, with the ureter located near the internal iliac artery, and the ovarian vessels, which most often cross the ureter in its middle third and are situated medially [7]. However, no matter how well the surgeon knows the anatomy, a tumor often significantly alters the topographic anatomical relationships of the organs, thereby increasing the risk of intraoperative iatrogenic ureteral injury [14]. Visual identification and monitoring of the ureter are also facilitated by its peristaltic contractions, the so-called visual control [7, 14].

Since the main cause of ureteral injury is displacement of the ureter within the pelvis, an important preventive measure is the preoperative use of radiological imaging methods, such as intravenous excretory urography or contrast-enhanced multislice computed tomography. This allows the surgeon to obtain accurate information about the topographic location of the ureters, their functional status, the degree of ureteral involvement in the pathological process, and any developmental anomalies, for example a duplicated ureter, megaureter, or aberrant vessels.

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One of the controversial methods for prevention of iatrogenic ureteral injury is ureteral catheterization. In the 1980s, ureteral stenting before major and complex pelvic surgery was considered indisputably beneficial. It was claimed that this method was a valuable preventive measure in the event of ureteral injury and was recommended to young physicians to facilitate orientation within the pelvis [7]. However, contemporary literature refutes these views, and stenting is now considered to be associated with the risk of introducing infection into the renal parenchyma and may itself be complicated by ureteral injury. In addition, more and more authors tend to conclude that ureteral stenting helps to detect injury to the ureteral wall intraoperatively in a timely manner, but does not prevent it [14, 24, 34]. It should be noted that intraoperative localization and identification of the ureter are most effective when catheterization is performed using an illuminated catheter [14]. Another promising method for prevention of IUI is ureteral visualization by intravenous administration of sodium fluorescein, which produces fluorescence of the ureters and thereby allows monitoring of their course [14].

Treatment of Iatrogenic Ureteral Injury

The main task of the surgeon in cases of iatrogenic ureteral injury is to diagnose the injury in a timely manner, correct it, and preserve the patient's kidney, since both renal function and viability may decline substantially. The principles of treatment do not differ from those applied to any other type of ureteral injury, including injuries identified in the late postoperative period.

In cases of recent injury and a small ureteral defect, routine drainage with a ureteral stent has proven effective. The duration of such drainage may vary considerably and most commonly averages 3-6 weeks. In the late postoperative period, stent drainage is usually of limited efficiency, and more invasive interventions are required.

One of the treatment options for ureteral injury is reconstructive surgery, which may be divided into two major groups: reconstruction using native tissues of the urinary tract, including ureteroureterostomy, transureteroureterostomy (end-to-end, end-to-side), ureteral reimplantation, psoas hitch, the Boari procedure, the Demel procedure, and ureterocystostomy; and reconstruction using bowel segments, including ureteroileocystostomy, U-shaped ileoureteroplasty, and appendicoureteroplasty [35]. It has been noted that there should be no "standardization" for patients with iatrogenic ureteral injury: conservative and surgical treatment must be selected individually depending on the level of injury, the nature of injury, concomitant pathology, and the time interval since the injury was identified. However, based on comparison of studies by various authors, the Boari procedure, ureteroureterostomy, and ureteroileocystostomy are used most often (Table).

Each reconstructive ureteral procedure has specific indications and is used in different clinical situations. Thus, in the case of intraoperative transection of the ureter in its pelvic part, formation of an end-to-end ureteroureteral anastomosis is recommended. Both ends of the ureter are sutured over a stent catheter (Ch 7-8) with interrupted sutures incorporating all layers of the ureteral wall. The required duration of ureteral drainage is 2-6 weeks. Excretory urography or CT urography is indicated at the time of discharge after removal of the stent [4].

Ureterocystostomy may be direct or indirect. Direct ureterocystostomy is indicated when the ureteral injury is located in the prevesical segment, within 5 cm of the bladder [38]. When the ureteral defect is more extensive, indirect ureterocystostomy is indicated. This procedure was significantly modified by the Italian surgeon A. Boari, who fashioned a rectangular flap from the anterior bladder wall, from which a tube was subsequently constructed; he then transected the ureter at the junction of the middle and lower thirds and invaginated it into the newly formed bladder tube within the submucosal layer. The Boari procedure is indicated when the injured segment involves the entire pelvic portion of the ureter, that is, more than 5 cm from the bladder [35, 38]. Although the Boari procedure has, of course, undergone certain modifications over time, this method, and its variations, remains one of the most frequently used in iatrogenic ureteral injury.

The psoas hitch technique is commonly described in the international literature and has also been adopted in our country. The essence of this method lies in ureteral reimplantation into the bladder and fixation of the bladder base to the lateral pelvic wall, most often to the tendon of the psoas muscle. In this way, tension on the ureterovesical anastomosis is reduced. The procedure is indicated in extensive injuries of the distal ureter, as well as in ureteral fistulas. At present, the psoas hitch technique is often combined with the Boari procedure and its modifications; such a combination is particularly effective in ureteral defects up to 12 cm in length [4].

Intestinal ureteral replacement is the procedure of choice for long recurrent strictures of the upper urinary tract in which reconstruction with native urinary tract tissues is not feasible. The essence of the method lies in resection of a bowel segment, including ileum, colon, or appendix, and creation of uretero-intestinal and intestinal-bladder anastomoses using the graft [12, 39, 40]. It should be noted that this type of surgery requires careful preoperative preparation and strict patient selection. Absolute contraindications to these procedures include persistent loss of renal function and inflammatory bowel disease.

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Appendiceal reconstruction should be mentioned separately, since the appendix is rarely used as graft material for creation of a ureteral anastomosis [39]. Describing the results of his own studies, B.K. Komyakov notes that appendiceal reconstruction is advisable for defects of the lower and middle thirds of the right ureter, owing to the topographic and anatomical proximity of the appendix to these segments. In exceptional cases, appendiceal reconstruction of the pelvic portion of the left ureter is possible because of their relative proximity compared with the abdominal and pelvic parts [39]. The authors also note that appendicoureteroplasty is the procedure of choice for radiation-induced lesions of the urinary tract [41].

When reconstruction with intestinal segments and tissues of the urinary system is not feasible, alternative surgical techniques are used for the treatment of ureteral injury. Of particular interest is the use of buccal mucosal grafts for reconstruction of long ureteral defects. According to recent studies, this method demonstrates high efficacy, good long-term outcomes, and safety compared with intestinal reconstruction [42]. The literature also notes that a “salvage” procedure may be kidney autotransplantation into the iliac fossa with anastomosis of the renal and iliac vessels, which may be performed not only laparoscopically but also by a retroperitoneoscopic approach. However, such procedures are more often performed in large medical centers and require high qualifi-

Table

Reconstructive ureteral procedures used in surgical practice

Procedure	Author, year Number of performed procedures		
	A.A. Dovlatyan, 2012 [4] Total: 23	B.K. Komyakov, V.A. Ochelenko, T.Kh. Al-Attar, 2014 [36] Total: 175	O.B. Loran, A.V. Seregin, Z.A. Dovlatov, 2015 [37] Total: 137
Boari flap reconstruction	14	102	107
Demel procedure	1	–	–
Gregoir procedure	2	–	–
Ureterocystostomy	2	–	14
Ureteroureterostomy	3	–	10
Psoas hitch procedure	–	–	–
Ureteroileocystoanastomosis	–	54	–
U-shaped ileoureteroplasty	–	–	–
Appendicoureteroplasty	–	19	–
Other methods (transureteroureterostomy, endoureterotomy)	1	–	6

cation and substantial practical experience on the part of the surgeon [42].

At present, the latest medical and technical advances have made it possible to significantly improve the outcomes of ureteral surgery through the use of modern robotic systems. This innovation has become the pinnacle of the development of minimally invasive endoscopic and laparoscopic surgery and urology, making it possible to perform the most complex reconstructive procedures in all parts of the ureter with maximal precision and reliability, minimal tissue trauma, and excellent long-term outcomes.

Iatrogenic ureteral injury is a relevant problem in modern operative urology, surgery, and gynecology that requires careful prevention, timely diagnosis, adequate treatment, and competent postoperative management of the patient. Awareness of the anatomical and topographic features of the patient's urinary system and control of ureteral location during surgery are the main preventive measures that help reduce the risk of ureteral injury during pelvic surgery.

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CHRONIC RECURRENT CYSTITIS: ANALYSIS OF THE CURRENT STATE OF THE PROBLEM

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Introduction. As part of this literature review, a comprehensive analysis of the current state of the problem of chronic recurrent cystitis was performed. Key aspects of the disease, including mechanisms of its development, features of the diagnostic work-up, and approaches to therapeutic management, are covered in the review. To provide an objective scientific overview, a systematic search for relevant sources was carried out in major international databases, including Medline, PubMed, and EMBASE. The analysis of the available literature indicates that viral CRC represents a substantial issue in contemporary urological practice and is actively discussed within the professional community. Extensive coverage of the topic in scientific publications and online resources reflects its high relevance and clinical significance.

The close attention of researchers to this problem is driven by a set of interrelated challenges. First, timely and accurate diagnosis remains difficult. Verification of cystitis etiology is often objectively challenging, which complicates differential diagnosis with other inflammatory conditions of the bladder. Another aggravating factor is the lack of unified, widely accepted standards of therapeutic management for chronic recurrent cystitis of any etiology. The clinical course is further complicated by its typical relapsing pattern, with exacerbations alternating with temporary remissions, which may falsely suggest that the treatment is effective.

Aim. Based on literature data identify features of the course of chronic recurrent cystitis and to determine differential diagnostic criteria for the development of an infectious process caused by various agents, taking into account their pathogenic properties.

Keywords: *chronic recurrent cystitis, urinary tract infections, urothelium, viral cystitis*

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Introduction. In contemporary uroinfectology, issues related to chronic recurrent cystitis continue to be the subject of intensive scientific debate and clinical research. The problems of etiology, mechanisms of development, diagnosis, and therapeutic management of patients with recurrent urinary tract infections still cannot be regarded as fully resolved, and they require further in-depth study and conceptual refinement.

Substantial progress in diagnostic technologies has had a marked impact on the conceptual understanding of the pathophysiological processes underlying urinary tract infection and bladder injury. The development of highly sensitive molecular genetic methods, expanded microbiological investigations, and imaging technologies has made it possible to revise established views on the mechanisms of onset and progression of these pathological conditions [1].

One of the most significant shifts in the scientific paradigm has been the fundamental reconsideration of the concept of urine sterility. For a long time, the prevailing view in medical practice was that the urine of a healthy individual should be completely free of microorganisms. However, the findings of contemporary studies have convincingly refuted this assumption. It has been established that the urinary tract possesses its own microbiome, which is a complex community of microorganisms that plays a certain role in maintaining local immunity and homeostasis. This fundamental revision of basic concepts has naturally led to a transformation in views on a number of key aspects of urological practice. In particular, concepts regarding the etiological structure of chronic cystitis have changed substantially. Whereas the bacterial theory previously predominated, the multifactorial nature of the disease pathogenesis is now recognized, including the potential role of viral agents, fungal flora, as well as dysbiotic alterations in the bladder microbiome [2, 3].

Such an evolution of scientific views is inevitably reflected in clinical practice as well. Approaches to the diagnosis of chronic recurrent cystitis are being reconsidered from routine laboratory tests to comprehensive investigations that make it possible to assess not only the presence of pathogens, but also the state of local immunity, morphological tissue changes, and biochemical markers of inflammation. Accordingly, therapeutic strategies are also being transformed: from the standard prescription of antibacterial agents to personalized treatment regimens that take into account the individual characteristics of the microbiome, the patient's immune status, and the specific features of the pathogenetic mechanisms underlying the disease [4, 5].

Aim. Based on the published literature, to identify the specific features of the course of chronic recurrent cystitis and to determine the differential diagnostic criteria for the development of an infectious process caused by various agents, taking into account their pathogenic properties.

Literature search strategy. An electronic literature search was carried out using the Medline, PubMed, EMBASE, and the Chinese databases CNKI and Wanfang to identify studies relevant to the analysis of CRC published up to December 2025. The following keywords were used: "chronic recurrent cystitis," "urinary tract infection," "viral cystitis," and "urothelium."

The literature search showed that contemporary medical literature demonstrates sustained interest in the study of chronic recurrent cystitis as a significant clinical problem. Analysis of published studies indicates that the concept of the bacterial nature of the disease has traditionally dominated the scientific community, since most studies focus on the role of pathogenic microflora in the formation of the etiopathogenetic mechanisms of bladder inflammation. At the same time, an important trend has emerged in recent years: the number of studies aimed at investigating the viral component in the development of infectious and inflammatory processes of the urinary tract is increasing. This opens new perspectives for understanding the multifaceted nature of chronic recurrent cystitis and calls for a revision of established diagnostic and therapeutic approaches [1, 2].

From a clinical perspective, chronic recurrent cystitis occupies one of the leading places in everyday urological practice, especially in the outpatient setting. Epidemiological observations show that the disease is most commonly diagnosed in sexually active women of reproductive age. This predilection is explained by a combination of anatomical and physiological features of the female body: a shorter and wider urethra, together with the close proximity of natural reservoirs of opportunistic microflora, namely the vagina and rectum, creates favorable conditions for the easier penetration of infectious agents into the urinary tract. As a result, women have a substantially increased risk of developing both primary episodes of cystitis and its recurrent forms. The course of chronic recurrent cystitis represents a complex, multifaceted pathological process characterized by marked resistance to therapeutic interventions. Even when all clinical recommendations are followed, prescribed medications are taken regularly, and preventive measures are observed, achieving stable, long-term remission often remains a difficult task. This is due to a combination of pathogenetic mechanisms that sustain chronic inflammation in the bladder wall and prevent complete restoration of its functional activity [6, 7].

The clinical presentation of the disease is characterized by marked severity and persistence of symptoms, substantially affecting the patient's quality of life. Intense pain comes to the forefront; it may be constant or fluctuate in intensity, is localized predominantly in the suprapubic region, but may also radiate to the perineum, lower back, or inner thighs. The nature of the pain varies from persistent dragging discomfort to acute burning or cutting episodes, especially aggravated by bladder filling or during urination. Pain intensity often reaches a level that significantly limits daily activity and disturbs sleep and the patient's psychologic and emotional state. Alongside pain, persistent urinary disturbances develop, forming a typical clinical triad of manifestations. Increased urinary frequency becomes an integral feature of the disease. The patient is forced to visit the toilet repeatedly throughout the day, including at night, which disrupts her usual routine and causes pronounced discomfort. Urination is accompanied by painful sensations ranging from mild burning to severe cutting pain, which may lead the woman to consciously restrict fluid intake, thereby aggravating metabolic disturbances in the bladder tissues [8].

Particularly problematic is the phenomenon of urgency, which is sudden, irresistible urges to empty the bladder that arise without warning and create a risk of uncontrolled urination. This not only physically exhausts the patient, but also imposes serious psychological limitations, forcing her to plan any movement with regard to the proximity of sanitary facilities. The clinical picture is further complemented by a persistent sensation of incomplete bladder emptying that remains even after urination has been completed. This sensation creates the illusion of the need for repeated voiding, thereby perpetuating the vicious circle of urinary symptoms [7, 8].

A significant factor aggravating the course of the disease is the state of immunocompromise identified in a considerable proportion of patients with chronic recurrent cystitis. This involves not only systemic immune disturbances, but also local dysfunction of the immune defense mechanisms of the urinary tract. As a result, the body's ability to effectively eliminate pathogenic agents is reduced, regulation of the inflammatory response is impaired, and regeneration of the damaged urothelium is delayed [9].

Immune disturbances form a peculiar vicious circle in pathogenesis: chronic inflammation itself exerts an immunosuppressive effect, further weakening the protective mechanisms of the bladder. This creates favorable conditions for persistence of the infectious or autoimmune process, prevents complete tissue repair, and makes it difficult to achieve clinical improvement even with adequate therapy. As a result, the disease acquires a fluctuating course with alternating periods of exacerbation and incomplete remission, and each subsequent exacerbation often proceeds with greater symptom severity and lower responsiveness to treatment [10, 11].

At present, cystoscopy is one of the principal methods for the diagnosis and differential diagnosis of various bladder diseases. In chronic recurrent cystitis, characteristic morphological changes in the bladder mucosa are identified, reflecting a chronic inflammatory process with alternating periods of exacerbation and partial remission. The visual picture is usually characterized by polymorphism and heterogeneity of changes across the bladder surface. The mucosa demonstrates signs of chronic inflammation: it loses its normal pale pink color and transparency, acquiring diffuse hyperemia of varying intensity, from moderate pink discoloration to deep red. In some cases, the hyperemia is focal, being concentrated predominantly in the region of the bladder neck, the trigone, or around the ureteral orifices; these areas most susceptible to microbial invasion and mechanical irritation. The mucosal surface often appears edematous and friable, with loss of its usual sheen and smoothness. In areas of pronounced inflammation, granularity may be observed, caused by lymphoid infiltration and hyperplasia of subepithelial elements.

In some areas, the mucosa may appear thickened and swollen, creating an impression of a "velvety" texture during examination in transmitted light [12, 13].

A characteristic feature of chronic recurrent cystitis is the presence of areas of epithelial metaplasia. Squamous metaplasia is the most common type and is visually manifested as whitish, slightly elevated lesions with indistinct borders. These areas may be isolated or may coalesce, forming more extensive fields of altered mucosa. In rare cases, areas of glandular metaplasia are detected, appearing as small cyst-like formations or elevated nodules with a smooth surface. During exacerbation, punctate hemorrhages, petechial bleeding, or small subepithelial hematomas may be identified against the background of hyperemic and edematous mucosa. In some cases, areas of superficial erosion with a dull base and indistinct margins, lacking a normal epithelial covering, are observed. On contact with the cystoscope, such areas may bleed easily, indicating increased vascular fragility and impaired tissue trophism. The vascular pattern of the mucosa undergoes substantial changes. The normal network of thin, evenly distributed vessels is replaced by chaotically arranged, tortuous, dilated vessels. In zones of pronounced hyperemia, the vascular pattern may be obscured because of the intense coloration of the tissues, whereas at the periphery of inflammatory foci the vessels appear markedly dilated, with multiple anastomoses and glomerulus-like formations. The ureteral orifices usually retain their normal round shape; however, the surrounding mucosa is often edematous and hyperemic. In some cases, slight deformation of the orifices may be observed due to periureteral fibrosis or edema. However, pronounced structural changes such as strictures or gaping are uncharacteristic of chronic cystitis and require exclusion of other diseases [14-16].

In a number of cases, deposits of salts or fibrinous overlays are found on the mucosa, especially in areas of erosion or microtrauma. These deposits may appear as whitish or yellowish films partially covering the mucosal surface. With prolonged disease duration, small pseudopolyps may form as focal mucosal proliferations in the setting of chronic inflammation. They have a smooth surface, a broad base, and usually do not exceed 3-5 mm in diameter.

In the phase of partial remission, the severity of hyperemia and edema decreases; however, signs of structural remodeling of the mucosa persist, including areas of metaplasia, irregularity of the vascular pattern, and mild granularity.

In some cases, small scars or fibrotic areas form at the sites of previous erosions or hemorrhages, giving the mucosa a mosaic appearance [16].

As for treatment, it represents a multilevel, differentiated strategy that requires consideration of the etiopathogenetic mechanisms of the disease, the individual characteristics of the patient, and the dynamics of the clinical process. The key objective of therapy is not episodic symptom relief, but the achievement of stable remission through correction of the underlying disturbances and prevention of recurrent exacerbations. The therapeutic approach is based on comprehensive etiopathogenetic correction. Identification and elimination of predisposing factors are of primary importance, including anatomical abnormalities of the urinary tract, urodynamic disturbances, hormonal imbalance, especially in peri- and postmenopausal women, dysbiosis of the vaginal biotope, and chronic infectious foci in adjacent organs. Without addressing these pathogenetic links, any drug therapy remains symptomatic and does not prevent recurrences [17].

Antibacterial therapy is used strictly when indicated, namely in the presence of confirmed bacteriuria and clinical signs of exacerbation. Drug selection is based on microbiological testing with determination of pathogen susceptibility. Preference is given to agents with high tropism for bladder tissues and the ability to maintain stable concentrations in the urothelium. In the acute phase, courses of standard duration are prescribed (1-5-7 days); however, in recurrent disease, prolonged regimens or low-dose prophylactic antibiotic therapy lasting 3-6 months may be considered. This approach reduces the frequency of exacerbations, but requires careful monitoring to prevent the development of resistance and dysbiosis [18, 19].

One of the key treatment directions is restoration of the protective glycosaminoglycan layer of the urothelium. Deficiency of mucopolysaccharides renders the mucosa vulnerable to bacterial adhesion and chemical irritation. Barrier repair is achieved by instillations of hyaluronic acid, chondroitin sulfate, or heparin preparations, which form a protective film on the epithelial surface. Oral glycosaminoglycan formulations complement the local effect by stimulating endogenous regeneration. This stage of therapy is of long-term importance, since glycocalyx stability directly correlates with the frequency of recurrences [20].

Anti-inflammatory correction is aimed at controlling chronic inflammation and reducing detrusor overactivity. Nonsteroidal anti-inflammatory drugs are used in short courses to reduce edema and pain, although their use is limited by the risk of ulcerogenic effects. A safer option is represented by herbal preparations with antiexudative and antispasmodic effects, such as extracts of bearberry, lingonberry leaf, and cranberry, which complement the main therapy without causing significant adverse reactions [21, 22].

In patients with hormonal disturbances, particularly estrogen deficiency, local estrogen therapy is of fundamental importance. Creams or vaginal suppositories containing estriol restore the trophism of the urogenital epithelium, increase glycogen production, and promote lactobacillus colonization, thereby strengthening local immunity and preventing bacterial invasion. Systemic hormonal correction is prescribed strictly when indicated after consultation with a gynecologist, taking into account contraindications and the individual risk profile [23]. The most extensively studied minimal daily dose of local estriol included in the meta-analyses cited by experts in the international clinical guidelines of IMS 2016 [24], NAMS 2020 [25], and EMAS 2021 [26] is 0.5 mg.

Physiotherapeutic methods are integrated into the treatment regimen to improve microcirculation, stimulate reparative processes, and reduce chronic inflammation. Electrophoresis with anti-inflammatory agents, such as dioxidine and lidocaine, applied to the suprapubic region ensures targeted drug delivery. Magnetotherapy and low-intensity laser radiation activate capillary blood flow and cellular metabolism, thereby accelerating urothelial regeneration. Hyperbaric oxygen therapy improves tissue oxygenation, which is particularly important in the presence of long-standing erosions and areas of metaplasia [27].

Non-pharmacological interventions constitute an integral part of the long-term strategy. An adequate hydration regimen (2-2.5 L of fluid per day) promotes natural bladder flushing and reduces the concentration of irritating metabolites. Dietary restrictions, including avoidance of spicy and acidic foods, caffeine, and alcohol, reduce chemical irritation of the mucosa. Bladder training and pelvic floor muscle exercises performed under biofeedback guidance help correct detrusor dysfunction and eliminate urgent urges to void. Psychotherapeutic support helps reduce anxiety, which often aggravates symptoms through neurogenic spasm [28].

In cases where recurrences are caused by anatomical defects, such as pelvic organ prolapse, urethral strictures, or bladder diverticula, surgical correction becomes a necessary component of treatment. Surgical interventions are aimed at restoring normal urodynamics and eliminating zones of urinary stasis, which substantially reduces the risk of recurrent infections [29].

Based on published data, it has been shown that in women a chronic inflammatory process in the bladder may be not the cause, but rather the consequence of functional disorders of the lower urinary tract associated with impaired neural regulation of these organs. The development of inflammation in the bladder wall against the background of lower urinary tract dysfunction may, in turn, perpetuate bladder and/or urethral dysfunction. In long-standing lower urinary tract dysfunction, the inflammatory process that has developed progresses over time; accordingly, without correction of impaired bladder and urethral function, antibacterial and anti-inflammatory therapy may prove insufficient. To eliminate functional disorders of the lower urinary tract and improve the function of these organs, drugs affecting the sympathetic and parasympathetic components of the autonomic nervous system may be used. Thus, pathogenetic treatment of chronic cystitis is based on breaking the "vicious cycle" of dysfunction-inflammation [30, 31].

Prevention of recurrence requires long-term monitoring and adaptation of therapy. Regular assessment of the urinary and vaginal microbiocenosis makes it possible to detect imbalance in a timely manner. Preventive courses of herbal preparations or low-dose antibiotics, when individually indicated, reduce the frequency of exacerbations. Intimate hygiene is also important, as is the treatment of concomitant infections, such as vaginitis and pyelonephritis, which may trigger recurrences. Treatment efficiency is assessed using a set of criteria: symptom dynamics, including urinary frequency, pain, and urgent urges to void, microbiological test results, cystoscopic findings, including reduction of hyperemia, edema, and erosions, as well as the patient's quality of life. In the absence of response to a standard regimen, more in-depth diagnostic evaluation, including urothelial biopsy and urodynamic testing, is required to exclude interstitial cystitis, neoplastic processes, or other rare disease entities [29].

Thus, analysis of contemporary data demonstrates that chronic recurrent cystitis cannot be regarded as an isolated inflammation of the bladder. Rather, it is a condition involving numerous factors in its development, including microbial composition, the state of local and systemic immunity, hormonal background, anatomical features of the urinary tract, concomitant diseases, and even the patient's psychologic and emotional status. This multicomponent pathogenesis explains why standardized treatment regimens often prove insufficiently effective and why recurrences occur even in the setting of formally adequate therapy. The issue of diagnosis deserves particular attention. As studies show, routine methods, including urinalysis and urine culture, are often insufficient to identify the true causes of recurrence. A comprehensive approach is required, including advanced microbiological investigation, cystoscopy with targeted biopsy, urodynamic testing, and, where necessary, molecular genetic methods. Only such detailed evaluation makes it possible to differentiate bacterial, interstitial, and mixed variants of chronic recurrent cystitis, which is critically important for selecting an appropriate therapeutic strategy [28].

In the treatment of chronic recurrent cystitis, a clear trend toward personalization has emerged. Moving away from standardized regimens and toward individualized drug selection based on etiology, disease phase, and concomitant conditions substantially increases the likelihood of achieving long-term remission. At the same time, not only pharmacotherapy, including antibacterial, pathogenetic, and symptomatic treatment, but also non-pharmacological methods, such as lifestyle modification, dietary therapy, physiotherapeutic interventions, and bladder training, are of key importance. A multidisciplinary approach is especially important in the management of peri- and postmenopausal patients, where close collaboration between the urologist and the obstetrician-gynecologist is required to correct hormonal disturbances.

It should also be noted that many aspects of chronic recurrent cystitis remain the subject of scientific debate. There is still no consensus regarding the role of viral agents in the genesis of recurrences, and the mechanisms of their formation and their influence on infection persistence remain insufficiently studied. The criteria for selecting patients for long-term prophylactic antibiotic therapy also require further clarification, as do the optimal regimens for the use of agents that restore the glycosaminoglycan layer of the urothelium [22, 23].

Thus, chronic recurrent cystitis represents a clinical reality in which each case requires careful analysis and an individualized approach. In view of all the presented data, it appears logical and necessary to revise the clinical guidelines "Cystitis in Women" so that they address the various possible pathogenetic aspects of CRC development, not only of bacterial origin, with presentation of an expanded diagnostic work-up and options for non-antibacterial drug treatment.

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THE USE OF AUGMENTED REALITY TECHNOLOGIES IN UROLOGICAL PRACTICE

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Introduction. Modern urology is undergoing a technological revolution, a key component of which is the integration of augmented reality (Augmented Reality, AR). By combining virtual 3D models with the real operating-room environment in real time, AR is transforming surgical planning, intraoperative navigation, and training. This technology creates opportunities to improve procedural accuracy, reduce invasiveness, and enhance clinical outcomes, particularly in robotic and laparoscopic surgery.
Aim. To systematize current data on the use of AR technologies in urology for surgical planning, intraoperative navigation, and training, and to assess their clinical efficiency.
Materials and methods. A systematic review of publications (2019–2023) was conducted in PubMed, Scopus, and IEEE Xplore in accordance with PRISMA. Inclusion criteria: clinical studies, technical reports, and reviews on the use of AR/VR in urological surgery or training with quantitative data. A total of 26 studies were included in the final analysis.
Results. Key findings:
1. Training: AR/VR platforms (HoloLens®, STAR®, RobotiX-Mentor®) substantially improve surgical skills by reducing procedure time and error rates (e.g., a 3.6-fold decrease in instrument collisions among novices) and increasing accuracy (nerve preservation 96.6% vs 72.8%). AR-based telepresence systems with AI-driven hand tracking (98% accuracy) and AI video analysis tools have also been developed.
2. Renal surgery: AR navigation during removal of complex tumors is associated with reduced estimated blood loss (~22 mL), shorter operative time (~23 min), lower rates of warm ischemia (by 50%) and shorter ischemia duration (~4 min), fewer collecting system injuries (10.4% vs 46.5%), and higher enucleation rates. Intraoperative concordance with the 3D plan reaches 86.7%.
3. Prostate surgery (RP): 3D models/AR improve the accuracy of tumor and neurovascular bundle identification (sensitivity/specificity ~90–95% for predicting extracapsular extension), reduce positive surgical margin rates (to 2.9–6.6%), and improve functional outcomes (continence up to 94.1%, potency up to 70.6%). AI systems enable accurate targeted biopsy (87.5% in pT3).
Limitations and challenges: high equipment and operating costs (up to $1500–2000 per procedure), real-time model registration accuracy issues (misalignment up to 12%), limited and heterogeneous evidence base, and the need to improve haptic feedback in VR.
Future directions: integration of AI for navigation and analysis, development of "digital twins", hybrid AR/VR platforms for telemedicine and training, and cloud-based solutions.
Conclusion. AR has demonstrated clinical relevance in urology by improving the accuracy, safety, and outcomes of surgery and transforming training. Despite existing technical and economic barriers, integration with AI and the development of personalized approaches are shaping the future of this technology as a key element of digital urology. Large-scale randomized clinical trials are needed to confirm long-term effectiveness and cost savings.

Key words: *urology, augmented reality, mixed reality, renal tumor, prostate cancer, partial nephrectomy, radical prostatectomy, training*

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Introduction. Modern urology is undergoing a technological revolution driven by the integration of digital innovations into clinical practice. Among these, augmented reality (AR) stands out as a tool transforming approaches to surgical planning, intraoperative navigation, and training. By combining virtual 3D models with the real environment in real time, AR can improve precision, minimize invasiveness, and optimize surgical outcomes, especially in the context of robotic and laparoscopic surgery [1–6].

AR is used in nephron-sparing surgery, radical prostatectomy, and reconstructive procedures of the urinary tract. For example, 3D reconstruction based on CT and MRI enables highly accurate visualization of anatomical structures, including vessels, renal parenchyma, cysts, tumors, and the collecting system, which is critically important for preoperative planning before nephron-sparing procedures for renal tumors [2, 7, 8]. Intraoperative overlay of the generated 3D models onto the surgical field in real time improves identification of renal structures and the renal pedicle, thereby reducing the risk of injury to healthy tissues [9].

The future prospects of AR in urology are associated with the development of hybrid operating rooms, where the combination of virtual reality, AR, and artificial intelligence will create interactive environments for training and conditions for remote consultation [5, 10, 11]. Already today, AR is becoming an integral part of the digital transformation of urology, opening the way to personalized, safe, and effective surgery [5, 12, 13].

Aim. To systematize current evidence on the use of augmented reality technologies in urology for surgical planning, intraoperative navigation, and training, and to evaluate their clinical efficiency.

Materials and methods. Study design: a systematic review of publications on the use of AR in urology published between January 2019 and December 2023 was performed. The review was conducted in accordance with PRISMA recommendations.

Search strategy: the literature search was performed in the PubMed, Scopus, and IEEE Xplore databases. Combinations of keywords with Boolean operators were used: ("augmented reality" OR "mixed reality") AND ("urology" OR "kidney surgery" OR "prostatectomy") AND ("education" OR "surgical training").

Inclusion criteria: the analysis included clinical studies, technical reports, and systematic reviews describing the use of AR/VR in urological surgery or training. The presence of quantitative data (accuracy, time, complications) and full-text availability of English-language publications were mandatory.

Exclusion criteria: in vitro and animal experimental studies, publications without a control group (for comparative analysis), duplicate publications, and studies with unclear methodology were excluded.

Selection process: the initial search identified 254 publications. After removal of duplicates (n=87) and screening of titles/abstracts (n=112 excluded), 55 articles were selected for full-text assessment. Full-text evaluation led to exclusion of 29 publications due to non-compliance with the eligibility criteria. A total of 26 studies were included in the final analysis.

Quality assessment: the quality of included clinical studies was evaluated using the modified Jadad scale (range 0–5 points), with a mean score of 3.8±0.6. Technical developments were analyzed according to IEEE criteria, including accuracy (⩾90%), reproducibility, and clinical validation.

Data analysis: qualitative thematic analysis was used to synthesize the identified advantages and limitations of AR technologies.

Ethical considerations: all included clinical studies had confirmation of approval by local ethics committees.

Limitations: the main limitations of the review include the potential risk of publication bias and the methodological heterogeneity of the included studies, including different AR platforms and evaluation criteria.

Statistical analysis: Student's t-test and ANOVA were used for group comparisons. Correlation analysis was performed using Pearson's correlation coefficient. Statistical significance was set at p<0.05.

Tools: bibliographic data management was performed using EndNote X9. Statistical analysis was conducted in R 4.3.1 (with the meta package) and GraphPad Prism 9.

Results

Training in urology using augmented and virtual reality technologies: transformation of surgical education

The integration of AR and virtual reality (VR) technologies into urological practice opens new perspectives for surgical education by combining interactivity, standardization, and objective skills assessment. Current studies demonstrate how these tools overcome the limitations of traditional training methods, enabling a transition to personalized and safe acquisition of complex procedures.

The systematic review by Rodler et al. (2023) [14] confirms the efficiency of AR platforms in urology. Analysis of 46 studies showed that the use of Microsoft HoloLens® reduces ureteroscopy task completion time and improves OSAT scores among trainees. STAR® and ImmersiveTouch technologies also demonstrated improvement in basic skills, including error reduction and greater accuracy. However, the authors noted several limitations, including methodological heterogeneity, small sample sizes, and a lack of data on long-term effects on clinical outcomes.

Innovations in AR telestration were presented in the study by Müller et al. (2022) [15], in which a three-level pipeline for tracking the surgeon's hands was developed: localization (YOLOv5s), segmentation (FPN-EfficientNet B3), and regression of 21 skeletal key points. In retrospective data (14,102 frames), detection accuracy reached 98%, regression error was 10.0 px, and the Dice coefficient was 0.95. Real-time implementation (20 frames/s) makes it possible to overlay AR visualization of the hands onto laparoscopic video, providing intuitive interaction between mentor and trainee. A prospective study (705 frames) confirmed the robustness of the method across changes in operators, gestures, and cameras.

The efficiency of VR simulators was further confirmed in the study by Ebbing et al. (2021) [16], in which 51 surgeons with different levels of experience performed robot-assisted radical prostatectomy (RARP) on the RobotiX-Mentor® platform. Experts demonstrated a marked advantage in precision: the number of intraoperative instrument collisions in novices was 3.6 times higher than in experienced surgeons (61 vs 17; p<0.01), while the time required for neurovascular bundle dissection was reduced by 44% (757±142 s vs 1352±294 s; p<0.01). Preservation of neural structures reached 96.6% in the expert group versus 72.8% in novices (p=0.04), highlighting the role of VR in minimizing iatrogenic risks.

Additional data were obtained in the study by Hvolbek et al. (2019) [17], in which participants with video gaming experience of ⩾6 hours/week showed an advantage in instrument handling: the number of movements with the left instrument (2122.5 vs 2571.5; p=0.012) and its path length (20,178 mm vs 25,304 mm; p=0.015) were significantly lower than in non-gamers. This confirms that gaming experience may enhance basic motor skills that are critical for robot-assisted surgery.

The development of artificial intelligence (AI) expands the possibilities for analysis of surgical data. In the study by Cheikh Youssef et al. (2023) [18], it was demonstrated that non-expert operators can participate in annotation of robot-assisted surgery videos. A novice medical student trained on the Proximie® platform achieved an accuracy of 93.06% in annotating the stages of RARP (n=17). The lowest scores (4.13/5 points) were recorded for labeling bladder neck transection, which was associated with anatomical variability. Computer vision tools such as VIA allow automation of surgical workflow analysis, which is essential for the development of AI algorithms capable of identifying surgical stages and evaluating technical performance.

Mixed reality (MR) for training in basic skills was investigated in the study by Schoeb et al. (2020) [19]. A randomized blinded study using Microsoft HoloLens for bladder catheterization demonstrated superiority of the MR group (n=57) in OSCE scores (21.49±2.27 vs 19.96±2.42 points; p<0.001) compared with traditional training (n=107). Despite the low usability rating of the system (System Usability Scale, SUS 56.6/100), MR provided standardization of instructions by eliminating variability in teaching. Limitations included the need for technical support (28.9% of participants) and discomfort associated with headset use; nevertheless, the method confirmed the potential of MR as a tool for autonomous learning.

AR/VR technologies are shaping a new paradigm in surgical education by providing standardization of training through reproducible VR scenarios and AR guidance that reduces the error rate by 67%, reduction of intraoperative risks through integration of AR platforms such as HoloLens® and STAR® to improve procedural precision, and creation of a hybrid ecosystem in which AR complements traditional methods, reducing cognitive load and accelerating the learning curve. Limitations include insufficient realism of haptic feedback in VR, the high cost of AR systems, and the need for validation in randomized clinical trials. Future prospects are associated with cloud-based platforms for remote training and adaptive AI algorithms. Further studies should assess the long-term impact of these technologies on clinical outcomes and their cost-effectiveness. Thus, AR/VR are transforming education by enhancing real surgical experience with digital tools for training highly qualified urologists.

Application of augmented reality technologies in kidney surgery

In contemporary urological practice, particularly during nephron-sparing surgery for renal tumors, achieving an optimal balance between oncological radicality and preservation of renal function is critically important. The introduction of AR technologies represents a promising direction, offering innovative approaches to this challenge and contributing to a change in the paradigm of intraoperative management during resection of complex renal masses.

The pioneering study by Porpiglia et al. (2020) [7] demonstrated the capabilities of a 3D-AR system integrated with the da Vinci robotic platform for intraoperative visualization of the tumor and the vascular-segmental anatomy of the kidney. In a comparative analysis of robot-assisted partial nephrectomy outcomes in 91 patients with complex renal masses (PADUA score ⩾10), the use of 3D-AR guidance, compared with standard ultrasound-guided navigation, was associated with a significantly lower rate of warm ischemia (45.8% vs 69.7% in the ultrasound group; p=0.03), a higher rate of enucleation (62.5% vs 37.2%; p=0.02), and a significantly lower number of collecting system injuries (10.4% vs 46.5%; p=0.003). These findings indicate the potential of 3D-AR to optimize perioperative outcomes and preserve renal function during resection of complex renal masses.

The results of the meta-analysis by Cheng et al. (2023) [9], which included 8 studies and 583 patients, confirm the advantages of augmented reality surgical navigation (ARSN) in kidney surgery. The use of ARSN was associated with a statistically significant reduction in estimated blood loss by 21.86 mL (p<0.00001) and operative time by 22.59 min (p=0.0001). ARSN use reduced the likelihood of global ischemia by 50% (relative risk 0.50; p=0.003) and shortened warm ischemia time by 3.96 min (p=0.009). A higher rate of enucleation was also observed (relative risk 1.72; p=0.005). These data indicate improved perioperative safety and better key surgical outcomes with ARSN.

The study by Schiavina et al. (2021) [20] presented the results of a 15-case series of robot-assisted partial nephrectomy using AR guidance. Analysis of 3D models significantly influenced the preoperative arterial clamping plan (p=0.03), and intraoperative management with AR corresponded to the 3D plan in 86.7% of cases. The median warm ischemia time was 9 minutes (interquartile range 6–12 minutes), and mean blood loss was 140 mL. Major postoperative complications (Clavien grade ⩾3) were observed in 6.7% of patients. The absence of positive surgical margins in 100% of cases and the low complication rate demonstrate the safety and precision of AR in this case series.

Technological progress in AR continues, including integration with machine learning methods. In the study by De Backer et al. (2023) [21], experience was described in improving AR during robot-assisted kidney surgery through real-time instrument segmentation based on deep learning. The developed algorithm, trained on 15,100 frames, demonstrated high accuracy of instrument detection (intersection over union, IoU 94.4%; Dice score 97.10%). Validation in 10 cases of robot-assisted kidney surgery showed the potential to improve the safety of AR navigation by reducing the overlap of instruments with virtual objects.

The use of AR also expands the possibilities for surgical interaction and training. In the study by Li et al. (2020) [13], the use of MR for navigation with virtual 3D models during laparoscopic nephrectomy made it possible to significantly increase the proportion of nephron-sparing procedures (from 46% to 82%, p<0.001), reduce the mean operative time (from 98.4 to 60.7 min, p<0.001), and shorten ischemia time (from 20.3 to 12.5 min, p<0.001). A statistically significant reduction in estimated blood loss was also observed (from 45.9 to 15.5 mL, p<0.001).

The systematic review by Khaddad et al. (2023) [22], which included 16 publications, confirmed the presence of potential advantages of AR based on analysis of the included studies, such as a lower rate of global ischemia, a higher rate of enucleation, and fewer collecting system injuries. Nevertheless, the authors of the review emphasized the limited level of current clinical evidence and the need for more rigorously designed studies to definitively confirm the advantages of AR in minimally invasive partial nephrectomy.

Alongside its clear promise, AR implementation is associated with a number of challenges, including the high cost of equipment (according to some reports, $1500–2000 per procedure) [23] and the need to improve the accuracy of registration between virtual models and real-time anatomy in order to overcome mismatches, reported in up to 12% of cases [23]. Personalization of surgery through patient-specific digital twins, mentioned, for example, in the context of the work by Checcucci et al. (2023) [5] based on 3D models, appears to be one of the key directions for further development, making it possible to account for individual anatomical variations in the modeling and performance of AR-guided procedures.

Conclusion. Analysis of the presented data indicates the substantial potential of augmented reality (AR) technologies for advancing kidney surgery, especially in minimally invasive nephron-sparing procedures. Available studies demonstrate promising results in improving perioperative outcomes, including shorter ischemia time, reduced blood loss, and optimization of surgical technique, for example, higher enucleation rates and fewer injuries to the collecting system. AR contributes to more accurate preoperative planning and intraoperative navigation, which may have a positive effect on preservation of renal function. Despite existing challenges, such as equipment cost and registration accuracy, the continuous development of the technology, including integration with machine learning and the concept of digital twins, opens prospects for further improving the safety and efficiency of kidney surgery. Further high-quality randomized clinical trials are needed to definitively confirm the clinical benefits of AR.

Application of augmented reality in prostate surgery

Radical prostatectomy is a procedure in which every millimeter matters: the entire tumor must be removed while preserving the neurovascular bundles responsible for erectile function. AR has become the “third eye” that helps surgeons see the invisible.

According to the systematic review by Rodler et al. (2023) [14], which analyzed 46 studies on novel imaging technologies in RARP, 19 studies focused on visualization of the primary tumor. The narrative review by Della Corte et al. (2024) [23], summarizing data from 16 studies, also emphasizes the substantial potential of three-dimensional virtual models (3D-VMs) and AR technologies in RARP. These technologies provide considerable support for preoperative planning, intraoperative navigation, and real-time decision-making, significantly improving visualization of complex anatomical structures, facilitating modulation of the nerve-sparing approach, and reducing the rate of positive surgical margins (PSMs).

The randomized clinical trial by Shirk et al. (2022) [24] (n=92) demonstrated improved oncological outcomes, with a significantly lower rate of detectable postoperative PSA (9% vs 31%; p=0.036) and a trend toward a lower PSM rate when virtual models were used for planning. Surgeons changed their operative strategy in 32% of cases based on model analysis, which led to a trend toward more frequent bilateral nerve sparing. A retrospective analysis by Checcucci et al. (2022) [25] also showed that the use of 3D models was a protective factor against PSMs. Similar results were obtained by Martini et al. (2022) [26] when comparing outcomes before and after implementation of 3D models created from 3T MRI data.

A major contribution to the development of AR-guided RARP was made by Porpiglia et al. in their 2019 study [27], which investigated robot-assisted radical prostatectomy with AR guidance based on hyperaccuracy three-dimensional reconstruction (HA3D™) technology. The authors demonstrated high accuracy of preoperative radiological prediction of capsular invasion. The sensitivity of HA3D™ for detecting CI was 90.9%, specificity 95.5%, positive predictive value (PPV) 90.9%, negative predictive value (NPV) 95.5%, and overall accuracy 94.1%. Pathological analysis confirmed the accuracy of HA3D™ in determining the location of the neurovascular bundles relative to the prostatic capsule.

In a subsequent study (2019) [8] involving 50 patients, Porpiglia et al. presented further development of the technique, including elastic registration of 3D models. In this study, the accuracy of HA3D™ in predicting CI was 90.0% for sensitivity, 95.0% for specificity, 90.0% for PPV, 95.0% for NPV, and 94.0% for overall accuracy. Intraoperative AR guidance using these models enabled precise identification of tumor location, neurovascular bundles, and areas of capsular invasion. The authors concluded that HA3D™-based elastic AR provides accurate prediction of capsular invasion and precise intraoperative guidance, which may potentially improve the results of nerve-sparing surgery and reduce the rate of PSMs.

Substantial progress has also been achieved in intraoperative visualization and navigation using AR. Samei et al. demonstrated the feasibility of real-time prostate motion tracking using ultrasound [28] and subsequently developed a system combining preoperative MRI data with intraoperative ultrasound with an accuracy of up to 3.2 mm [29]. The study by Kratiras et al. (2019) [30] showed that tablet-based AR systems are actively used during the most critical stages of RARP, including bladder neck dissection, apical dissection, and nerve sparing. In the study by Schiavina et al. (2020) [31], involving 26 patients and using 3D models overlaid onto the robotic video stream, it was demonstrated that AR-3D technology changed the nerve-sparing plan in 38.5% of cases at the patient level and in 34.6% of cases at the side-specific level, with an overall appropriateness of changes of 94.4%. Model accuracy for detecting the index tumor was 92% (sensitivity 70%, specificity 100%) in the analysis of 32 prostate regions. The overall PSM rate was 15.4%, and 11.5% at the level of the index tumor. Functional outcomes at 6 months included urinary continence in 92.3% of patients and recovery of erectile function in 65%. Porpiglia et al. also confirmed the feasibility of AR guidance in their studies (2018 [32], 2019 [27]), with model accuracy ranging from 1 to 5 mm, while in 85% of cases the discrepancy was less than 3 mm. The elastic AR model developed by them (2019) [8] showed superiority over 2D visualization for intraoperative detection of capsular invasion. Canda et al. (2020) [33] successfully integrated positron emission tomography data with prostate-specific membrane antigen (PSMA PET) into a VR model, demonstrating the clinical feasibility of the approach in five cases of RARP.

A promising direction is the integration of AR with AI technologies. In the study by Checcucci et al. (2023) [34], a 3D automatic augmented reality (AAR) system with AI guidance was presented for selective neurovascular bundle biopsy during nerve-sparing RARP. In this prospective study of 34 patients with suspected tumor contact with the capsule or extracapsular extension on MRI, AAR guidance enabled accurate identification of tumor location on the neurovascular bundle in 87.5% of cases among patients with pT3 disease. Selective biopsy under AAR guidance resulted in a low rate of positive surgical margins: 0% in patients with pT2 disease and 7.1% in patients with pT3 disease at the biopsy margin. The overall rate of positive surgical margins in this series was 2.9%.

Favorable functional outcomes were also reported at 12 months, with urinary continence in 94.1% of patients and recovery of potency in 70.6%. Development of deep learning frameworks for automatic real-time registration of 3D models is also actively underway. In the study by Padovan et al. (2022) [35], such a framework was presented and tested, in particular, in RARP. The system uses convolutional neural networks for semantic segmentation of instruments or organs (IoU accuracy >80%, and 0.7296 for the prostate) and for rotation estimation. For organ registration, a combination of a neural network and an optical flow algorithm is applied. After additional training on real images, the accuracy of prostate rotation estimation reached a level at which the error was less than 10 degrees in nearly every frame, demonstrating the potential of automatic registration without additional external sensors. Tanzi et al. (2021) [36] also investigated the use of deep learning for real-time semantic segmentation for AR-assisted surgery and achieved an IoU of 0.894. Surgeons also subjectively rate the usefulness of AR during RARP highly [37].

AR is also being applied in intraoperative diagnostics. Andrews et al. (2020) [38] demonstrated the use of AR for navigation during intraoperative frozen section assessment, which allowed a significant reduction in the rate of PSM at the level of the index tumor (5% vs 20%; p=0.01).

According to the narrative review by Della Corte et al. (2024) [23], studies show that AR technologies based on highly accurate 3D reconstructions have the potential to improve the precision of preoperative planning and intraoperative performance of RARP, which may lead to better oncological and functional outcomes. For example, in one study, the rate of positive surgical margins on frozen sections decreased from 22.5% to 11.3%, and on permanent sections from 13.1% to 6.6%. In another study, the group with 3D models had a lower rate of PSM (25% vs 35.1%, p=0.01) and a higher rate of full nerve sparing (20.6% vs 12.7%). Intraoperative management with AR corresponded to the 3D plan in 86.7% of cases. Despite the limitations noted in the review, such as small patient cohorts and the absence of standardized techniques, as well as challenges related to equipment costs, reported in some studies to reach up to $1500–2000 per procedure, and registration accuracy, with mismatches reported in up to 12% of cases [23], the integration of 3D virtual models and AR appears to be a promising direction in urologic oncology. The future of AR in prostate surgery is closely linked to the personalization of surgery, including the development of patient-specific digital twins, as mentioned, for example, in the context of the work by Checcucci et al. (2023) [5] based on 3D models.

Discussion. The results of our review are generally consistent with those of similar studies, including the meta-analysis by Cheng et al. [9] and the narrative reviews by Khaddad and Della Corte [22, 23], and confirm the potential of AR navigation to improve perioperative outcomes in partial nephrectomy and RARP. At the same time, the findings require critical interpretation. The overwhelming majority of included studies are small retrospective case series with substantial methodological heterogeneity: different AR platforms, non-uniform outcome measures, and the absence of standardized registration protocols do not allow direct comparison of results across centers. The only full-scale randomized clinical trial, by Shirk et al. [24], did not reach significance for its primary endpoint, namely the rate of positive surgical margins, which precludes any conclusion of a high level of evidence for most claims regarding the clinical advantages of the technology.

The economic aspect also deserves special attention: the cost of AR navigation reaches $1500–2000 per procedure, whereas a formal cost-effectiveness analysis is still lacking in the literature. Reduction in warm ischemia time and intraoperative complications could potentially offset these costs; however, this assumption requires dedicated economic evaluation [23].

Overcoming the main technical barrier, namely registration error of up to 12%, appears most promising through integration with deep learning algorithms for automatic real-time segmentation of organs and instruments. To definitively confirm the clinical benefits of AR, multicenter randomized clinical trials with standardized protocols and clearly defined primary endpoints are required [5, 10, 11].

Conclusion. Augmented reality has moved from the category of experimental technologies into the group of clinically relevant tools that have demonstrated efficiency in urology. However, its full potential cannot be realized without addressing technical, economic, and ethical challenges. Further development of AR should be directed toward the creation of integrated ecosystems combining AI, telemedicine, and educational platforms, in line with global trends in the digital transformation of healthcare.

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