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ООО "БИОНИКА МЕДИА"

CONTENTS

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RESULTS OF PERCUTANEOUS NEPHROLITHOTOMY USING TWO ACCESSES IN THE TREATMENT OF PATIENTS WITH STAGHORN STONES

N.A. Lopatkin Research Institute of Urology and Interventional Radiology – branch of the National Medical Research Radiological Center; Moscow, Russia

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Introduction. In order to improve clinical efficiency and reduce the risk of postoperative complications in patients with staghorn stones, we compared the results of original technique of two-access percutaneous nephrolithotomy (PCNL) with the standard PCNL.

Materials and methods. A total of 221 patients with staghorn stones of K3–K4 was included in the study. The two-access PCNL was used in 109 patients, while the control group consisted of 112 patients. Inclusion criteria were stone size ⩾2 cm, age over 18 years, absence of coagulopathy and width of the renal parenchyma ⩾1 cm. On 1st postoperative day, ultrasound or plain urography was performed, while in patient with radiolucent stones, multi-slice computed tomography was used. In addition, complete blood count and biochemical profile were done.

The main difference from the standard PCNL with sequential renal tracts is the simultaneous creation of the main and additional accesses when performing two-access PCNL. This method allowed two surgeons to simultaneously and synergistically perform lithotripsy and stone extraction from two accesses using a standard nephroscope in the main tract of 24 Ch and a miniaturized nephroscope in the additional tract of 16.5 Ch.

Results. The stone-free rate in the group of two-access PCNL was 80.7% (n=88), compared to 72.3% in the control group (n=81). Secondary interventions and additional procedures were required in 29 (26.6%) and 40 (39.2%) cases, respectively. The total number of infectious and hemorrhagic complications was higher in the control group.

Discussion. According to our data, significant advantages are observed in the group of two-access PCNL compared to the standard technique.

Conclusion. Two-access PCNL can be recommended as a promising advancement of the technique traditionally used in the clinical practice.

K e y w o r d s: urolithiasis, percutaneous nephrolithotomy, staghorn stones

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Introduction. The widely accepted method for the surgical treatment of staghorn kidney stones is percutaneous nephrolithotomy (PCNL) [1, 2]. However, its efficiency is significant lower in those with complete staghorn stones (stages K3–K4) [3]. In order to overcome this problem, multi-tract PCNL is usually used, but this technique leads to an increase in the operating time, as well as hemorrhagic and infectious complications in the postoperative period [3, 4]. An alternative method of stone removal such as retrograde intrarenal surgery (RIRS), although being associated with a low risk of postoperative complications, is less effective than PCNL in the treatment of staghorn stones [5, 6].

The use of mini-PCNL significantly reduces renal trauma and has a number of advantages, such as more delicate manipulation of the instrument in the collecting system and increased opportunities for tubeless procedure, but it can prolong operation time in case of complete staghorn stones, which also leads to higher risk of complications [7-11].

Taking into account the modest clinical efficiency and complication rate, advancement of PCNL can be done by optimization of the techniques [12, 13]. To overcome technical difficulties in the treatment of staghorn stones of stages K3–K4, a technique of two-access PCNL has been developed.

Our aim was to analyze the results of two-access PCNL and to valid of its use in clinical practice [14].

Materials and methods. A total of 221 patients with staghorn stones of K3–K4, who were undergone to PCNL in N.A. Lopatkin Research Institute of Urology and Interventional Radiology – branch of the National Medical Research Radiological Center, were included in the study. The patients were divided into two groups. The first included patients who underwent two-access PCNL (n=109). In the second (control) group a standard PCNL was performed, when two percutaneous tracts were created with staged lithotripsy through each access (n=112).

The standard PCNL was done under endotracheal anesthesia. After performing cystoscopy in the lithotomy position and placing the ureteral and urethral catheter, the patient was turned over to the prone position. Then, under combined ultrasound and fluoroscopic guidance, the puncture of the collecting

Table 1

Baseline patients' characteristics

Indicator	Group of patients		p^a	p^b
	Group 1 (n=109)	Group 2 (n=112)		
Age, years, Me [25%; 75%] (min, max)	50 [41; 57] (21–76)	54 [39,5; 60] (20–75)	0,25	–
Females/males	69/40	74/38	–	0,67
Side of the procedure, right/left, %	71,6/28,4 (31)	65,2/34,8 (39)	–	0,31
Maximal stone size, mm, Me [25%; 75%] (min, max)	61 [45; 72] (37–121)	55 [45; 69] (38–120)	0,33	–
Stone area, mm2, Me [25%; 75%] (min, max)	2704 [1356; 3672] (840–9620)	2052 [1357; 3108] (882–10180)	0,14	–
Stone density, HU, Me [25%; 75%] (min, max)	872 [663;1100] (394–1879)	848 [647; 1120] (364–1857)	0,89	–
A deterioration of the excretory function of ipsilateral kidney, % Me [25%; 75%] (min, max)	29 [18; 46] (0–86)	31,5 [18; 44] (0–88)	0,52	–
Bacteriuria, %	48,6	52,6	–	0,54

Note. [a] – Mann–Whitney coefficient, [b] – χ^2-Pearson coefficient, differences were significant if $p<0.05$.

system was done. After confirming the precise location of the needle, a superstiff guidewire was advanced. If necessary, to achieve the maximum efficiency, several accesses were created. To do this, a stiff guide wire was passed through the needle after each successful puncture, then the needle was removed. After advancing the guidewires, a two-component introducer was placed in the main access. Then, a safety guidewire was passed, followed by dilatation of the percutaneous tract using Alken dilator set. After lithotripsy and stone extraction, the collecting system was drained by a nephrostomy tube (balloon or Malecot). In order to ensure the complete removal of the fragments, the additional access was used. In the absence of bleeding, the additional tract was not drained.

To perform two-access PCNL, a method for minimally invasive surgical treatment of kidney stones in adults has been developed [15]. The main difference from the standard PCNL technique with staged dilating of the tracts is the simultaneous creation of the main and additional accesses. Using them, two surgeons work in parallel. This requires the installation of two endoscopic systems in the operating room. The technique of cystoscopy and tract dilation does not differ from the standard one. When creating accesses under combined ultrasound and fluoroscopic control, the guidewires are simultaneously advanced in the collecting system.

An additional percutaneous access is used to provide manipulations in the collecting system in difficult-to-reach calyxes. When choosing the location of accesses, their perpendicular position seems to be optimal. Through the main access a nephroscope of 24 Ch with lithotripter is used. For second access, a miniaturized nephroscope of 16.5 Ch and a holmium laser is chosen. Two surgeons perform simultaneous and synergistical lithotripsy. After fragmentation of the stones from the additional access, large particles are displaced to the working area of the main access for further extraction. After complete stone removal, the nephroscope from the additional access is first moved away. If there is no active bleeding at the end of the procedure, nephrostomy tube is put only through the main tract.

Inclusion criteria were stone size ⩾2 cm, age over 18 years, absence of coagulopathy and thickness of the ipsilateral renal parenchyma ⩾1 cm.

Exclusion criteria: anatomically or functionally single kidney, an acute inflammatory process of any localization, a stricture and/or a stone of the ipsilateral ureter, congenital anomalies of the kidney (number and position), ipsilateral kidney tumor, evidence for a crossing vessel with the dilatation of the collecting system, a presence of a nephrostomy tube, chronic kidney disease of the 4-5th stages, other chronic diseases in the stage of decompensation.

Comparative criteria: clinical efficiency (stone-free status or the presence of clinically insignificant fragments less than 4 mm in size, according to follow-up imaging studies), operation time, stone-free rate after primary procedure, length of stay.

All patients had standard preoperative evaluation, which included history taking, physical examination, general clinical and laboratory studies, ultrasound examination of urinary tract, plain and intravenous urography, computed tomography of the retroperitoneal space, and dynamic scintigraphy. All patients received antibacterial prophylaxis 2 hours before surgery.

On the 1st postoperative day, the clinical efficiency was assessed using a plain urography and ultrasound of the kidneys or CT in patients with radiolucent stones. In addition, complete blood count and biochemical tests were also performed. Febrile fever (⩾38.5°C) for more than a day was regarded as persistent febrile hyperthermia.

Results. No significant differences were found in any of the studied parameters (*Table 1*). The stone-free rate in the first group was 80.7% (n=88), compared to 72.3% (n=81) in the second group. The median operative time was significantly less in the first group (85 [70; 95; 45–135) vs. 105 [90; 130; 60–205]) min (*Table 2*).

Table 2

Comparative data between groups

Indicator	Group 1 (n=109)	Group 2 (n=112)	p^a	p^b
Operation time, min, Me [25%; 75%] (min, max)	85 [70; 95] (45–135)	105 [90; 130] (60–205)	< 0,0001	–
Efficiency of primary intervention, n (%)	88 (80,7)	81 (72,3)	–	0,15
Final clinical efficiency, n (%)	98 (89,9)	99 (88,3)	–	0,71
Length of stay, days, Me [25%; 75%] (min, max)	7 [6; 10] (3–21)	9 [7; 13] (3–32)	0,0015	–

Note. [a] – Mann–Whitney coefficient, [b] – χ^2-Pearson coefficient, differences were significant if $p<0.05$.

Table 3

Comparative evaluation of the need in additional interventions

Intervention	Group 1 (n=109)	Group 2 (n=112)	p
Ureteral stenting, n (%)	12 (11)	20 (17,8)	0,18
Extracorporeal shock-wave lithotripsy, n (%)	9 (8,2)	13 (11,6)	0,5
Ureteroscopy with lithotripsy, n (%)	6 (5,5)	8 (7,1)	0,78
Re-PCNL, n (%)	4 (3,6)	7 (6,2)	0,53
Nephrostomy, n (%)	1 (0,9)	2 (1,8)	1,0
Total number, n (%)	29 (26,6)	40 (35,7)	0,14

Note. The χ^2-Pearson coefficient and Fisher's exact test were used, the differences were significant if $p<0.05$.

In regard to the location of the main and additional tract, in the first group a lower-pole access was performed in 89 (81.6%) cases, while upper-pole and middle-pole was done in 12 (11%) and 15 (13.7%) patients. In the second group, the respective figures were 76 (67.8%), 48 (42.8%) and 41 (36.6%), respectively. Additional access was more often created through the middle pole in the first group compared to upper pole in the second group.

Additional interventions and procedures after PCNL were required in 29 (26.6%) cases in the first group compared to 40 (39.2%) patients in the second group. As shown in the *Table 3*, there were no significant differences in the rate of additional interventions.

After the removal of residual fragments using additional interventions, stone-free status was obtained in 98 and 99 patients in the first and second group, respectively. As a result, the final stone-free rate was 89.9% and 88.3%, respectively.

Table 4 shows a comparative characteristic of groups of patients according to the frequency of complications. A description of complications is following. Severe bleeding, precluding endoscopic visualization and requiring aborting the procedure, developed in 3 (2.7%) cases in the first group, but it was more often in the second group (n=6; 5.3%). There was no need for superselective embolization in the first group; in the second group, 1 patient (0.9%) was undergone to this procedure.

In addition, in the control group, there was a higher rate of persistent febrile hyperthermia (25.8 vs. 14.6%), systemic inflammatory response syndrome (15.7 vs. 6.4%), a need to augment antibacterial therapy with use of additional interventions (23.2 vs. 13.7%) and sepsis (4.5 vs. 1.8%). Accordingly, we can conclude that the likelihood of developing infectious complications is lower when using two-access PCNL.

Intraoperative hemorrhagic complications were more often in the control group (10.7 vs. 6.4%). Most likely, this is due to the use a miniaturized nephroscope in the first group when working through an additional access, which allows to reduce the risk of kidney injury.

The total rate of postoperative complications was 38.3 vs. 25.6% in control and main group, respectively. The length of stay was 9 vs. 7 days, which is due to lower clinical efficiency and a greater likelihood of complications.

Discussion. A distinct feature of PCNL in patients with complete staghorn stones is an increase in the operation time for destruction of the stone and extraction of fragments, as well as an higher risk of developing inflammatory complications and less optimal visualization due to hemorrhage, which complicates endoscopic visualization, affecting the efficiency of the procedure.

One of the options for reducing the morbidity of the intervention is a use of staged mini-percutaneous PCNL. Disadvantages of this method included low primary stone-free rate (45%), operation time (76–175 min), and the need to perform two-stage procedure in most cases [16]. At the same time, the relationship between postoperative complications and operation time has been proven [17, 18]. With an increase in the number of tracts, the operation time is prolonged, regardless of the use of the minipercutaneous or the standard PCNL technique [19, 20].

According to the results of studies, which were previously carried out in our clinic, when performing PCNL in patients with complete staghorn stones (n=938; stages K3–K4), one access was used in 51.8% of cases, while two vs. three or more tracts were created in 39.6% and 8,4% of patients, respectively. Efficiency with single tract was only 53.6% compared to 83.8% for multiple-tract procedure. The operative time depended on number of accesses and increased from 74.2±29.9 to 144.0±12.2 minutes for single-tract and four-tracts PCNL, respectively. In addition, in case of multi-tract PCNL the rate of postoperative complications raised from 20.3 to 25.5% [3].

Table 4

Comparative evaluation of complication rates

Complications	Grade according to the Clavien–Dindo	Group 1 (n=109)	Group 2 (n=112)	p (ОШ; 95% ДИ)
Persistent fever, n (%)	I	16 (14,60)	29 (25,8)	0,040 (0,49; 0,25–0,97)
Systemic inflammatory response syndrome, n (%)	II	7 (6,4)	17 (15,7)	0,041 (0,38; 0,15–0,96)
Change in antibiotic therapy, n (%)	II	15 (13,7)	26 (23,2)	0,075 (0,52; 0,26–1,06)
Bleeding, requiring blood transfusion, n (%)	II	7 (6,4)	12 (10,7)	0,25 (0,57; 0,21–1,51)
Procedures under X-ray control, n (%)	IIIa	14 (12,8)	24 (21,4)	0.09 (0,54; 0,26–1,11)
Sepsis, n (%)	IVa	2 (1,8)	5 (4,5)	0,27 (0,40; 0,07–2,10)
Hydropneumothorax, n (%)	IVa	0	2 (1,8)	0,30 (0,20; 0,01–4,25)
Treatment in the intensive care unit, n (%)	IVa	3 (2,7)	8 (7,1)	0,14 (0,36; 0,09–1,42)
Total number, n (%)	I–IVa	28 (25,6)	43 (38,3)	0,044 (0,55; 0,31–0,98)

In order to reduce the risk of complications and increase the efficiency, a combined approach to the treatment of kidney stones was proposed with simultaneous using of RIRS and PCNL. Compared with a monotherapy, it can significantly reduce the length of stay and the total operation time, despite an average duration of the procedure also remains quite high (143 min) [21].

Our data on the use of two-access PCNL show a significant advantage in almost all outcomes. By synchronizing the work of two surgeons through two percutaneous accesses, it was possible to minimize the time required for the complete removal of the staghorn stones.

In addition, simultaneous work with displacing fragments from difficult-to-reach areas for main-tract nephroscope allows to reduce the mechanical load on the instrument, which leads to lesser kidney trauma and deterioration of endoscopic visualization. This effect can be achieved through the use of a miniaturized nephroscope through an additional access. The reduction of hemorrhagic complications due to the small diameter of the working channel and the possibility of disintegration of the stone into large particles with further extraction from the main access allows to effectively use miniaturized nephroscope in the treatment of staghorn stones.

The rate of infectious complications in the postoperative period, such as hyperthermia or sepsis, was significantly higher in the control group. Most likely, this is due to a decrease in operation time when using two-access technique. Moreover, two accesses allow free outflow of the irrigation fluid from the collecting system, reducing intrapelvic pressure.

Moreover, it should be noted that, owing to two-fold less using of the upper-pole tract during two-access PCNL, one may not only decrease the risk of developing pneumo- and hydrothorax, but also reduces discomfort in the postoperative period, which is associated with the location of nephrostomy tube near to intercostal nerves [22, 23].

Some of the most important compared outcomes are clinical efficiency and the need for additional interventions. An integral indicator that combines these data is the coefficient of efficiency (EQ), calculated by the formula: EQ = (frequency of stone-free status at the end of treatment in %) / (100% + frequency of repeated interventions in % + frequency of additional procedures in %). An increase in the efficiency of minimally invasive treatment of renal stones is reflected in the EQ coefficient approaching 1. When using the two-access PCNL, it was 0.71, while for the standard technique with the sequential creation of accesses, this value was 0.65.

Conclusion. Comparing the results of two-access PCNL with the standard technique with sequential creation of percutaneous tracts for treating patients with staghorn stones, a significant advantage of a former method is shown, despite the comparable baseline characteristics. The use of the new technique allows to decrease the operation time by 20% ($p<0.0001$), the need for additional interventions and procedures by 25.5% ($p=0.14$), the total number of complications by 33.1% (38.3 vs. 25.6%; $p=0.04$), length of stay by 22.3% ($p=0.0015$) and increase clinical efficiency by 8.4%, as well as the EQ by 10% by compared with traditional PCNL technique.

The use of two-access PCNL shows high clinical efficacy and safety, demonstrates significant advantages over the traditional approach, and is a promising advancement of the technique traditionally used in the clinical practice for the treatment of patients with staghorn kidney stones.

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RETROSPECTIVE ANALYSIS OF THE RESULTS OF WHOLE-BODY PET/CT AS A POSSIBLE TOOL FOR CLINICAL EXAMINATION OF THE POPULATION IN ORDER TO IDENTIFY SUBCLINICAL MANIFESTATIONS OF CHRONIC KIDNEY DISEASE (PILOT STUDY)

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Introduction. Every year in Russia, more than 200 thousand whole body PET/CT are performed for various diseases in patients without clinical and laboratory manifestations of chronic kidney disease (CKD). However, only the "area of interest" of the attending physician is analyzed, while the rest of the organs or rather their metabolic activity is neglected during the standard procedure of this contemporary and high-tech research method.

Aim. To perform a retrospective study of whole-body PET/CT as a tool for prophylactic clinical examination of the population in order to identify subclinical manifestations of chronic kidney disease

Materials and methods: The results of whole-body PET/CT with ^{11}C-choline were retrospectively analyzed for the detection of CKD in 100 patients of the Tyumen region who underwent a study for various indications outside the genitourinary system without history, clinical and laboratory manifestations of CKD.

Results: According to the results, 22% of patients had different manifestations of ^{11}C-choline hypometabolism, indicating a decrease in the viability of the parenchyma. In 14% of patients, there was a local decrease in the uptake of ^{11}C-choline without CT-signs of kidneys damage, and in 8% of cases there was a total decrease in their metabolism, coinciding with X-ray signs of renal scarring.

Conclusions. The possibility of early molecular study of nephropathy can be used for wider retrospective PET/CT clinical examination as one of the highly effective methods for detecting CKD, which needs further research.

Key words: PET/CT, prophylactic clinical examination, chronic kidney disease

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Introduction. Over the past 5 years, more than 150,000 PET/CT scans have been performed in Moscow for anatomic and functional disorders of various organs. This science-intensive and high-technologic study provided an answer to one specific question of the referring physician in electronic form, while the rest of the body, or rather the state of its different parts, didn't have special attention. However, back in 2010, one of the first scientific papers was published in the Oxford Academic Medical Journal in the section "Imaging in Nephrology", pointing to the potential of PET/CT technology as an alternative to renal biopsy [1]. In 2014, C.R. Christopher et al. were among the first who suggest that a retrospective study of PET/CT in young people can contribute to the detection of asymptomatic pathology [2].

According to World Health Organization, chronic kidney disease (CKD), is one of the leading causes of disability and mortality among the working population. It is characterized by a decrease in kidney function for at least 3 months, regardless of the cause [3]. CKD usually presents with pathological changes in the parenchyma, detected by imaging, biopsy, or based on laboratory markers, such as the manifestation of a nephrotic syndrome with increased albuminuria and a progressive reduction of glomerular filtration rate [4]. Data from imaging studies or in-vivo morphological examination, even performed once, may be enough to diagnose CKD, if irreversible structural changes in the kidney are present. At the same time, changes that may be detected during a clinical examination showing the pathological processes in the kidney can be marker of kidney damage [5]. The concept of CKD does not replace the nosological approach to the diagnosis of kidney diseases. It is a universal tool for determining the degree of renal dysfunction in various disorders, reflecting the occurrence and progression of nephropathy. Depending on the clinical situation, the diagnosis of CKD can be based on the detection of any morphological or clinical markers of kidney damage [6].

The study of tissue viability at the molecular-cellular level by the method of PET/CT has been widely used for 10 years in oncology, cardiology, functional studies, and in recent years in nephrology and urology [7–9]. An analysis of lipid metabolism is carried out using the ^{11}C-choline isotope, which is a precursor of membrane phospholipids and makes up to 60% of their mass. The content of the main fractions of the membrane bilayer (lysolecithin, phosphatidylcholine, sphingomyelin) provides sufficient physiological fluidity to ensure cell-cell communication. When the bilayer is depleted due to a decrease in the content of choline-containing phospholipids, the membranes become rigid, the cellular homeostasis is disturbed and the apoptotic process is activated, followed by

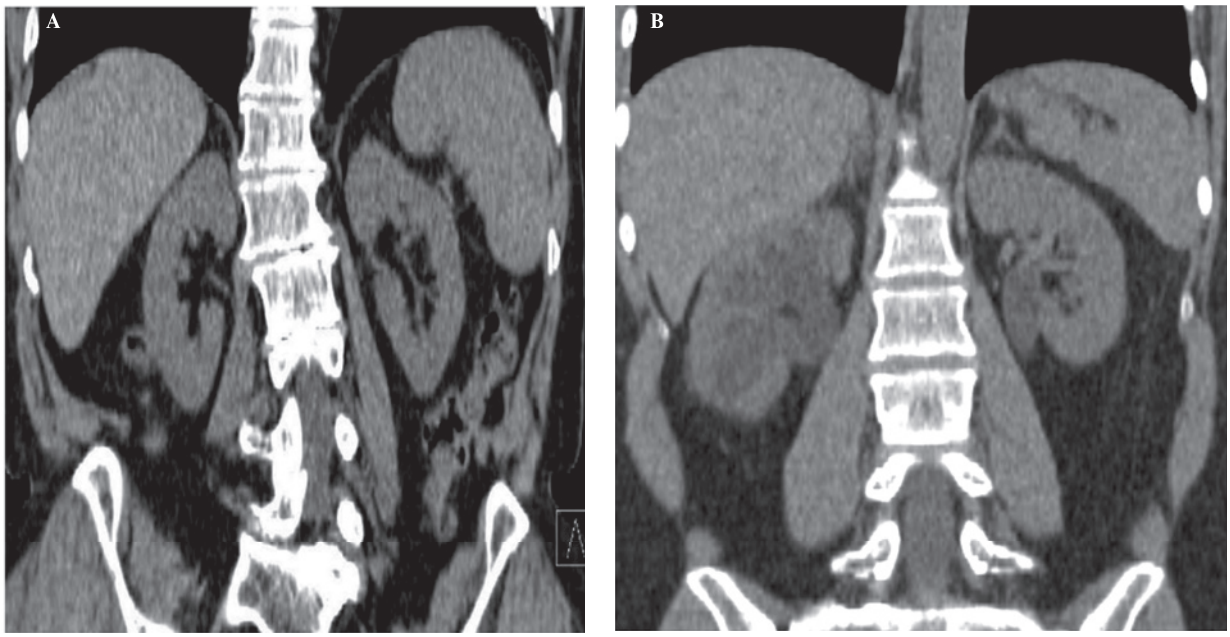


Fig 1. Non-contrast-enhanced computed tomography of the kidneys.
A — normal variant; B — in chronic kidney disease.

the replacement of the region with scar tissue. Regardless of the cause of disturbing the process of regeneration of the lipid bilayer, whether it is the action of bacterial toxins, immune complexes or toxic drugs, PET/CT study allows to visualise these areas and to calculate the level of reduction in the uptake of tracer. Labeled biomolecules emit a proton pulse, which is used for visual and quantitative stereochemical positioning and provides high-precision detection [10–14].

PET/CT study is based on the principle of analyzing the affinity of labeled tracers to the structures of actively functioning cells. At the same time, visual color analysis from white to yellow or orange and a quantitative calculation of the pulse in g/ml are used as objective criteria reflecting the viability of tissues with a sensitivity of 90% and a specificity of up to 85% [15–19].

According to the World Health Organization, up to 20% of the world's population has various clinical and laboratory manifestations of CKD, however, in the available literature, we did not find any data on the possibility of detecting CKD at the molecular and cellular level based on a retrospective analysis of PET/CT scans of people without renal disorders, which pointed us to the aim of our pilot study.

Aim: to perform a retrospective study of whole-body PET/CT as a tool for prophylactic clinical examination of the population in order to identify subclinical manifestations of CKD.

Materials and methods. To achieve this goal, on the basis of a random sampling method, the results of PET/CT with ^{11}C-choline were retrospectively analyzed for the detection of CKD. A total of 100 residents of the Tyumen region with various diseases aside genitourinary disorders who underwent a study at the radiological center of the GAUZ TO MK MC "Medical City" of Tyumen in 2016–2020 were included. There were 52 men and 48 women with a median age of 44.6 (42;55) years who did not have history, clinical and laboratory manifestations of renal pathology. PET/CT was performed according to the standard technique using a device from Siemens (Biograph). The analysis of the obtained data was carried out by a visual method with a 3D image reconstruction.

In this study, functional changes in the kidney parenchyma were evaluated by uptake of ^{11}C-choline. Visual control was supplemented by a quantitative assessment. Areas of active metabolism were analyzed automatically according to the level of uptake (SUVmax in g/ml). The study began 10 minutes after the administration of the drug at dose 3 ng/kg. The isotope was prepared in the radiological center on a compact cyclotron of the Swedish company Scanditronix.

Statistical analysis was carried out in accordance with international requirements for the processing of data from scientific research, using the program for personal computers Statistica for Windows (version 11.5). Continuous variables are presented as mean ± standard error of mean. The significance of the differences was assessed by Student's t-test.

Results. In total, more than 10,000 PET/CT studies have been carried out at the Tyumen Radiological Center over the past 5 years. After undergoing specialized treatment, patients, having the remission of the underlying pathology, including a relapse-free period of oncological diseases, were referred for further follow-up and treatment to local outpatient clinic, having an electronic media with comprehensive information on the viability of all viscera located from the level of the thyroid gland to the acetabulum. During this study, we performed a retrospective analysis of PET/CT examinations with ^{11}C-choline of 100 patients in order to detect early manifestations of CKD at the molecular and cellular level. Studying the indications for PET/CT, which necessarily contained history and additional information about concomitant diseases, we proved that there were no participants who had known kidney pathology.

According to the analysis, regardless of the indications to PET/CT, 22 participants had various manifestations of decreased ^{11}C-choline uptake, indicating a reduce in viability of the parenchyma (*fig. 1, 2*). From them, in 14 patients a local decrease in ^{11}C-choline uptake (SUVmax) was seen, which was not accompanied by radiological signs of kidney damage, and 8 patients a total decrease in its uptake was found, which coincided with CT signs of renal scarring (abnormalities of contour, deformation of the collecting system and reduced

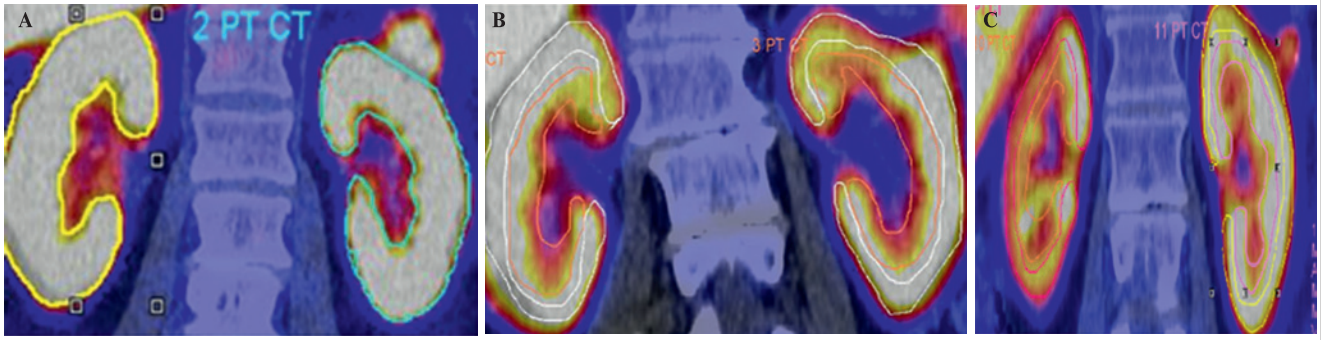
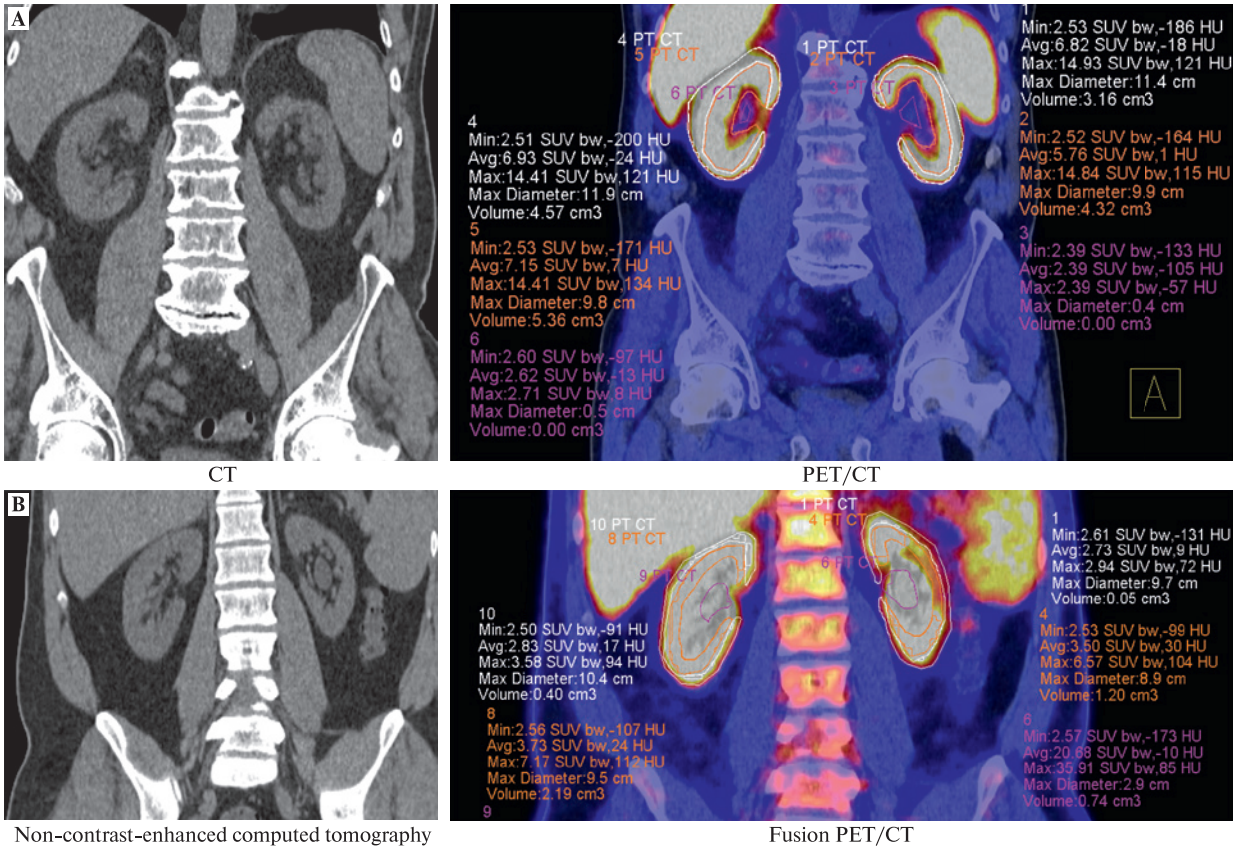


Fig 2. Variants of visual color changes in 11C-choline PET/CT in the kidney parenchyma in residents of the Tyumen region who do not have clinical and laboratory manifestations of CKD
A – normal variant; B – in decreased metabolism; C – in scarred kidneys.



CT PET/CT

Non-contrast-enhanced computed tomography Fusion PET/CT

Fig 3. Results of a standard comparative analysis of PET/CT images, selected for retrospective study (on the right, simultaneous visual and mathematical calculation of ^{11}C-choline activity in the kidney parenchyma)
A – normal variant, B – features of CKD

Table

Results of PET/CT of lipid metabolism in the renal parenchyma using by ^{11}C-choline uptake (SUVmax) in patients without clinical and laboratory manifestations of CKD (M±mean)

^{11}C-choline	SUVmax in g/ml	*P*
Normal structural and functional state of the parenchyma (*n*=78)	11,6±1,0 100%	
Decreased functional viability of the parenchyma (*n*=14)	10,8±0,7 -21,7%	<0,05
Decreased structural and functional viability of the parenchyma (*n*=8)	7,5±04 -35,3%	<0,05

*P<0.05 differences are significant relative to the structurally and functionally unaffected renal parenchyma (Student's t-test).

size). Thus, these changes were regarded as a reliable marker of parenchymal damage.

The values of ^{11}C-choline uptake on PET/CT, reflecting the viability of the kidney parenchyma, are presented in the table. A decrease in the parenchymal uptake of ^{11}C-choline by up to 20% compared to structurally and functionally unaffected parenchyma was not accompanied by deformities of the kidney contour on CT. A decrease in parenchymal uptake by more than 30% coincided with the radiological signs of irreversible changes in the renal parenchyma (abnormalities of the contour, deformation of the collecting system, reduced size) (*fig 3*). Based on the results of a comparative visual and mathematical analysis of the PET/CT images, it can be concluded that patient B., like patient A., who did not have history, clinical and laboratory manifestations of CKD at the time of the examination, had a decrease in the uptake of the tracer in cortex and medulla of both kidneys by more than 40% relative to the calculated normal values (SUVmax~11.6±1.0 g/ml), which was accompanied by a decrease in the renal parenchyma thickness by 10%.

All patients with radiological manifestations of CKD identified during PET/CT were referred to a nephrologist for further diagnosing the causes of renal parenchyma damage.

Discussion. The pilot retrospective analysis of the results of ^{11}C-choline PET/CT performed in 100 residents of the Tyumen region who did not have history, clinical or laboratory manifestations of CKD allows to identify and quantify a reduce of viability of the kidney parenchyma in 22% cases, while in 8% participants irreversible radiological signs of kidney damage were revealed.

Conclusions. The possibility of early molecular study of nephropathy can be used for wider retrospective PET/CT clinical examination as one of the highly effective methods for detecting CKD, which needs further research.

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PRACTICE OF UROLOGICAL DEPARTMENTS DURING THE COVID-19 PANDEMIC

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Introduction. The pandemic of novel coronavirus infection has had a strong impact on the whole medical system, including urological departments.

Material and methods. We assessed the impact of restrictions due to the pandemic on the work of urological departments of private (Medical Center "Avicenna", Novosibirsk) and community (KGBUZ "City Clinical Hospital No. 11, Barnaul") hospitals; GBUZ of the Novosibirsk region "City Clinical Emergency Hospital" (GBUZ CCEH) No. 2, Novosibirsk) clinics, as well as the urogenital department of the TB Research Institute of Ministry of Health of Russia during the period from 2019 to 2020. The changes in the spectrum of surgical procedures, as well as the structure of patients' visits to a urologist were evaluated.

Results. In March 2020, the urogenital department of the TB Research Institute of Ministry of Health of Russia was redesigned into an observational one. Community departments worked with small restrictions or without any limitations. In KGBUZ "City Clinical Hospital No. 11, Barnaul", an increase in the number patients with bladder cancer, ureteral stones, concomitant kidney and ureteral stones by 3-27% was noted ($p<0.05$), as well as those with acute epididymo-orchitis, including testicular abscess. At the same time, a significant decrease in the number of patients with varicocele, pyelonephritis, chronic cystitis, chronic prostatitis, and phimosis was found. A surgical department of GBUZ CCEH from October to December 2020 was restructured to an infectious hospital; this led to a decrease in the volume of urological care and the number of procedures. The Avicenna Medical Center also established anti-epidemic measures, which made it possible not only not to reduce, but in a number of procedures to increase the volume of surgical care.

Conclusion. Owing to anti-epidemic measures, including the patient flow distribution, an introduction of mandatory testing, an early detection of patients and carriers among employees, mask regime, the opening of an observational department, single rooms, the lack of contact between patients, short length of stay, it was possible to prevent an outbreak of coronavirus infection among patients and personnel. Both in the municipal and private urological clinics, well-organized work precluded the negative impact of the pandemic.

Key words: coronavirus infection, urology, urological care, COVID-19, tuberculosis, BCG

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Doi: https: //dx.doi.org/10.18565/urology.2022.1.35-40

Introduction. At the end of 2019, the world faced an infectious disease that was unprecedented in its consequences. The pandemic of a new coronavirus infection, as of February 9, 2022, caused 5,784,434 deaths, including 334,039 in Russia. More than 400 million people worldwide have had COVID-19 [1]. In the Novosibirsk region, as of February 9, 2022, 124,006 people had a diagnosis of COVID-19, of which 4,746 died. In the Altai Territory, including Barnaul, a new coronavirus infection by this time was diagnosed in 159,187 patients, and 7,543 died [1]. The sudden influx of patients led to the forced re-profiling of many departments and hospitals, which could not but affect the results of diagnosis and treatment of those with other diseases. Thus, the inability to receive medical care led to a sharp decrease in the early detection of tuberculosis, which results in a twofold increase in mortality [2]. Representatives of many medical specialists (urologists, gynecologists, cardiologists, otorhinolaryngologists) had to treat patients with a new coronavirus infection, since there was an urgent lack of infectious disease specialists.

Materials and methods. The role of forced restrictions due to the pandemic of a new coronavirus infection on the work of urological departments of various clinics was studied. The statistical reports of a private center (MC "Avicenna", Novosibirsk) and municipal clinics, including the City Clinical Hospital No. 11, Barnaul, and the City Clinical Emergency Hospital No. 2, Novosibirsk were analyzed. Statistics of the urogenital department of the Novosibirsk Research Institute of Tuberculosis (FGBU NNIIT) for 2019 and 2020 is also presented. The changes in the spectrum of surgical interventions, as well as the structure of patients' visits to the urologist were compared.

Statistical processing was performed using the Microsoft Office package 2007, Biostat, 2009. Differences between groups were determined using the χ^2 test. The hypothesis of the lack of a statistically significant effect of the factor was rejected at $p>0.05$.

Results. In March 2020, due to the deteriorating epidemic situation, the urogenital department of the FGBU NNIIT was reprofiled into an observational department for a new coronavirus infection. This department admitted patients with tuberculosis not only of the genitourinary system, but also of the lungs. Hospitalization was carried out only in the presence of a

Table 1

Comparison of the main results of the urologic department of the City Clinical Hospital No. 11, Barnaul, for 2 years

Disorder	Number of patients in 2019	Number of patients in 2020	Dynamics	*P*
Prostate cancer	82	49	-40%	<0,05
Bladder cancer	33	34	+3%	>0,05
Varicocele	30	7	-77%	<0,05
Acute tubulointerstitial nephritis	432	367	-15%	<0,05
Acute pyelonephritis	53	40	-24%	<0,05
Hydronephrosis	79	62	-21%	<0,05
Kidney abscess	19	19	0	>0,05
Kidney stones	616	564	-8%	>0,05
Ureteral stones	1060	1105	+4%	>0,05
Kidney and ureter stones	167	212	+27%	<0,05
Acute cystitis	88	82	-7%	>0,05
Chronic cystitis	25	16	-36%	<0,05
Urethral strictures	48	30	-38%	<0,05
Benign prostatic hyperplasia	211	186	-12%	<0,05
Acute prostatitis	126	123	-2%	>0,05
Chronic prostatitis	8	6	-25%	<0,05
Acute epididymo-orchitis, including testicular abscess	76	80	+5%	>0,05
Phimosis/paraphimosis	34	14	-59%	<0,05
Pyelonephritis in pregnant women	36	34	-6%	>0,05
Hospital admissions per year	3457	3209	-7%	>0,05

negative test for COVID. Moreover, on the day of admission, patients were re-tested using a polymerase chain reaction. Then, they were in the observational department for two weeks; with a positive test, patients were transferred to a specialized hospital, while those with a negative result for COVID-19 were admitted to the therapeutic or pulmonary surgical department. Patients with tuberculosis of the genitourinary system were admitted mainly for performing highly specialized surgical procedures, and specialized examinations were minimized.

Municipal branches worked either in full or with slight restrictions. The dynamics of the work of the municipal urological clinic of Barnaul is shown in *Table 1*.

In total, the number of patients in the year of the pandemic decreased by 7%, but this value is within the statistical error. There was an increase in the influx of patients by 3–27% admitted for bladder cancer, ureteral stones and concomitant kidney and ureteral stones ($p<0.05$), as well as those with acute epididymo-orchitis, including abscessing. At the same time, a significant decrease in the number of patients with varicocele, acute pyelonephritis, chronic cystitis, chronic prostatitis, and phimosis was found. Less patients with benign prostatic hyperplasia and urethral stricture were treated as well ($p<0.05$).

Strict adherence to strict sanitary and hygienic measures allowed to prevent the outbreak of coronavirus infection on the territory of the department, despite the fact that patients were urgently admitted.

In April 2020, quarantine was introduced in the surgical building of the City Clinical Emergency Hospital No. 2. All visits to patients were prohibited, planned hospitalization and admission in the day patient department were also canceled. In October 2020, the institution was re-profiled into an infectious hospital. On December 18, 2020, hospitalization of patients with a new coronavirus infection was completely stopped. From December 21 to December 25, sanitization of all facilities was carried out; on December 28, the institution fully returned to its usual profile and work schedule. Reprofiling could not but affect the volume of urological care, which is demonstrated in *Table 2*.

The restrictions due to reprofiling led to a decrease in surgical care, which is shown in *Table. 3*.

Despite strict anti-epidemic measures, the volume of surgical care in the private medical center "Avicenna" has not decreased, although the range of operations has changed, as shown in *Table 4*. For example, in the year of the pandemic, the number of flexible ureteroscopies increased by 3 times, but rate

Table 2

Urological care provided in City Clinical Emergency Hospital No. 2, Novosibirsk, in 2019–2020

	2019 г.	2020 г.	Dynamics, %	*p*
Patients treated	2492	2116	-15	$p<0,05$
Length of stay	7,4	7,2	-3	$p>0,05$
Urgent admission	2373	2083	-12	$p>0,05$
Planned admission	119	33	-72	$p<0,05$
Emergency procedures	978	756	-23	$p<0,05$
Planned procedures	82	66	-19	$p<0,05$

Table 3

The structure of surgical procedures performed at the City Clinical Emergency Hospital No. 2, Novosibirsk, in 2019–2020

	2019	2020	Dynamics, %	*P*
Puncture suprapubic cystostomy	154	122	-21	<0,05
TURP	36	13	-64	<0,05
TURBT	36	14	-61	<0,05
Percutaneous nephrostomy	41	21	-49	<0,05
Ureteroscopy with stone extraction	60	43	-28	<0,05
Ureteral stenting	75	74	-1	>0,05
Ureteroscopy with lithotripsy	152	111	-27	<0,05

Note. TURP – transurethral resection of the prostate, TURBT – transurethral resection of bladder tumor

Table 4

The volume and structure of all surgical procedures at Avicenna Medical Center for 2019–2020

Surgical procedures	2019	2020	Dynamics, %	*P*
Interventions on the genitals	238	189	-21	<0,05
Interventions on the prostate	185	191	+3	>0,05
Interventions on the bladder	113	93	-18	<0,05
Interventions on the kidney, ureter	311	335	+8	>0,05
Diagnostic procedures and manipulations	128	110	-14	<0,05
Urogynecological procedures	14	25	+79	<0,05
Percutaneous interventions	217	266	+23	<0,05
Other procedures	30	25	-17	<0,05
Total	1226	1234	+0,7	>0,05

of ureteroscopies after extracorporeal shock-wave lithotripsy decreased by 86% (*Table 5*). In general, the number of surgical interventions for urolithiasis increased by 6%. The structure of prostate procedures has also changed. The number of transurethral resections has increased by 16%, while prostate biopsies were performed by 12% less (*Table 6*).

The number of cystectomies and nephrectomies for malignant tumors of was not different between 2019 and 2020, and the number of partial nephrectomies increased by 19% (<0.05). The data are clearly presented in *Table 7*.

In addition, in MC "Avicenna" in 2020 such interventions as laparoscopic pyeloplasty with simultaneous ureteroneocystostomy and laparoscopic partial nephrectomy were performed significantly more often, however, the number of laparoscopic hernioplasties decreased by 40%, as presented in *Table 8*.

Discussion. The organization of medical care in the context of the COVID-19 pandemic is a great challenge. According to the recommendations of the World Health Organization, any surgical intervention should be postponed in regions with a high incidence of COVID-19 [3].

Table 5

The volume and structure of procedures and interventions for urolithiasis at Avicenna Medical Center for 2019–2020

Procedure	2019	2020	Dynamics, %	*P*
Cystolithotripsy	20	12	-40	<0,05
Extracorporeal shock-wave lithotripsy (ESWL)	69	70	+1	>0,05
Repeated sessions of ESWL	9	10	+11	>0,05
Ureteroscopy after ESWL	7	1	-86	<0,05
Ureteroscopy	12	5	-58	<0,05
Ureteroscopy with lithotripsy	109	122	+12	>0,05
Percutaneous nephrolithotomy	192	238	+24	<0,05
Flexible ureteroscopy with lithotripsy	3	9	+200	<0,05
Total	421	447	+6	>0,05

Table 6

The volume and structure of procedures on the prostate at Avicenna Medical Center for 2019–2020

Procedure	2019	2020	Dynamics, %	*P*
TURP, enucleation of the prostate, TUIP	106	123	+16	<0,05
Laparoscopic radical prostatectomy	69	68	-1	>0,05
Prostate biopsy	103	91	-12	<0,05
Total	278	282	+1	>0,05

Note. TUIP – transurethral incision of the prostate.

Table 7

The volume and structure of procedures and interventions for oncological diseases at Avicenna Medical Center for 2019–2020

Procedure	2019	2020	Dynamics, %	*P*
Radical prostatectomy	69	68	-1	>0,05
Prostate biopsy	103	91	-12	>0,05
TURBT	67	60	-10	>0,05
Radical cystectomy	15	16	+7	>0,05
Nephrectomy	21	19	-9	>0,05
Partial nephrectomy	26	31	+19	<0,05
Pelvic exenteration	0	1	+100	>0,05
Retroperitoneal/pelvic Lymph node dissection	5	1	-80	<0,05
Orchidectomy	5	5	0	>0,05
Resection of a retroperitoneal tumor	3	5	+67	<0,05
Total	314	297	-5	>0,05

Table 8

Volume and structure of laparoscopic procedures at Avicenna Medical Center for 2019–2020

Procedure	2019	2020	Dynamics, %	*P*
Laparoscopic excision of kidney cysts	15	11	-27	<0,05
Laparoscopic nephrectomy	18	19	+6	>0,05
Laparoscopic pyeloplasty + ureteroneocystostomy	23	51	+122	<0,05
Laparoscopic nephrectomy	22	31	+41	<0,05
Laparoscopic prostatectomy	69	68	-1	>0,05
Laparoscopic adrenalectomy	1	4	+300	<0,05
Laparoscopic hernioplasty	15	9	-40	<0,05
Laparoscopic cystectomy	10	10	0	>0,05
Total	173	203	+17	<0,05

A new coronavirus infection is a systemic disease that affects not only the lungs, but also other organs and systems. Acute kidney injury is one of the important complications of the COVID-19, which occurs in up to 7% of cases in general and in 3–23% of patients in the intensive care unit [4–5]. The role of SARS-CoV-2 in the development of lower urinary tract symptoms, including high rate of dysuria, has not yet been fully elucidated. The development of lower urinary tract symptoms in patients with coronavirus infection in the absence of bacteriuria and with elevated urinary levels of cytokines has been called "de novo urinary symptoms" or "COVID-19 associated cystitis" [6]. In the studied departments, there were no cases of coronavirus kidney diseases, neither in the first period of the pandemic [7], nor now.

SARS-CoV-2 can infect the testicles, potentially affecting testosterone levels, as well as having a destructive effect on male reproductive potential. Orchitis can be a complication of COVID-19. Damage to testicular tissue is possible due to direct infection with the virus, secondary autoimmune reaction, hyperthermia and thrombosis of testicular microvessels [8]. A greater susceptibility to coronavirus infection of men has been shown. In moderate and severe disease, a reduced testosterone level is detected in 46.7% of cases. With successful treatment of a new coronavirus infection, a significant increase in testosterone levels is observed without any special intervenions [9].

An experience suggests that patients with diabetes mellitus and arterial hypertension receiving angiotensin-converting enzyme inhibitors had more severe course of COVID-19, and they develop complications more often [10].

A.M. Belyaev et al. [3] analyzed changes in the work of the oncourological department during the first wave of the COVID-19 pandemic in the National Medical Research Center for Oncology named after N.N. Petrov in St. Petersburg. The authors studied the results of 96 patients admitted in the surgical department for the period from March 16 to May 18, 2020. Surgical treatment was done in 79.2%, while chemotherapeutic treatment was performed in 12.5% of cases, and 8.3% of patients were discharged without specialized treatment. Indications for surgical treatment in 76 (79.2%) patients were as follows: renal cell cancer (n=18; 23.6%), prostate cancer (n=20; 26.3%), bladder cancer (n=27; 35.7%) patients.

During this period, a new coronavirus infection was diagnosed in 11 (11.5%) patients, and a severe course of the disease, requiring mechanical ventilation, developed in 3 (3.1%). Mortality during hospitalization was 3.1%, another 2 (2.1%) patients died within a month after discharge. The authors note a short waiting time for surgery in the hospital, which was 1.8±1.7 days. Postoperatively, patients were discharged on average after 7.3±7.7 days [3].

The re-profiling of the health care system due to a massive influx of infectious patients has significantly limited the opportunity to receive timely specialized medical care. This led, in particular, to a significant decrease in the number of newly diagnosed patients with tuberculosis and at the same time doubled the number of deaths from this disease [2]. The consequences of late diagnosing of urogenital tuberculosis [11] will undoubtedly affect the post-COVID era. It was the impossibility of obtaining timely medical care that led to an increase in the rates of emergency admissions and surgical interventions [12].

Currently, the inability to provide a visit for patients has led to the rapid development of telemedicine. Modern communication technologies allow to receive a consultation online [13]. In our opinion, this is a suboptimal medical care, since the physician can only question the patient and evaluate the laboratory results, while a full examination, including palpation, is impossible.

In a number of countries, medical institutions can use online consultations and get paid accordingly. However, there are a

number of restrictions in the Russian Federation. For example, remote counseling requires a licensed room, and it is forbidden to make a diagnosis and prescribe treatment [13]. In addition, for some patients, due to insufficient computer literacy and appropriate equipment, such a variant of medical care is still unavailable.

In one of the urological centers in New York, during the COVID-19 pandemic, the number of video consultations increased by 8729% [14].

According to the results of an online survey of 1021 Russian urologists, conducted by a working group of the chief urologist of the Ministry of Health of Russia, the number of scheduled consultations and elective surgeries decreased by approximately 75% and 71%, respectively; the proportion of planned oncourological procedures was 30%, while the volume of emergency procedures increased, reaching 70%. In addition, 32% of respondents expressed confidence that the medical institutions in which they work will be reprofiled, and 54% of participants believed that urologists would be involved in the treatment of patients with COVID-19 [12].

During a pandemic, the number of elective surgeries should be reduced [15], since the development of a coronavirus infection that was not diagnosed prior to surgery increases the likelihood of severe complications in the postoperative period by a third; mortality in this group of patients was 20% [16].

Now the principles of organizing the work of the urological department have been developed [12], which allow to significantly reduce the risk of developing outbreak of COVID-19 in a hospital.

Conclusion. Despite the tense epidemic situation, urological departments both in municipal hospitals and in a private center were able to provide specialized care in full or with slight restrictions. This was possible owing to strict anti-epidemic measures, including the patient flow distribution, an introduction of mandatory testing for COVID-19 before and during hospitalization, an early detection of patients and carriers among employees, introduction of mask regime, the opening of an observational department with admission of patients for 14 days, maximum isolation of patients with preferential placement in single rooms and short length of stay.

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PATHOGENESIS AND TREATMENT OF POSTCOITAL CYSTITIS: ARE OUR APPROACHES CORRECT?

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Aim. To study the pathogenetic factors in the development of postcoital cystitis and the efficiency of extravaginal transposition of the urethra.
Materials and methods. Literature data and our point of view on the causes of postcoital cystitis are described. Case histories of 438 patients aged 18 to 61 (mean 24±1.3) were analyzed. The efficiency of extravaginal transposition of the urethra for the prevention of recurrence of postcoital cystitis was evaluated.
Results. The long-term results of operations in 315 patients were studied. A positive effect was noted in 297 (94.3%), which means the complete recovery or reduction in the frequency of cystitis to 2 or less times a year, while complete recovery occurred in 214 patients. In 18 (5.7%), the surgical procedure was ineffective, which required repeated interventions.
Discussion. According to our observations, the external opening of the urethra is located in patients with postcoital cystitis and in healthy women at the same level - before the introitus. During sexual intercourse, everyone experiences vestibulo-vaginal frictional dislocation of the urethra, however, exacerbations of the inflammatory process in the bladder occur only in some females, which is associated with the multifactorial nature of the disease.
Conclusion. Postcoital cystitis develops as a result of a complex of factors, the most significant of which are the state of the vaginal microflora, the virulence of uropathogenic bacteria, the anatomical features of the urethra and vagina, its narrowness with a mismatch with the penile size, the intensity and duration of sexual intercourse, severe, complicated childbirth and surgical procedures in this area. Performing extravaginal transposition of the urethra according to Komyakov demonstrated high efficiency in the prevention of recurrence of postcoital cystitis.

K e y w o r d s: *urethra, poctcoital cystitis, transposition of distal urethra*

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Doi: https: //dx.doi.org/10.18565/urology.2022.2.27-32

Introduction. Postcoital cystitis is a special form of recurrent bladder infection in women, which occurs after sexual intercourse. The national clinical guidelines and recommendations of the most authoritative urological communities (AUA, EAU) suggest the general principles for preventing recurrences of the cystitis. Of all these measures, only the postcoital antibiotic prophylaxis has proved efficiency, but is associated with known side effects and the development of antibiotic resistance in uropathogens. Currently, there are no recommendations regarding the women, in whom all measures taken, including long-term antibacterial prophylaxis, are ineffective.

Historically, it is believed that a prerequisite for the development of postcoital cystitis is the displacement of the external urethral orifice into the vagina during coitus, associated with the anatomically "low" location of the urethra and/or its high mobility. This problem was first described in 1959 by R.P. O'Donnell [1]. He found the low position of the meatus in women suffering from postcoital cystitis and called this condition female relative hypospadias. The author suggested that in combination with hymen remnants in the form of folds extending radially from the urethra, it may cause permanent route for infection into the bladder during intercourse. O'Donnell considered these anatomical features associated with incomplete rupture of the hymen at the onset of sexual activity, which leads to the formation of hymenal folds, the overgrowth of the hymen remnants over the urethra like a "hood" and its displacement towards the introitus. In that work, he first proposed a method of surgical prevention of recurrence of postcoital cystitis, which was called hymenotomy. The procedure involved the division of the hymenal folds, which, in his opinion, should lead to the release of the urethra and reduce the frequency of recurrences. However, this technique did not meet expectations, since external urethral orifice remained in the same position and may be displaced during sexual intercourse into the vagina with the subsequent relapses of cystitis. Subsequently, the ideas of O'Donnell were developed by other authors. For example, R.C. Hirschhorn [2] developed procedure that he called "urethrolysis", which involved transverse division of the urethro-vaginal gap with its longitudinal suturing. In 1992 L. I. Van Bogaert [3] was the first who suggested mobilizing the urethra and then transposing it up, closer to the clitoris, using a single vertical incision, which was then sutured over the urethra. This method, called urethral transposition, began to be used in a number of clinics, including Russia [4, 5]. However, this approach had not gained popularity due to insufficient transposition of the urethra from the introitus and its weak fixation in a new position, which led to the wound dehiscence with dislocation of the meatus to its original place and recurrence of the disease.

As a result, this technique is no longer used, as shown by the absence of publications in foreign literature over the past three decades. To overcome this problem, we have developed a method for surgical correction of the meatal dystopia in women with postcoital cystitis [6, 7].

Aim. To study the pathogenetic factors in the development of postcoital cystitis and the efficiency of extravaginal transposition of the urethra.

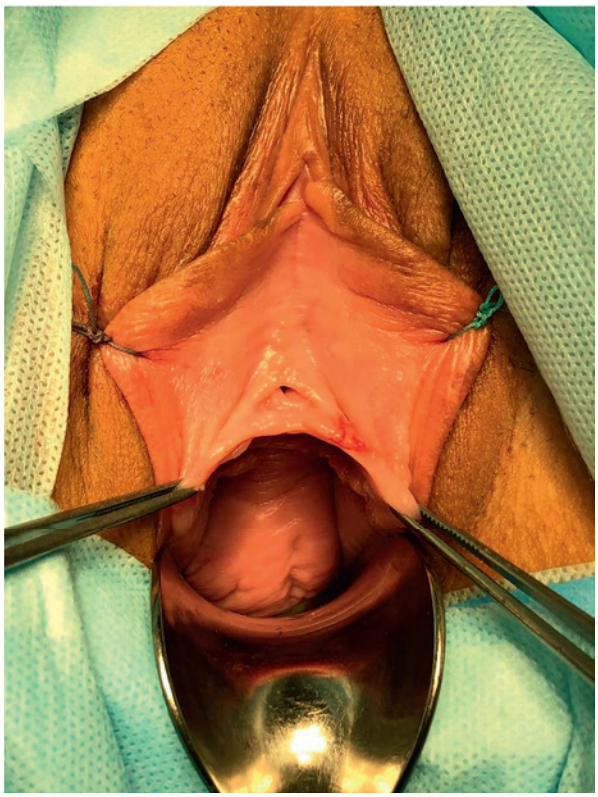

Fig. 1. The typical location of the external urethral orifice in front of the vestibule. The hymenal remnants diverge radially from it

Fig. 2. Long vaginal vestibule with a distally located urethral meatus

Fig. 3. Short vaginal vestibule with the same typical location of the meatus

Materials and methods. A total of 438 women aged 18 to 61 years (mean 24±1.3 years) with extravaginal transposition of the urethra were treated in our clinic from 2005 to 2020, according to the method, which was developed and then improved by our team (patents for invention No. 2686948 from 2011 and No. 2408296 from 2018). The examination included the history taking, physical examination, evaluation of the external genital organs, urinalysis and urine culture and bladder ultrasound. In almost all women, the urethra was located above the introitus in the area of the hymen remnants. The hymenal folds diverging from the urethra were especially well visualized during vaginal speculum examination (Fig. 1). In most patients, a significant distance from the urethra to the clitoris was detected (Fig. 2), but in some cases this distance was short (Fig. 3). The urethral meatus in all women was located in the same place, namely in front of vestibule. The cystitis developed after each or almost every sexual intercourse. In most cases, frequent recurrences of urinary tract infections were seen from the beginning of sexual activity, in others they were associated with a change of sexual partner, childbirth, surgical interventions in this area, acute infectious diseases, etc.

Our surgical technique is based on the mobilization of the entire urethra, followed by its pulling through submucosal tunnel to the clitoral area, where it is diverted through a separate incision and fixed with interrupted sutures. The posterior wall of the urethra is sewed during closing of the vaginal incision [6]. This method allowed to significantly improve the outcomes, which contributed to its widespread adoption. During the first 3 years in our clinic there were 17 such procedures, after that their number rapidly increased, and as a result, over the three years from 2017 to 2019 a total of 190 women were treated. In 2020, their number decreased due to the epidemiological situation. The dynamics of the number of procedures is shown in the Fig. 4.

Recently, this procedure has received universal recognition and is used in many clinics in our country [8, 9]. In addition, it has attracted interest at the congresses of the European and American Urological Associations [10, 11].

Results. Out of 438 women, who were undergone to our technique, 315 (71.9%) had long-term follow-up. In 297 (94.3%) patients, a successful outcome was observed: 214 (72%) women achieved complete cure, while 77 (25.9%) had recurrences of cystitis no more than 2 times a year. Moreover, recurrences were not always associated with sexual intercourse. The procedure

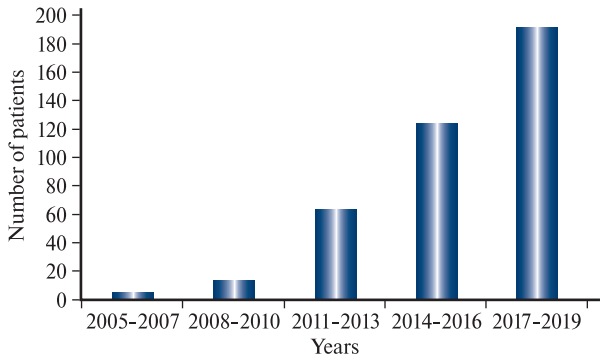

Fig. 4. Distribution of the number of treated patients by years

was ineffective only in 18 (5.7%) cases, including 11 females with displacement of the urethra to the original place with the recurrence of cystitis and 7 patients with the same recurrence rate after sexual intercourse 3 years after the intervention. Reoperation was performed in 8 patients; in 7 of them it was effective.

Discussion. Until recently, the anatomically low location of the meatus was considered the main cause of the development of postcoital cystitis, since it was prone to deep displacement into the vagina during intercourse. Such a location of the urethra was called female hypospadias, relative hypospadias, vaginal ectopia or dystopia of the meatus, or urethral vaginization. In addition, urethral mobility was regarded as hypermobility of the urethra. All these terms, in our opinion, are incorrect. It is impossible to extrapolate hypospadias in men, which includes a serious anomaly not only of the urethra, but also of the penis, to women. In Russian and foreign literature, there is no generally accepted definition of female hypospadias, although different classifications are described. The authors, who consider this term valid, define hypospadias as the location of the meatus on the anterior wall of the vagina, proximal to the hymenal ring, and in extremely rare and severe cases, the fusion of the bladder neck and vagina with the development of urinary incontinence [12]. This rare pathological condition, which is more correctly called ectopia or dystopia of the urethra, has no association with postcoital cystitis. In hundreds of our patients, the external urethral orifice was always located on the border of the vestibule and the vagina in the area where the hymenal remnants were found. It should be noted that there is no clear concept of the normal location of the meatus in females. An anatomy textbook edited by M.G. Prives [13] describes its location approximately 2 cm below the clitoris glans. In the latest edition of the classic textbook Gray`s anatomy [14], the location of the meatus on the anterior wall of the vagina is described as normal.

The term "urethral hypermobility", in our opinion, is also unacceptable and cannot regarded as a diagnosis. It means an increased displacement of the urethra, but in the normal state it has a static position. Even more so, the degree of its mobility during intercourse has not been established. To detect hypermobility, a test, described by O'Donnell and then Hirschhorn, was proposed: two fingers are inserted into vagina, which results in a complete displacement of the meatus into the vagina. In our experience, this test is almost always positive, including healthy women, since a sufficiently deep insertion of two fingers leads to displacement of the meatus into the vagina in all subjects. On fig. 5 the vestibule in a 57-year-old woman who had a regular sexual life, without any episodes of cystitis in history, is shown. At the same time, she has all the anatomical attributes described by O'Donnell and other authors (a fold of the vestibular mucous membrane, overlying the urethra like a hood, a low location of the urethra on the border between the vestibule and the vagina, hymenal folds radially diverging from it). The woman also has a positive O'Donnell-Hirschhorn test (Fig. 6).

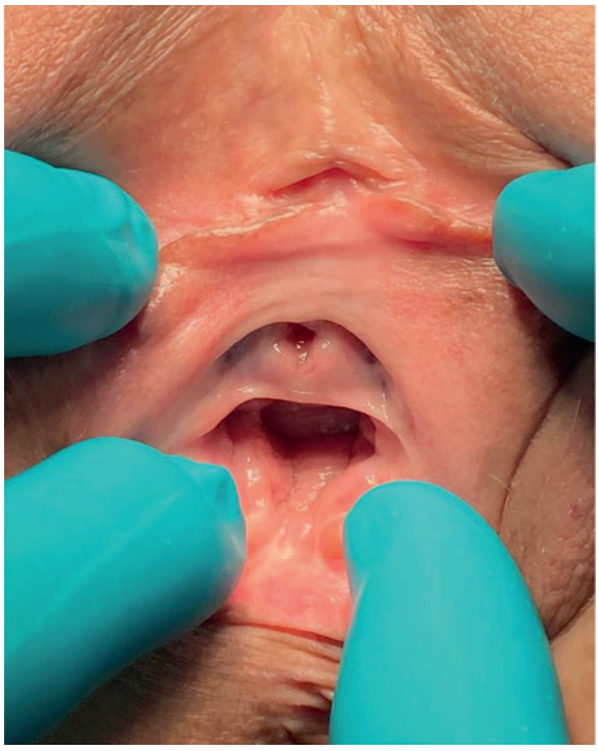

Fig. 5. The urethra and vestibule in a 57-year-old woman without any previous episodes of cystitis

Fig. 6. Positive O'Donnell-Hirschhorn test in this woman

According to our data, the urethra in the vast majority of women is located directly above the vaginal vestibule, and the visual sensation of its "low" external opening is created due to the different lengths of the vaginal vestibule and different distances from the urethra to the clitoris. It is more correct to consider that it is not the urethra that is low, but the clitoris is located high.

In the cited publications, the location of the external urethral orifice was determined only visually. T.M. Hotoon [15] was the first to carry out morphometric studies. They established that the distance from the urethra to the anus in women with recurrent urinary infections was shorter than in healthy women, although the difference constitutes only 2 mm on average.

V.N. Lesovoy [16] et al. measured the distance between the urethra and clitoris. They showed that in healthy women it was less than 3 cm compared to ⩾3 cm in those with postcoital cystitis. The authors also compared the size of the penis in partners of healthy women and patients with postcoital cystitis. Their conclusion was that penile size is not a risk factor for the development of the cystitis, which contradicts our data.

In a study by K. Gyftopoulos et al. [17], the authors evaluated the anatomical relationships in patients with recurrent postcoital cystitis and healthy women, and calculated the prognostic value of each variable. It was found that the external urethral orifice in healthy women is indeed located higher relative to the vagina, while the length of the vestibule is bigger, although the difference for both variables was insignificant (difference of the medians was 5 mm). The most reliable prognostic factor for the development of postcoital cystitis was the distance from the urethra to the vagina, which was a half the vertical size of the introitus. The difference in the median of this variables between the groups was significant: in patients with postcoital cystitis, it was 10 mm higher. The rationale for this association is probably that the smaller size of the introitus naturally leads to greater tension and deformation of the urethra during intercourse.

Regardless of which anatomical feature plays a main role, a necessary prerequisite for the development of cystitis is the repeated displacement of the urethra into the vagina during intercourse, namely the vestibulo-vaginal frictional dislocation of the urethra. At the same time, it is not only dislocation, but also deformation, which leads to its contamination and the development of an inflammatory process. Perhaps due to the longitudinal repetitive compression and dilation of the urethra, the vaginal flora may get into the bladder according to the principle of the plunger. As a result, the basis for the development of cystitis is not static, but dynamic, namely a displacement of the external urethral orifice into the vagina. Since the O'Donnell-Hirschhorn test, as noted above, was positive in all women, it should be assumed that these processes occur constantly. However, not all women develop recurrent postcoital cystitis. The reason is probably related to the differences in urethral displacement, which is influenced by following factors: the narrowness of the vestibule and its inconsistency with the size of the penis, the length and width of the urethra, its elasticity, the distance from the urethra to the introitus, hymenal folds, intensity and duration of sexual intercourse, difficult, complicated childbirth and surgical procedures in this area. To a certain extent, after the elimination of even one of the factors, some women note a positive effect, for example, the division of the hymenal folds or the suburethral injection of urethral bulking agent. In addition, the change in the frequency of recurrence may depend on the size of the penis. With extravaginal transposition of the urethra, it is moved from the zone of tension and from the vestibule. Its length and structure, as well as quality of paraurethral tissues also change. During this procedure, the external urethral orifice is also dissected from the hymen remnants, which can also be the area of colonization by uropathogens [17].

In addition to the anatomical factors, one of the causes of postcoital cystitis is a disturbance of the vaginal microbiota. In some cases, it is possible to establish an association with vaginal dysbiosis during a pelvic exam, when discharge and other signs of inflammation are present. However, when a woman does not have signs of vaginitis, a more thorough examination is required. In a review article by A.E. Stapleton [18] it was established that lactobacilli play a role in preventing the colonization of the vagina by E. coli, one of the main causative agents of cystitis. A decrease in the content of these bacteria leads to both inflammatory and non-inflammatory disorders of the vagina, and the development of recurrent cystitis. A. Aydin [19] showed the influence of the anatomy of the labia minora on the development of cystitis. It was also found that in women with recurrent cystitis, the vaginal pH is more alkaline than in healthy women, which may be a consequence of disturbed microbiota. The significance of these factors is confirmed by the fact that in a number of patients, postcoital cystitis may develop after antibiotic therapy, which naturally leads to vaginal dysbiosis. At the same time, some studies have shown the efficiency of probiotics containing lactobacilli in the prevention of urinary tract infections [20].

Conclusion. The external urethral orifice in healthy women and in those with recurrent postcoital cystitis is located approximately at the same level before the vestibule. This is not low, as previously thought, but a completely normal location of the meatus. From this point of view, it remains not clear why only a number of women after the onset of sexual activity experience frequent recurrences of postcoital cystitis. Currently, we consider a combination of different risk factors, the most significant of which are the vaginal microflora, the virulence of uropathogens, anatomical features of the urethra and vagina, narrowness of the vagina and its inconsistency with the penile size, the intensity and duration of sexual intercourse, complicated childbirth and surgical interventions in this area. Extravaginal transposition of the urethra according to our method allows for eliminating its deformation and displacement into the vagina during frictions, preventing infection from entry into the bladder. The main indication for the procedure is the clear relationship of episodes of cystitis with sexual intercourse. The best results are achieved with the correct selection of patients and compliance with all the technical features of the technique developed in our clinic.

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KIDNEY CARBOXYCRYOABLATION. PILOT STUDY

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Aim: The aim of this experimental study was to evaluate the effect of low temperatures of carbon dioxide on a "living" blood-supplying organ (pig kidney), to determine the possibility of performing cryoablation of kidney tissue with carbon dioxide (carboxycryoablation), as well as to establish experimentally modes of carboxycryoablation of the kidney.
Materials and methods. To carry out this experimental study, a female of the mini-pig line was used. We performed laparoscopic access to the kidney for carboxycryoablation. During the freezing of the kidney, three modes were compared: 60, 90, and 120 s on one kidney of one animal. Immediately after the completion of cryoablation, nephrectomy was performed, and the removed kidney was sent for histological examination. According to the histological study, the results of the use of carbon dioxide during cryoablation of porcine kidney tissue were evaluated.
Results. Cryoablation based on carbon dioxide (carboxycryoablation) leads to irreversible death (necrosis) and destruction of the affected tissue. A direct relationship between the exposure mode and the size of the cryonecrosis zone was noted. Thus, the most extensive zone of necrosis with a diameter of 10 mm was achieved when performing cryoablation in the exposure mode of 120 s.
Conclusion. This experiment showed that carbon dioxide-based cryoablation remains a feasible procedure that leads to irreversible death (necrosis) and destruction of the affected tissue. However, further studies on the safety and efficacy of cryoablation of kidney tissue with carbon dioxide are required.

K e y w o r d s: *carboxy cryoablation, cryoablation of the porcine kidney, carbon dioxide, necrosis, cryonecrosis*

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Introduction. The medical application of low temperatures has been studied for a long time as a surgical technique, which is used in cosmetology and for creating focal zones of destruction in tumor cells [1–3]. Cryoablation is a process of deep, local freezing and devitalization of tissues, allowing for targeted creation of a cryonecrosis area of the predetermined shape and size for the destruction of tumor cells and adjacent healthy cells [2]. Technological advancements in medicine have led to the creation of several types of cryodevices that are based on the gas-throttling effect. Liquid nitrogen, carbon dioxide, nitrous oxide, helium or argon are commonly used. In modern urological practice, cryoablation is performed in patients with kidney cancer and prostate cancer on third- and fourth-generation argon-helium based systems [4–6].

Some experimental and clinical studies have demonstrated that cryoablation of kidney tissue using percutaneous or laparoscopic approaches can be well tolerated [7–9].

Aim: The aim of this experimental study was to evaluate the effect of low temperatures of carbon dioxide on a "living" organ with preserved blood flow (pig kidney), to determine the possibility of performing cryoablation of kidney tissue with carbon dioxide (carboxycryoablation), as well as to establish experimentally modes of carboxycryoablation of the kidney.

Materials and methods. In this experiment, for carboxycryoablation of the kidney, we used 6 months old female mini-pig weighing 35 kg. The cryoablation was performed by laparoscopic access on a "living" organ using a flexible cryoprobe Erbecryo-2 from ErbeElectromedizin (Germany), designed and registered for use in thoracic surgery for cryoextraction (tumor, tissue biopsy, removal of a foreign body, blood clots and mucous plugs), cryo-recanalization, as well as for cryo-devitalization [10–12]. Cold temperature leads to crystallization of intracellular and extracellular fluid. Cell walls are destroyed due to the formation of crystals and recrystallization during thawing, which contributes to the devitalization (destruction) of tissues [13–15]. Our experience was the first, when carboxycryoablation of renal tissue on the Erbecryo-2 was done.

In this experiment, a flexible cryoprobe Erbecryo-2 with a diameter of 2.4 mm and a length of 1.15 m from ErbeElectromedizin (Germany) was used to perform cryoablation of the kidney tissue. The freezing effect of Erberyo-2 is based on the Joule-Thomson effect. It consists in changing the temperature of the gas as a result of a constant reduction of pressure in a gas flow forced through a throttle – local hydrodynamic resistance point, for example, a porous partition. The freezing point of CO2 is minus 78.5°C [16]. Carbon dioxide under high pressure is supplied from a gas cylinder to the cryoprobe (*fig 1*) through the cryosurgical unit *(fig 2)*.

The cryosystem allows to control the flow of carbon dioxide and the freezing time. Passing through the narrow tube of the

Fig. 1. Cryoprobe Erbecryo-2 (ø 2.4 mm)

probe (*fig 3a*), carbon dioxide flows the hollow tip of the probe *(fig 3b)*. At the moment of moving from the narrow segment of the cryoprobe tube to the wide part of the tip, carbon dioxide undergoes a sharp decompression due to a large pressure difference. At that moment, due to the Joule-Thomson effect, the gas freezes the probe tip very quickly (*fig 4*, the probe tip with an ice ball is seen). Depending on the CO2 pressure in the system and the size of the probe, temperatures ranging from -35°C to -50°C is generated at the tip of the flexible cryoprobe.

All animals on the eve of the experiment were deprived of food intake. After premedication with atropine 0.05 mg/kg, anesthesia was induced with zoletil 10 mg/kg and xylazine 0.2 mg/kg IM. After placing ear vein cannula, the animal was intubated. For anesthesia the following drugs were used: propofol 5 mg/kg IV, veropipecuronium 0.02 mg/kg IV and 1.3–3.0% inhalation concentration of AErrane.

Pneumoperitoneum was created by inserting a Veress needle into the paraumbilical space and achieving a pressure of 12 mm Hg. After placing a 12-mm laparoscopic trocar near the umbilicus, the animal was moved to the lateral position; then two additional ports 5 mm in diameter were placed lateral to the rectus abdominal muscle, proximal and distal to the umbilicus. After that, through 5 mm trocar, an endoscopic puncturing needle with a diameter of 3 mm was inserted (*Fig. 5*) for puncturing the lower, middle and upper renal segments to a depth of 2 cm.

Subsequently, a cryoprobe was advanced through the lumen of the endoscopic puncturing needle into the kidney parenchyma (*Fig. 6*). The exposure time in the lower segment was 120 s, while the thawing time was 80 s (*fig. 7*). The same manipulations were performed in the middle and upper segments of the kidney. The freezing time in the middle and upper segments was 90 and 60 s, and the thawing time was 70 and 60 s, respectively. After that, nephrectomy with an extraction of the kidney through a midline incision was performed (fig. 8). At the end of the experiment, the animal was euthanized with a use of drugs to stop cardiac activity. The removed kidney was sent for pathomorphological examination.

Experiment results

According to the pathomorphological study, massive hemorrhages, represented by clusters of red blood cells, were seen in all areas of the cryoprobe insertion. Massive zones of irreversible death of kidney tissue (necrosis) were observed along the periphery of the cryoprobe insertion point. Areas of necrosis included separate glomeruli and tubules with karyopyknosis (nuclei in epithelial cells were present, but dramatically wrinkled and decreased in size) and karyolysis

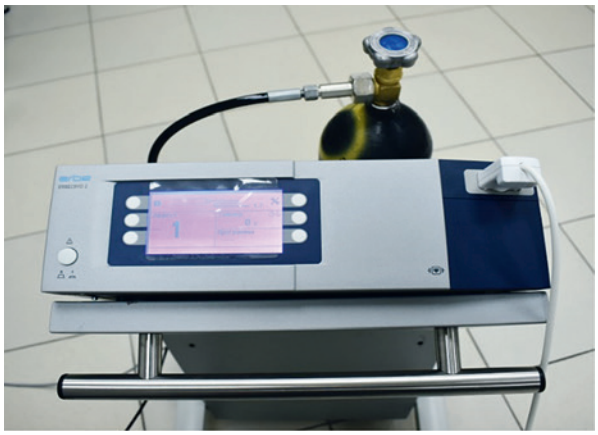

Fig. 2. Cryosurgical unit Erbecryo-2 with carbon dioxide cylinder

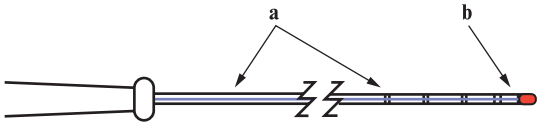

Fig. 3. Scheme of the cryoprobe. a – a tube for gas flow; b – cryoprobe tip

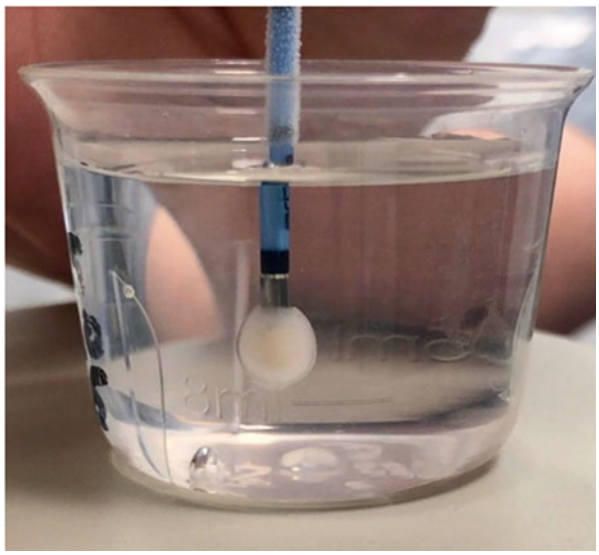

Fig. 4. Photo of the ice ball at the tip of the probe

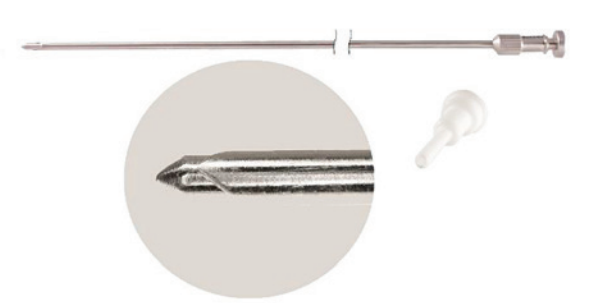

Fig. 5. Endoscopic puncturing needle (LLC "NPF "ELEPS")

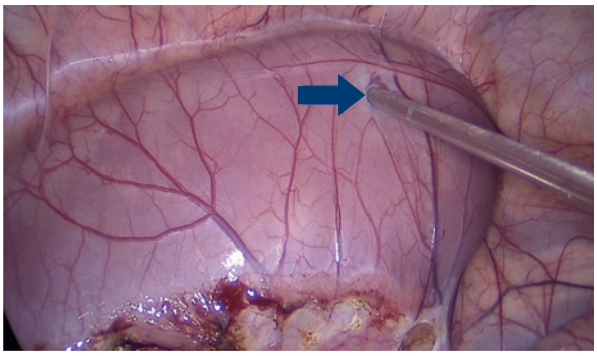

Fig. 6. Puncture of the lower renal segment using an endoscopic puncturing needle (indicated by an arrow)

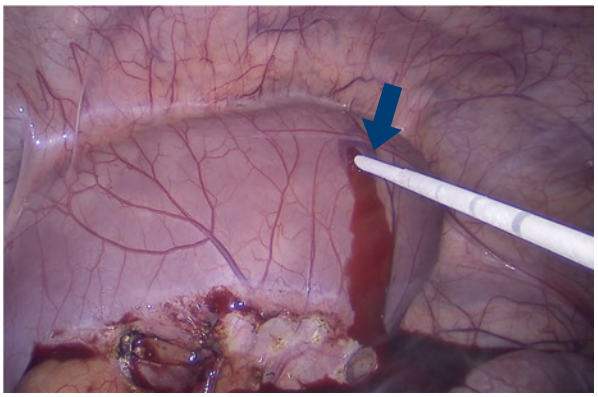

Fig. 7. Advancement of a flexible cryoprobe through the lumen of the needle, followed by cryoablation

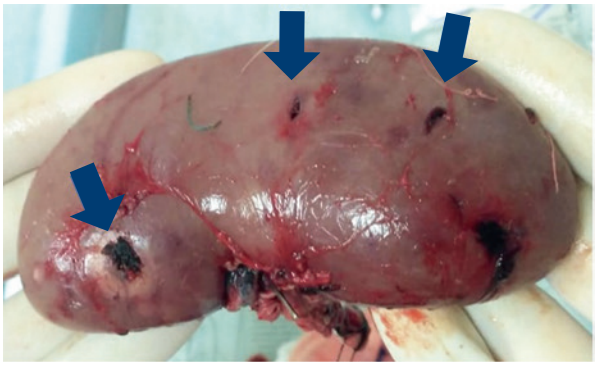

Fig. 8. Removed porcine kidney. Cryoprobe insertion point are indicated by the arrows

(an absence of nuclei in some epithelial cells of the tubules was noted).

The necrosis zone at a distance of 1.0 cm from the cryoprobe insertion points was seen in all areas subjected to cryoablation. Moreover, in all samples of the renal tissue, the area of necrosis was limited by demarcation inflammation, representing foci of hemorrhages and separate sharply expanded full-blooded vessels (*Fig. 10 a, b*).

Protein dystrophy of renal tubular epithelium in the demarcation zone with hyaline droplets and hydropic degeneration was seen. It should be noted that pronounced polymorphonuclear leukocytes infiltration, which is usually characteristic of inflammatory infiltration in various forms of necrosis, was not determined in this case. Only occasional solitary leukocytes were present. At a distance of 2 and 3 cm

Fig. 9a. The area of the renal parenchyma that was exposed to cryoablation No. 1 (exposure time of 120 sec). The zone of necrosis (dark brown, irregular in shape) extends from the cryoprobe insertion point into the kidney parenchyma to a depth of 1.0 cm

Fig. 9b. The area of the renal parenchyma that was exposed to cryoablation cryoablation No. 2 (exposure time of 90 sec). The zone of necrosis (dark brown, irregular in shape) extends from the cryoprobe insertion point into the kidney parenchyma to a depth of 0.8 cm

Fig. 9c. The area of the renal parenchyma that was exposed to cryoablation cryoablation No. 3 (exposure time of 60 sec). The zone of necrosis (dark brown, up to 0.2 cm thick) extends from the cryoprobe insertion point into the kidney parenchyma to a depth of 0.5 cm

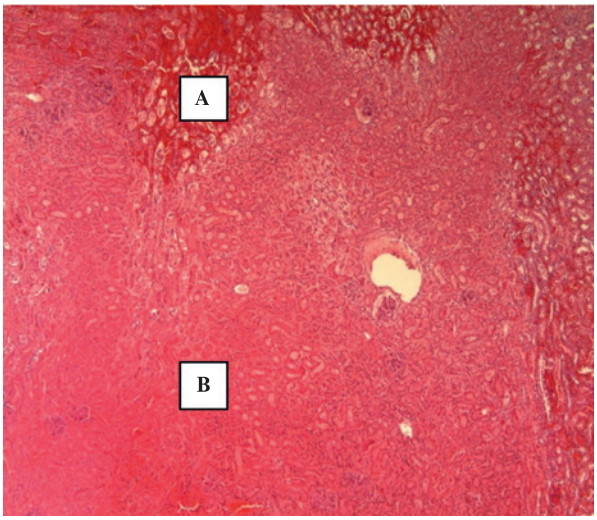

Fig. 10a. Microphotogram of a porcine kidney
A – cryoprobe insertion point, represented by foci of hemorrhages
B – an extensive area of necrosis of the renal parenchyma at a distance of 0.2 cm from the cryoprobe insertion point. Hematoxylin and eosin staining, X50 magnification.

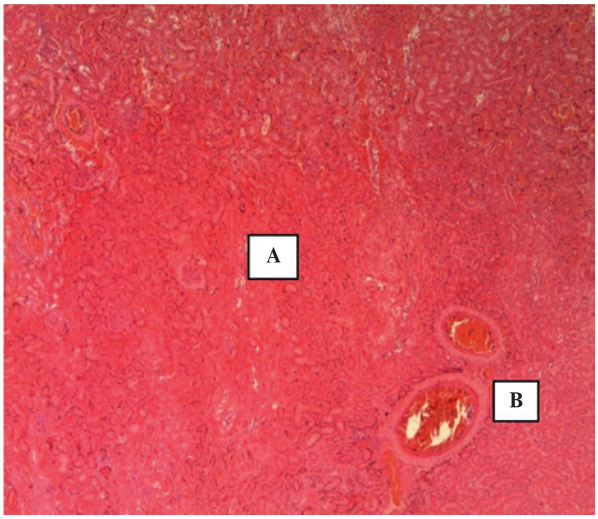

Fig. 10b. Microphotogram of a porcine kidney.
At a distance of 0.5 cm from the cryoprobe insertion point, a massive zone of necrosis (A) and sharply expanded full-blooded vessels (B) are seen. Hematoxylin and eosin staining, X50 magnification.

from the cryoprobes insertion point, dystrophic changes in the tubular epithelium persisted and focal lymphocyte and macrophage infiltration was shown. Hemorrhage and necrosis did not extend to the renal pelvis. In some areas, hyperplasia of the transitional epithelium lining the pelvis was noted. The pelvis wall was infiltrated with lymphocytes and macrophages with isolated lymphoid follicles.

The most extensive zone of necrosis was presented in the lower renal segment with an exposure mode of 120 s (section No. 1). On the preparation, the area of necrosis was dark brown. Starting from the cryoprobe insertion point, these changes of kidney parenchyma were present to a depth of 0.3 to 1.0 cm. In all fragments of 0.2 cm thick, the necrosis area was determined.

Results. Cryoablation based on carbon dioxide (carboxycryoablation) leads to irreversible death (necrosis) and destruction of the affected tissue. A direct relationship between the exposure mode and the size of the cryonecrosis zone was noted. Thus, the most extensive zone of necrosis with a diameter of 10 mm was achieved when performing cryoablation in the exposure mode of 120 s.

Conclusion. This experiment showed that carbon dioxide-based cryoablation remains a feasible procedure that leads to irreversible death (necrosis) and destruction of the affected tissue. However, further studies on the safety and efficacy of cryoablation of kidney tissue with carbon dioxide are required.

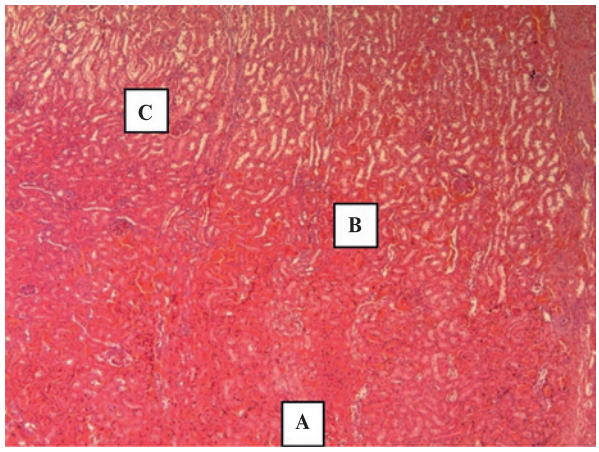

Fig. 11a. Microphotogram of a porcine kidney.
An area of the renal parenchyma at a distance of 1 cm from the cryoprobe insertion point. Hematoxylin and eosin staining, X50 magnification.
A – an extensive zone of necrosis, represented by the tubules with karyolysis.
B – demarcation inflammation, representing foci of hemorrhages and single sharply expanded full-blooded vessels.
C – intact renal tissue with single glomeruli and tubules, the epithelium of which has signs of protein dystrophy.

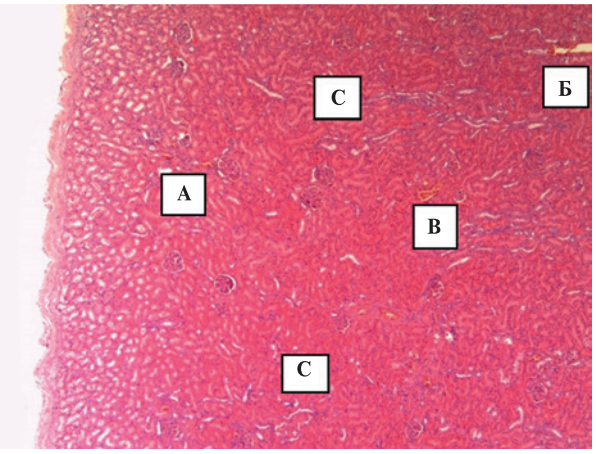

Fig. 11b. Microphotogram of a porcine kidney.
An area of the renal parenchyma at a distance of 2 cm from the cryoprobe insertion point. Hematoxylin and eosin staining, X50 magnification.
The morphological image is represented by kidney tissue with intact glomeruli (A) and thin-walled full-blooded vessels (B). There are signs of protein dystrophy of renal tubular epithelium (hyaline droplets) (C). Pronounced leukocyte infiltration is absent

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URACHUS DISEASES IN ADULTS: FEATURES OF DIAGNOSTIC AND TREATMENT TACTICS, MULTICENTER STUDY

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Introduction. Urachus pathology is a complex problem in modern medicine due to a wide variety of clinical and morphological forms, low occurrence, both in children and especially in adulthood, the lack of publications related to the analysis of large groups of patients, and, consequently, algorithms and diagnostics. treatment of this pathology. In addition, there are unambiguous recommendations that determine the surgical access in the case of planned surgery, as well as the sequence and priority of the stages of treatment of purulent complications.

Purpose. Analyze the experience of treating urachus pathology in adults and use rational diagnostic and treatment algorithms.

Materials and methods: Analyzed case histories 37 patients were operated on from 6 clinics: mean age 33.8±14.8 years, 36 patients undergoing surgical treatment for urachus pathologies, out of 12 patients were operated with an «open» method and 24 - with a laparoscopic one.

Results and discussion. The results of surgical treatment were assessed. It was determined that the method of choice for surgical treatment of patients with urachus pathology is laparoscopic excision of the urinary duct structures. An algorithm for the diagnosis of urachus pathology in adults is proposed.

K e y w o r d s: urachus, diagnosis and treatment, urachus adenocarcinoma, urachus cyst

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Introduction. Urachal diseases represent an extremely complex problem in medicine, due to a number of objective reasons [1–5]. Firstly, there are a lot of anatomical variants of obliteration of ductal remnant at the stages of embryogenesis, which also gives rise to a variety of clinical and morphological abnormalities, which can greatly differ in clinical manifestations, diagnostic and therapeutic approaches. Secondly, due to the low incidence of such diseases in childhood and the extremely low probability of their manifestation in adults, publications related to this problem are rare. This circumstance makes it impossible to carry out a reliable analysis of huge clinical experience. Thirdly, these diseases, especially in adults, are an interdisciplinary problem, since such patients fall into the "field of view" of various specialists, including urologists, abdominal surgeons, oncologists, etc. This circumstance causes additional difficulties in developing a coordinated treatment and diagnostic strategy. Fourthly, the anatomical features of the organ, its "borderline" position in relation to adjacent structure do not always allows to "standardize" the clinical manifestations and often leads to difficulties in differential diagnosis with a number of other diseases of the urinary tract and abdominal organs.

As a result, there is the lack of widespread algorithms for diagnosing urachal diseases that determine the sequence of diagnostic methods, using their minimum number [6–8]. The therapeutic tactics remains a controversial issue, starting from determining the indications for surgical treatment and ending with the its aggressiveness, from maximum "conservative" methods to the radical removal of urachus [5, 9, 10].

When deciding on surgical treatment, there are no clear recommendations that determine the method, open or laparoscopic [10]. Currently, there is no consensus about the timing and method of surgical procedure in case of purulent complications. The possible options include one-stage excision, puncture or minimally invasive drainage of a purulent focus with subsequent excision of urachal elements.

Aim. To analyze the experience of treating urachal pathology in adults and use of rational diagnostic and treatment algorithms.

Materials and methods. We evaluated the results of treatment of 37 patients from 6 clinics with various urachal diseases aged 18 to 71 years (mean age 33.8±14.8 years). Among patients, there was a predominance of men over women in the ratio of 20:17. The average age of men was 29.1±7.6 years, while the average age of women was 40.1±19.0 years. The structure of urachal diseases, clinical manifestations, diagnostic methods according to indications (ultrasound, computed tomography, magnetic resonance imaging, cystoscopy, fistulography, cystography, intravenous urography) and

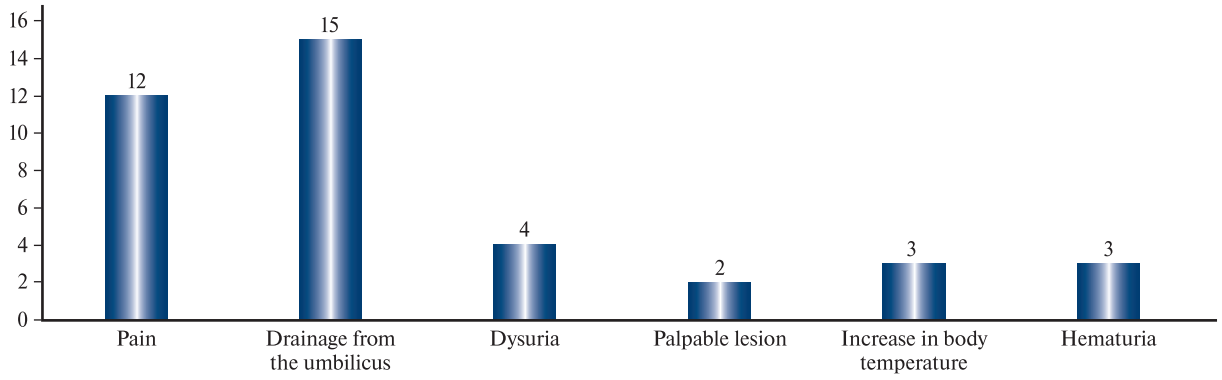

Fig 1. Clinical manifestations of urachal diseases

treatment tactics were analyzed. Surgical treatment was performed in 36 patients, of which 12 patients underwent an "open" procedure and 24 patients underwent laparoscopic techniques. There were no cross-over between groups.

Results. When analyzing the structure of diseases, data are similar to those obtained in most publications with the predominance of urachal cysts among other variants. A significant role of tumors in the structure of these diseases was also noted in the complete absence of urachal bladder diverticula.

Of the 37 patients, in two cases the urachal cyst was completely asymptomatic and was diagnosed incidentally on during ultrasound (*fig 1*).

Despite the congenital nature of these diseases, only three patients previously had clinical manifestations: in young men 18 and 21 years old, prolonged healing of the umbilical wound in the neonatal period with relapses of omphalitis was found, while in a patient of 37 years old, periodic discharge of purulent fluid from the umbilicus with an unpleasant odor from childhood until the moment of admission for a specialized medical care in adulthood occurred.

The clinical picture was characterized by a classic set of symptoms, including abdominal pain, palpable mass, local inflammation in the umbilical fossa, and symptoms of intoxication.

Purulent discharge from the umbilicus, both during the period of acute inflammation and in-between, was noted much less frequently than in pediatric practice. Urine leakage from the umbilical region also rarely occurs in adult practice and was seen in only one patient.

In contrast to childhood, a typical symptom was hematuria. In three cases, it was of a moderate grade, accompanied by mild dysuria. In one patient, the disease manifested with severe hematuria. Despite the absence of comorbidities, it was due to erosion of the vessel, which was located at the bladder base.

On the *fig. 2* and *3* the external view of the anterior abdominal wall of patients with inflammatory urachal diseases is shown.

Patients underwent the following diagnostic studies: ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), cystography, cystoscopy, excretory urography.

Fig 2. Patient S., 31 years old. Diagnosis: urachal sinus with recurrent infection. Photo on the 6th day of antibacterial and local anti-inflammatory therapy

Fig 3. Patient M., 25 years old. Diagnosis: infected urachal cyst. Inflammatory process in the umbilical fossa

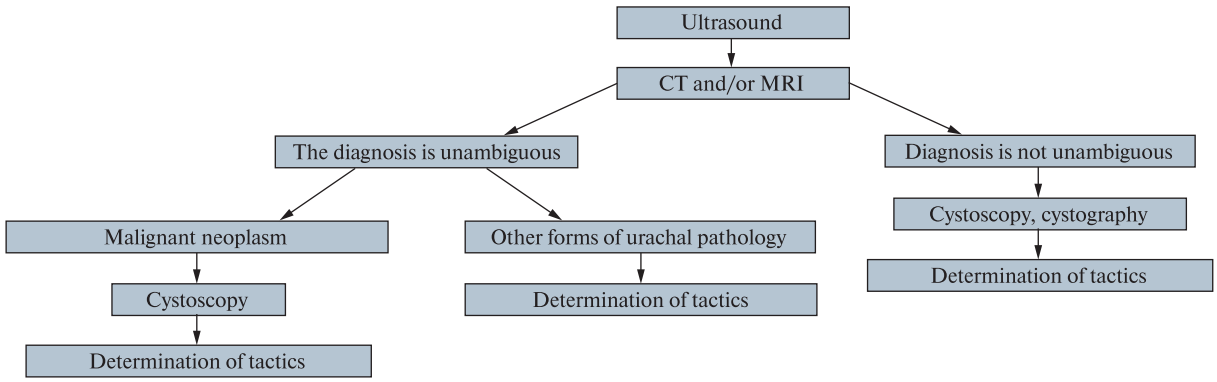

Fig 4. Algorithm for diagnosing urachal diseases in adults

Ultrasound examination was performed in all cases as screening method, regardless of the form of urachal pathology. It can be used both for routine examination and in an urgent situation, while the result is available immediately after the procedure. CT and MRI are highly accurate methods and, unlike in pediatric patients, they allow a more accurate assessment in adults. The diagnostic accuracy of the methods is approaching 100%; CT and MRI are regarded as mandatory in the diagnosis of urachal diseases in adults due to the large percentage of oncological diseases. Both methods allow to specify the localization, size, extension, relationships with neighboring organs, and the presence of invasive growth. In our study, all patients underwent contrast-enhanced imaging study. Cystography was used for the examination in only 8 patients, since it plays a minor role in adults due to the distinct urachal cyst. The efficiency of the method was 12.5%. Cystoscopy was performed in 12 patients. The accuracy of information depends on the type of urachal pathology. Among 8 patients with non-tumor disorders, the valuable information was obtained only in 1 (12.5%) case, where a urachal fistula was diagnosed. During cystoscopy, an opening of the fistula with a perifocal inflammatory reaction was visualized.

Intravenous urography was performed in five cases preoperatively to assess the upper urinary tract urodynamics, considering concomitant diseases. This method, in our opinion, has no diagnostic value. Fistulography was done in three patients with sinus and urachal fistula. The length of contrasting does not exceed 3 cm and cannot be interpreted as the volume of the structure. Due to the thicker anterior abdominal wall in adults, this manipulation can be very demanding, and is associated with complications; therefore, it shouldn't regard as effective and is not recommended. Fistuloscopy was also performed in three cases (two patients with urachal fistula and one with urachal sinus). Although the maximum visualization depth was 3.5 cm, it did not give reliable information about the form of the disease. In addition, it may result in an exacerbation of the inflammatory process.

Based on our data, we have developed an algorithm for diagnosing urachal diseases in adults (*fig. 4*).

In our study, 36 patients were undergone to surgical treatment, including 12 open procedures and 24 laparoscopic excisions. One patient, due to the presence of an asymptomatic urachal cyst measuring 30x28x30 mm, is still on active surveillance with a follow-up ultrasound every 6 months. Of 12 "open" procedures, three were performed for urachal tumors with wide excision (partial cystectomy and pelvic lymph node dissection). In addition, there were two emergency interventions for infected urachal cyst. One more procedure was an urgent, since it was an accidental finding during hernioplasty, and only in one case, with a large urachal cyst, the indications for open surgery were elective and determined by the possible technical difficulties during laparoscopic approach.

The operation time, the volume of blood loss, and the length of the surgical scar were compared between two groups ("open" procedure [n=8] vs. laparoscopic [n=18]). Patients with urachal tumors were excluded from the comparative analysis, considering performing a major procedure with wide excision (see table).

Our data suggest that laparoscopic procedure have a significant advantage over open interventions according to all criteria (shorter operation time and, consequently, the duration of anesthesia, total scar length, volume of blood loss) and can be recommended as the method of choice in urachal disease in adults.

Clinical case No.1

Patient C 36 years old. Diagnosis: urachal cyst. The cyst is located above the bladder base and has no communication; however, the intimate proximity did not allow to dissect it without opening the bladder (*fig. 5*).

Table

Comparison of open and laparoscopic approaches in surgical treatment of urachal abnormalities in adults. For statistical evaluation, the Mann-Whitney U-test was used, $p<0.05$ in all cases

	Laparoscopic access	Traditional access	Test	Level of significance, p
	$M\pm m$, n=18	$M\pm m$, n=8		
Operation time, min	70,7±26,7	97,3±25,4	U=30,5	p=0,01
Volume of blood loss, ml	24,2±16,3	67,8±27,3	U=3	p=0,0001
Length of postoperative scar (including total length), mm	23,5±7,3	87,8±33,1	U=2	p=0,0001

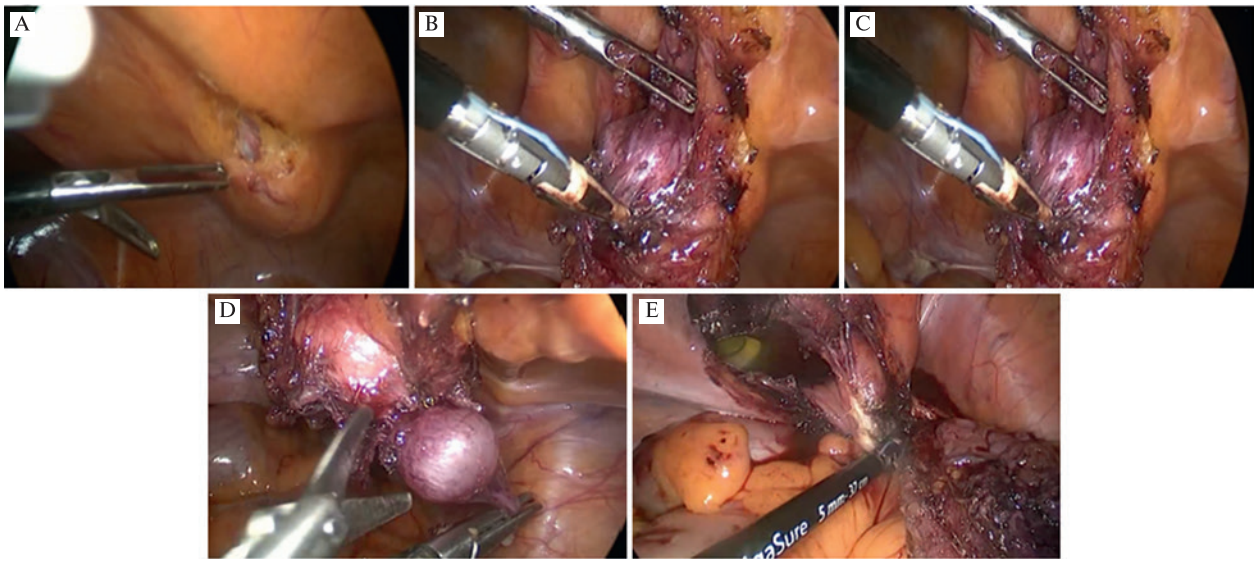

Fig 5. Stages of laparoscopic procedure for urachal cyst
A. The cyst is dissected from the preperitoneal fat tissue. B. Mobilization of the anteroposterior wall of the cyst. C. Mobilization of the posterior wall of the cyst. D. The cyst is dissected almost completely, the intimate adhesions with the bladder base are preserved, which do not allow to completely isolate the cyst. E. The bladder base was opened (Foley catheter is visualized inside), then the cyst was completely mobilized and resected.

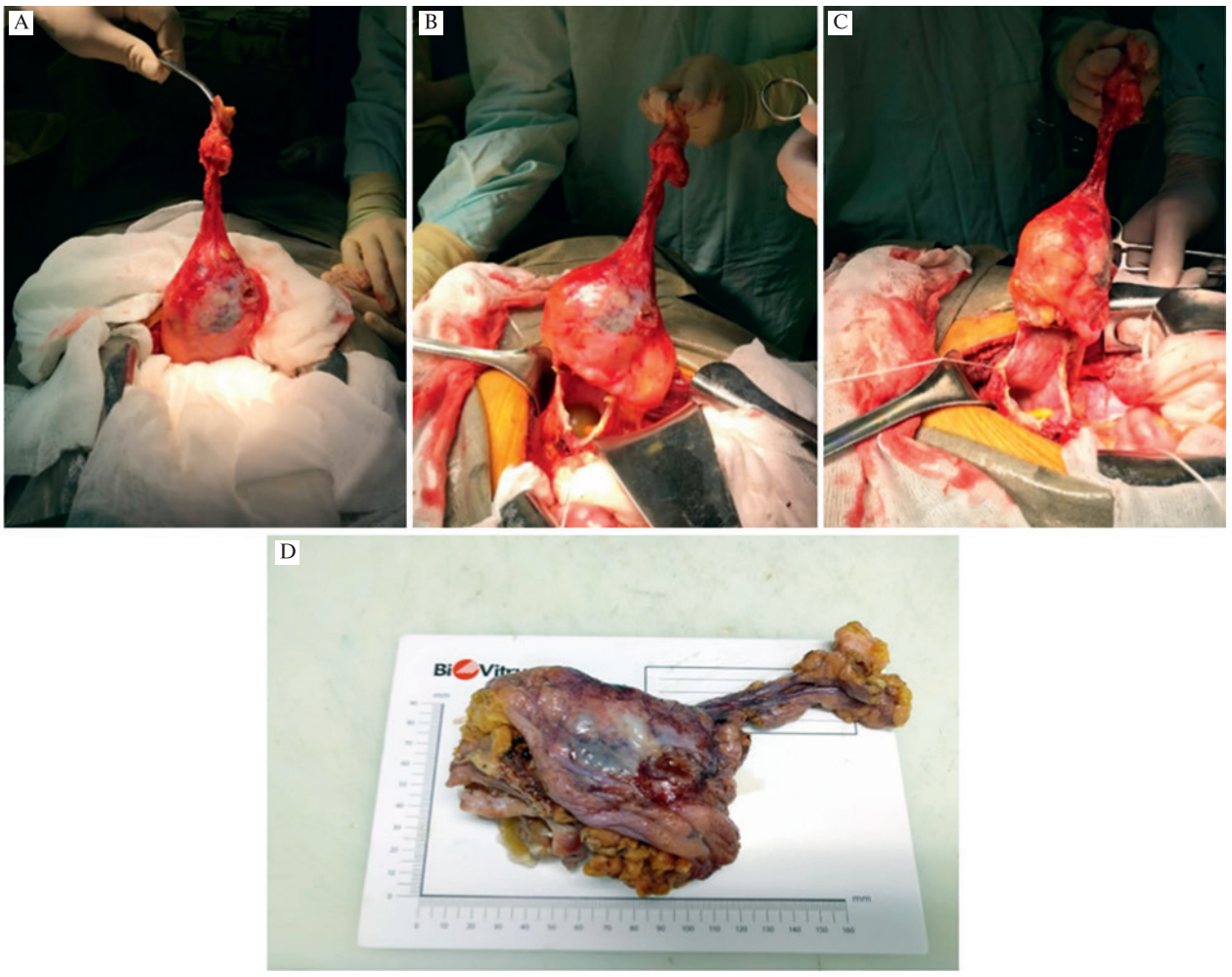

Fig 6 Stages of open surgery for mucinous cystadenocarcinoma of the urachus
A, B, C – laparotomy. Excision of the median umbilical ligament together with the umbilicus; excision of the urachal lesion with partial cystectomy and pelvic lymph node dissection. (Clinical case was presented by professor A.I. Novikov, S.Yu. Tareev, St. Petersburg Clinical Research and Practical Oncology Center); fig D – gross pathology

Clinical case No.2

Patient S., 34 years old (2019). Diagnosis: mucinous cystadenocarcinoma of the urachus (*fig 6*). Pathomorphological study: urachal mucinous cystadenocarcinoma growing into the subepithelial tissue of the bladder without mucosal invasion. The parietal peritoneum was invaded with the formation of a fistulous tract that communicates with the peritoneal cavity. In the seven lymph nodes on the right and four on the left, metastases were not detected. A stage IIIC (Sheldon staging system; *fig 6d*) was established.

Conclusions. According to our results, several methods for diagnosing urachal diseases should be distinguished. Ultrasound is the primary diagnostic method due to its availability, as well as good sensitivity in adults, and is regarded as mandatory. High-precision imaging methods (CT and MRI) play a major role in diagnosis, considering good specificity. They are required to clarify the form of the disease and assess the relationship between the urachal structures and adjacent organs. Cystoscopy is an optional method required to evaluate the bladder wall if invasive tumor growth is suspected. Cystography, fistulography and fistuloscopy do not significantly contribute to the visualization of urachal structures, and should be considered as a last resort only in the absence of above methods.

Laparoscopy is considered the preferred method of the surgical treatment of urachal diseases in adults. The laparoscopic approach demonstrates less volume of blood loss and the operation time, as well as a length of postoperative scar. A small number of surgical interventions and the heterogeneity of urachal diseases precludes a reliable comparative analysis; however, the advantages of the laparoscopic approach are additionally confirmed by both its predominant use and the lack of conversion to the open procedure.

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INTRAVESICAL PROSTATIC PROTRUSION AS A PREDICTOR OF THE FUNCTIONAL OUTCOME OF SURGICAL TREATMENT OF BENIGN PROSTATIC HYPERPLASIA

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Aim. To evaluate the effect of intravesical prostatic protrusion on the functional results of bipolar transurethral resection of the prostate and retropubic adenomectomy.
Materials and methods. From September 2019 to December 2021 in the clinic of urology on the basis of the GKB. S.P. Botkin, 210 patients underwent surgical treatment of prostatic hyperplasia, 101 of them – bipolar transurethral resection of the prostate (group I), 109 patients – retropubic adenomectomy (group II). Depending on the size of intravesical prostatic protrusion – more than 5 mm and less than 5 mm, the corresponding subgroups «a» and «b» are distinguished. Functional results were assessed 6 months after the operation: IPSS scores, including filling and emptying IPSS, QoL, maximum urination rate, residual urine volume.
Results. Comparing the functional results of the quality of urination 6 months after surgical treatment by the method of bipolar TURP in patients with PPI, a significantly significant decrease in IPSS scores, including both emptying and filling, a decrease in QoL scores, and improvements in maximum urination rate in patients ($p<0.05$). There were no significant differences in the reduction in residual urine volume ($p=0.89$). Similar functional results were demonstrated in the group of patients who underwent retropubic adenomectomy. Six months after surgery, in patients with PPI >5 mm, a significantly significant decrease in IPSS scores was found, including emptying and filling, a decrease in QoL scores, and an improvement in maximum urination rate ($p<0.05$). There were no significant differences in the volume of residual urine ($p=0.49$).
Conclusion. A significantly more significant decrease in the results of the IPSS scale was revealed, especially in emptying symptoms, QoL and an increase in the maximum urination rate after 6 months in patients with intravesical prostatic protrusion over 5 mm. Comparing bipolar transurethral resection of the prostate and retropubic adenomectomy, the latter showed a significantly more significant decrease in the above indicators in the group with intravesical prostatic protrusion over 5 mm, while in the group with intravesical prostatic protrusion less than 5 mm, there were no significant differences between the quality of urination.

K e y w o r d s: *intravesical prostatic protrusion, bipolar transurethral resection of the prostate, retropubic adenomectomy, personalized approach*

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Introduction. Benign prostatic hyperplasia (BPH) is one of the most common diseases in urological practice, which causes lower urinary tract symptoms (LUTS) in the elderly [1]. The prevalence of BPH progressively increases after 40th, reaching more than 90% by the age of 90 [2]. LUTS/BPH significantly impairs the quality of life (QoL) [3, 4]. According to various publications, by the age of 80 every 4th man will need treatment for BPH. The social significance and urgency of this problem are emphasized by the demographic studies, which were carried out by the World Health Organization. According to the results, growth of the world's population over the age of 60 has much higher pace than growth of the population as a whole, regardless of the country.

Intravesical prostatic protrusion (IPP) is a relatively new parameter that reflects bladder outlet obstruction (BOO) [5]. The association between IPP and BOO, as well as its influence on the choice of conservative therapy for BPH, is clearly demonstrated in the thesis of A.D. Bolotov [6].

One of the main methods of surgical treatment of BPH is bipolar transurethral resection of the prostate (Bi-TURP) and open retropubic simple prostatectomy (OSP). Currently, the personification of the treatment approach is of importance, and it can be possible by identifying predictors that affect the outcome of treatment.

Aim. To evaluate the effect of IPP on the functional results of Bi-TURP and OSP.

Materials and methods. On the basis of the Federal State Educational Institution of Additional Professional Education "Russian Medical Academy of Continuous Professional Education" of the Ministry of Health of the Russian Federation, University Clinical Hospital. S. P. Botkin, in accordance with the Declaration of Helsinki of the World Medical Association "Ethical principles for medical research involving human subjects" and the regulations of Good Clinical Practice in the Russian Federation, approved by order No. 266 of the Ministry of Health of Russia dated 19.06.2003, a retrospective study was performed. An analysis of treatment of 210 consecutive patients, who admitted to the urological clinic of the S. P. Botkin City Clinical Hospital with LUTS caused by BOO due to BPH, from September 2019 to December 2021, was carried out.

Inclusion criteria: informed consent; absence of severe comorbidities; the presence of LUTS caused by BOO (IPSS>20

or Qmax <10 ml/s) due to BPH, the inefficiency of drug therapy with alpha-blockers and 5α-reductase inhibitors.

Exclusion criteria: refusal to participate in the study, the presence of severe comorbidities, age less than 50 years, the presence of prostate cancer, treatment-resistant diabetes mellitus or diabetic neuropathy, history or signs of neurological diseases, surgical interventions or injuries in the pelvic region, a history of sexually transmitted diseases, the use of drugs that can affect the bladder function, the presence of bladder neck stenosis.

A total of 210 patients with BPH, who met these criteria, were undergone to surgical treatment. Transabdominal ultrasonography was performed on Acuson XP 128/10 device using a convex abdominal probe (frequency 3–3.5–5 MHz). IPP was measured during ultrasonography according to the standard technique presented in the fig. 1.

Depending on the degree of value IPP, each of the groups was additionally divided into subgroups: subgroup "a", where IPP was less than 5 mm (Ia, *n*=49, IIa, *n*=53), and subgroup "b", where IPP was more than 5 mm (Ib, *n*=52) and IIb, *n*=56). Uroflowmetry was carried out on a portable apparatus URODIN 1000 from DANTEK. The questionnaires were filled out according to the rules of GCP (Good Clinical Practice), i.e., without the participation of a doctor.

Depending on the method of surgical treatment and prostate volume, all patients were randomized into two groups. The first group included those with a prostate volume of less than 80 cm^3 who underwent Bi-TURP (*n*=101). In the second group consisting of patients with a prostate volume of more than 80 cm^3, OSP was done (*n*=109).

After 6 months of follow-up, all patients underwent examinations, including measurement of prostate volume, IPP, maximum urine flow rate (Qmax), postvoid residual volume. Treatment outcomes were assessed by IPSS score (with additional evaluation of storage and emptying symptoms) and the QoL score.

An analysis of the data was carried out using Excel-2010 statistical software package (arithmetic mean, standard deviation). A sample representativeness was assessed by testing it for normal distribution according to the Kolmogorov test. In addition, the percentage of the ratios were calculated. The hypothesis of differences between the proportions was tested according to Student's t-test. Differences were significant if $p<0.05$.

Results. There were no differences between baseline parameters, with the exception of prostate volume (less than 80 cm^3 in the BI-TURP group and more than 80 cm^3 in group of OSP) (*Table 1*).

Functional results after 6 months are presented in *Table 2*. When comparing the quality of urination after Bi-TURP in patients with IPP more and less than 5 mm (subgroups Ia and Ib, respectively), a significantly significant decrease in IPSS scores was found (4.5±0.5 and 6.4±0.7; $p<0.05$), including both emptying (2.5±0.2 and 3.3±0.3; $p<0.05$) and storage symptoms (2.0±0.3 and 3.1±0.4; $p<0.05$), as well as a decrease in QoL scores (0.8±0.1 and 1.3±0.2; $p<0.05$) and improvement in Qmax (23.5±1.2 and 19.9±0.9; $p<0.05$). With regard to postvoid residual volume (PVR), there were no significant differences between two subgroups (21.5±10.3 and 19.5±10.7; $p=0.89$).

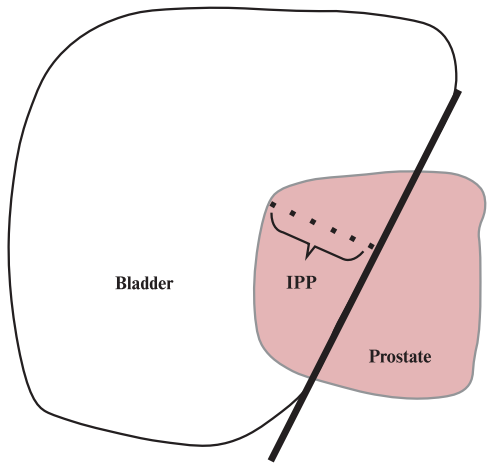

Fig 1. A technique for evaluation of intravesical prostatic protrusion (IPP) during transabdominal ultrasound

Similar functional results were demonstrated in the group of patients who underwent OSP. After 6 months, a decrease in IPSS scores (4.2±0.6 and 6.1±0.7; $p<0.05$), including both emptying (2.3±0.2 and 3.1±0.3; $p<0.05$) and storage symptoms (1.9±0.3 and 2.8±0.3; p <0.05), as well as a decrease in QoL scores (0.7±0.2 and 1.1±0.1; $p<0.05$) and improvement in Qmax (24.1±1.3 and 20.3±1.2; $p<0.05$) were more pronounced in patients with IPP more than 5 mm (subgroup IIa) than in those with IPP less than 5 mm (subgroup IIb). However, there were also no significant differences in PVR (30.1±11.2 and 41.2±11.8; $p=0.50$).

Comparing the functional results of Bi-TURP and OSP in subgroups of patients with IPP >5 and <5 mm (Ia vs. IIa and Ib vs. IIb, respectively), there were no significant differences in IPSS score (4.5±0.5 vs. 4.2±0.6, $p=0.70$, 6.4 ±0.7 vs. 6.1±0.7, $p=0.751$), including storage (2.0±0.3 vs. 1.9±0.3, $p=0.813$, 3.1± 0.4 vs. 2.8±0.3, $p<0.549$) and emptying symptoms (2.5±0.2

Table 1

Baseline patients' characteristics

Variable	Bi-TURP	OSP	*p*-value
n	101	109	
Prostate volume, cc	53,95±13,5	114,5±17,5	**0,006**
IPSS	20,1±3,4	19,9±3,3	0,96
Voiding symptoms	10,1±1,5	9,8±1,6	0,89
Storage symptoms	9,9±1,4	9,1±1,5	0,69
QoL	3,8±0,5	3,7±0,6	0,89
Qmax, ml/sec	7,5±2,2	7,3±1,9	0,94
Residual urine volume, ml	72,15±31,12	95,10±39,22	0,64

Note. TURP – transurethral resection of the prostate, IPP – Intravesical prostatic protrusion, IPSS – International Prostate Symptom Score, QoL – Quality of Life, Qmax – maximum urinary flow rate.

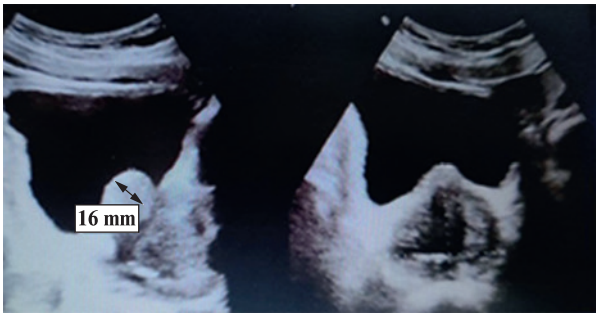

Fig 2. Severe IPP in patient A. Transabdominal ultrasound

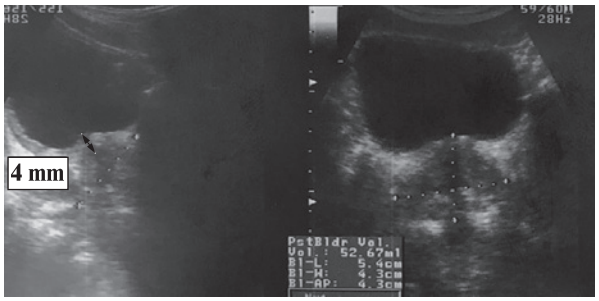

Fig 3. Absence of IPP in patient K., according to transabdominal ultrasound

vs. 2.3±0.2, p=0.481, 3.3±0.3 vs. 3.1±0.3, p<0.638), QoL score (0.8±0.1 vs. 0.7±0.2, p=0.655, 1.3±0.2 vs. 1.1±0 ,1, p=0.373), Qmax (23.5±1.2 vs. 24.1±1.3, p=0.735, 19.9±0.9 vs. 20.3±1.2, p=0.791), and PVR (21.5±10.3 vs. 30.1±11.2, p=0.573, 19.5±10.7 vs. 41.2±11.8, p=0.175), which suggest the comparable efficiency of both surgical methods.

Clinical case No. 1 Patient A., 65 years old had complaints about urinary disturbances with a weak stream, discomfort in the suprapubic area, a feeling of incomplete bladder emptying, nocturia up to 5 times for more than 1 year. He took the combination therapy with an α1a-blocker (Tamsulosin 0.4 mg q.d.) and inhibitor of 5α-reductase of types 1 and 2 (Dutasteride 500 μg q.d.) without any effect. The total IPSS score was 26 points, QoL of 5 points and serum PSA level of 1.9 ng/ml. According to digital rectal examination, there was no abnormalities in the prostate. At uroflowmetry, Qmax was 6.9 ml/s at the voiding volume of 140 ml. The prostate volume on transabdominal ultrasonography was 61 cc with IPP of 16 mm (*fig 2*).

Taking into account the presence of BOO, associated with BPH, the patient underwent surgical treatment by Bi-TURP. The urethral catheter was removed on the second postoperative day after bladder filling to a moderate urge to urinate with saline in a volume of 250 ml. After 6 months, a follow-up examination showed the total IPSS score of 4 points (two points for storage and emptying symptoms), QoL of 1 point, Qmax of 25 ml/s, and PVR of 20 ml.

Clinical case No. 2. Patient K., 67 years old with complaints about urinary disturbances with a weak stream, a feeling of incomplete bladder emptying and nocturia up to 3 times for more than 5 years. During last 4 years, he received combination therapy with an α1a-blocker (Tamsulosin 0.4 mg q.d.) and inhibitor of 5α-reductase of types 1 and 2 (Dutasteride 500 μg q.d.) similar to that described in clinical case No. 1). Drug therapy hadn't durable effect. The patient noted progressive deterioration in quality of urination for the last six months. The total IPSS score was 25 points, QoL of 5 points and serum PSA level of 1.5 ng/ml.

According to digital rectal examination, there was no abnormalities in the prostate. At uroflowmetry, Qmax was 7.3 ml/s at the voiding volume of 160 ml. The prostate volume on transabdominal ultrasonography was 52 cc with IPP of 4 mm (*fig 3*).

Taking into account the presence of BOO, associated with BPH of 56 cc in volume, the patient underwent surgical treatment by Bi-TURP. The urethral catheter was removed on the second postoperative day after bladder filling. After 6 months, a follow-up examination showed the total IPSS score of 6 points (three for storage and emptying symptoms), QoL of 2 points, Qmax of 19 ml/s, and PVR of 25 ml.

Discussion. Despite a large number of different surgical methods for the treatment of BPH, there are no clear indications for each of them. According to the current guidelines of the Russian Society of Urology, approved by the Ministry of Health of the Russian Federation [7] and the European Association of Urology [8], the choice of the treatment method depends on the prostate volume, concomitant diseases, a possibility of performing a procedure under anesthesia, patient choice, safety profile, accessibility of surgical techniques and preferences of the surgeon. In a paper of D.V. Enikeev et al. [9] comparing the guidelines of the European Society of Urology, the American Society of Urology, the National Institute of Health and Clinical Excellence, a heterogeneity of indications for surgical treatment of BPH was clearly demonstrated, which makes it relevant to identify predictors of the functional results in order

Table 2

Functional results after 6-months follow-up

Variable	Bi-TURP			OSP		
	Subgroup Ia (IPP >5 mm)	Subgroup Ib (IPP <5 mm)	p-value	Subgroup IIa (IPP >5 mm)	Subgroup IIb (IPP <5 mm)	p-value
IPSS	4,5±0,5	6,4±0,7	**0,029**	4,2±0,6	6,1±0,7	**0,041**
Voiding symptoms	2,5±0,2	3,3±0,3	**0,028**	2,3±0,2	3,1±0,3	**0,028**
Storage symptoms	2,0±0,3	3,1±0,4	**0,030**	1,9±0,3	2,8±0,3	**0,036**
QoL	0,8±0,1	1,3±0,2	**0,027**	0,7±0,2	1,1±0,1	**0,042**
Qmax, ml/sec	23,5±1,2	19,9±0,9	**0,018**	24,1±1,3	20,3±1,2	**0,034**
Residual urine volume, ml	21,5±10,3	19,5±10,7	**0,893**	30,1±11,2	41,2±11,8	**0,496**

Note. TURP – transurethral resection of the prostate, IPP – Intravesical prostatic protrusion, IPSS – International Prostate Symptom Score, QoL – Quality of Life, Qmax – maximum urinary flow rate.

to provide a personalized approach to a choice of method of surgical treatment of BPH.

Recently, the interest in IPP has been growing. G.G. Krivoborodov et al. [5] in a review article demonstrated that IPP was a relatively new parameter that can be used to assess the significance of BOO. Also, A.D. Bolotov [6] demonstrated the effect of IPP on the conservative treatment of BPH as part of his thesis.

There are different data regarding the IPP threshold. Some publications [10–13] suggest that IPP <5 mm, from 5 to 10 mm and more than 10 mm corresponds to I, II and III degree, respectively. For example, Reis et al. [12] considered the threshold value of IPP for the presence of BOO as 5 mm with a sensitivity of 95% and a specificity of 50%. Shin et al. [13] showed a sensitivity of 66.7% and a specificity of 80.5% for a IPP of 5 mm. A. D. Bolotov et al. [6] in the thesis determined the threshold for IPP, equal to 10 mm, with a sensitivity of 67.4% and a specificity of 100% in relation to the presence of BOO. It should be noted that all the above studies evaluated the effect of IPP on the efficiency of drug therapy in BPH. However, IPP threshold values for surgical treatment was not proposed. In this regard, we choose IPP equal to 5 mm as the threshold value for division into subgroups, however, taking into account our results, it is recommended to carry out more studies with other threshold values of IPP.

Conclusions. Considering the heterogeneity of the data and the lack of clear indications for different methods of surgical treatment in patients with BPH, we may formulate the concept of a personalized approach, the constitutes of which are presented in this paper. All above studies suggest that patients with IPP more than 5 mm have the better functional results 6 months after bi-TURP than those with IPP less than 5 mm. A significantly more significant improvement of IPSS score, especially in voiding symptoms, QoL and Qmax was seen after 6 months in patients with IPP more than 5 mm. Comparing to Bi-TURP, OSP is associated with more pronounced improvement of IPSS score, QoL and Qmax in those with IPP over 5 mm, while in the group with IPP less than 5 mm, there were no significant differences in urination quality between two methods.

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GENITOURINARY ADVERSE EVENTS IN MEN USING NON-MEDICAL TESTOSTERONE PREPARATIONS

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Introduction. In recent years, there has been an active use of testosterone and anabolic steroids by athletes for non-medical purposes, which results on undesirable effects from the urinary tract and reproductive organs.
Aim. To study the structure of urogenital adverse events in men who attended gyms and used testosterone and anabolic steroids for non-medical purposes.
Materials and methods. A clinical and statistical analysis of 64 men aged 22-46 years was carried out. Prior to the start of testosterone or anabolic steroids use, all men had no history of the urinary tract or genital disorders. When evaluating patients, validated questionnaire scales were used, including International Prostatic Symptom Score (IPSS) and International Index of Erectile Function (IIEF5). In addition, laboratory tests and imaging studies were performed, such as microscopic examination of the ejaculate, serum level of total Ts, FSH, LH, prolactin, estradiol, and ultrasound with Doppler mapping of the penile vessels.
Results. Erectile dysfunction, marital infertility, and testicular hypotrophy were among the adverse events. Less common were lower urinary tract symptoms, anejaculation, and gynecomastia. In some cases, chronic kidney diseases and a testicular tumor were diagnosed.
Conclusion. Unreasonable use of testosterone and anabolic steroids can be accompanied by a wide range of adverse events in the urinary tract and reproductive organs. These negative effects should be explained to men. It is important to develop a system for the treatment of adverse events.

K e y w o r d s: *Testosterone preparations, anabolic steroids, testosterone, hypogonadism, adverse events.*

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Introduction. Testosterone (Ts) and its active metabolite dihydrotestosterone play an important role in the male body. Ts has not only androgenic, but also anabolic effects, regulates the reproductive function of men by inducing spermatogenesis and ensuring sexual desire, and also predetermines the physiological support of mental activity. The main biological effects of Ts are manifested in target tissues, including seminiferous tubules, seminal vesicles, epididymis, prostate, penis. Clinically, the androgenic properties of Ts determine the development of the genital organs, the appearance of secondary sexual characteristics and the formation of sexual desire and sexual behavior. The congenital low level of androgens disrupts the formation of sexual characteristics, leading to defects in the development of the male reproductive and endocrine systems [1, 2]. The anabolic properties of Ts determine its role in the regulation of the metabolism of calcium, nitrogen, phosphorus, carbohydrates and proteins, which determines the development and increase in muscle mass and bone tissue formation [3–5].

With age in men, there is a decrease in Ts level by 0.4–2.0% starting from the age of 30 [6, 7]. In middle-aged men without comorbidities, the prevalence of hypogonadism is 6%, but it increases in those with obesity and uncontrolled diabetes mellitus to 50% or more [8].

For men with clinical manifestations of hypogonadism and low Ts levels, hormonal replacement therapy is recommended by modern clinical guidelines to correct testosterone deficiency [9–12]. The goal of treatment is to alleviate the symptoms of hypogonadism by restoring Ts levels to normal physiological values. The choice of drug for treatment is determined by the form of the disease, risk factors and necessity of having reproductive function. It should be remembered that possible transient decrease in Ts level can be associated with acute or decompensated chronic diseases, which should be excluded with a thorough clinical examination and repeated measurement of Ts levels [13].

However, in recent years there has been an active use of Ts preparations by athletes for non-medical purposes [14]. Due to the fact that the use of Ts for non-medical purposes is forbidden in many countries, its prevalence remains unclear. Moreover, those who seek medical help hide the fact of using steroids in 50% of cases [15, 16].

Considering the aggressive use of Ts for non-medical purposes is unreasonable, doctors have to deal with adverse events (AEs) from many organs and systems. It is incorrect to consider this approach as exogenous testosterone therapy, since its goal is not to correct a disorder, but to intentionally increase the level of Ts, despite normal value at baseline [17, 18]. At the same time, after long-term use of Ts, eugonadal men develop various types of hypogonadism.

In this regard, timely diagnosis and effective treatment of pharmacologically-induced hypogonadism seem to be an understudied public health problem. There are no clinical guidelines and standards for the diagnosis and treatment of secondary hypogonadism after the use of Ts by non-professional athletes [17-19]. The presented problem is interdisciplinary and requires detailed study.

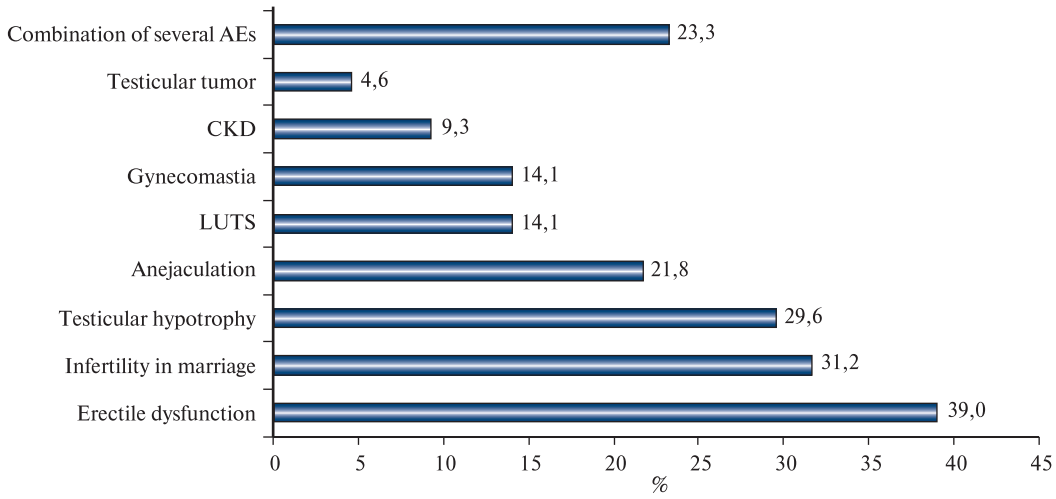

Fig 1. Genitourinary adverse events

Aim. To study the structure of urogenital adverse events in men who attended gyms and used Ts and anabolic steroids for non-medical purposes.

Materials and methods. A clinical and statistical analysis of 64 men aged 22-46 years, who attended urologist, andrologist, and endocrinologist with various complaints from the urinary tract and genital organs during or after taking Ts or anabolic steroids, was carried out. Prior to the start of their use, all men had no history of the urinary tract or genital disorders. Initially, the level of sex hormones (Ts, luteinizing hormone [LH], follicle-stimulating hormone [FSH], prolactin, estradiol) was within normal range. The total Ts level in all cases was above 12.1 nmol/l. Ts use was initiated without any medical indications by men or employees of sports centers. The duration of taking Ts or anabolic steroids in all patients was more than 1 year.

When evaluating patients, validated questionnaire scales were used, including International Prostatic Symptom Score (IPSS) and International Index of Erectile Function (IIEF5). In addition, laboratory tests and imaging studies were performed, such as microscopic examination of the ejaculate, serum level of total Ts, FSH, LH, prolactin, estradiol, and ultrasound with Doppler mapping of the penile vessels.

The obtained data were processed using Microsoft Excel spreadsheets from the Microsoft Office 2007 software package. Statistical analysis was performed with the statistical package STATISTICA, 6.1 (StatSoftInc., USA). The calculations and interpretation of the results were carried out according to the manual of O.Yu. Rebrova. The assessment of the normality of distribution of the parameters was carried out using the Shapiro–Wilk test. The threshold level of significance was set at $p<0.05$.

The study was approved by the Local Independent Ethics Committee of the Rostov State Medical University No. 20/21t on 12/23/2021.

Results. In the structure of adverse events the ED was predominated ($n=25$; 39.0%), followed by infertility in marriage ($n=20$; 31.2%) and testicular hypotrophy ($n=19$; 29.6%) ($p<0.05$) (*fig. 1*). The most commonly used drugs were as following: testosterone propionate, testosterone enanthate, Omnadren® 250 (*fig. 2*). In 65.6% of cases, men received combined therapy, while 60% of patients took three or more drugs. The injection route of administration was the main one ($p<0.05$) (*fig 3*).

The majority (59.3%) of men used Ts preparations or anabolic steroids within 1–3 years, while 43.7% of patients received therapy for more than 3 years ($p<0.05$).

When assessing the level of Ts, in 78.1% cases it was below 12.1 nmol/L. At the same time, a correlation was found between

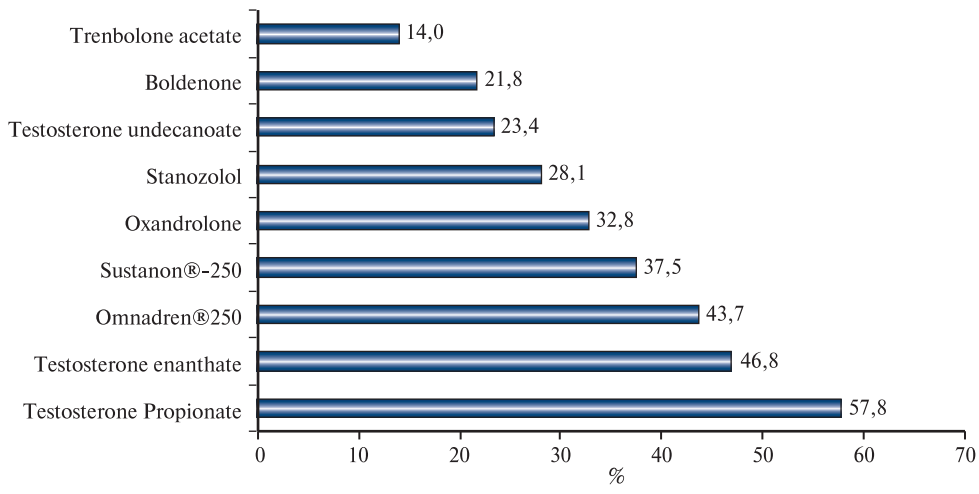

Fig 2. Testosterone preparations and anabolic steroids, used for non-medical purposes

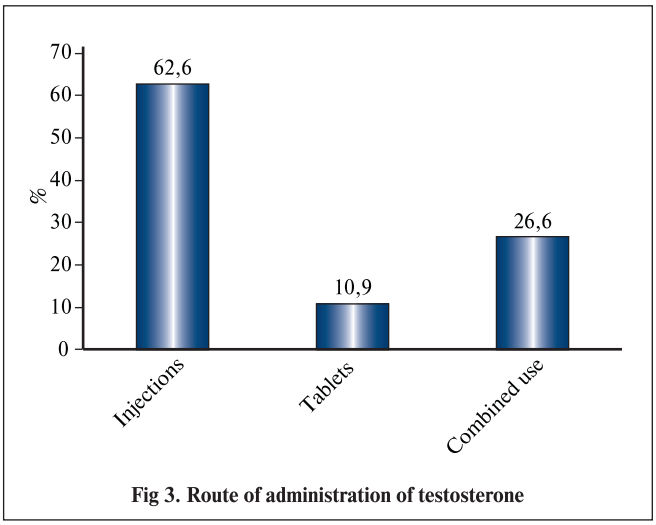

Fig 3. Route of administration of testosterone

the level of Ts and the duration of the use of Ts preparations or anabolic steroids. The longer was therapy, the lower the Ts level was seen ($p<0.05$).

Erectile dysfunction. ED of varying severity was diagnosed according to the IIEF-5 questionnaire in 25 (39.0%) men. Mild (1–20 points), moderate (11–15) and severe symptoms (5–10 points) were documented in 8 (12.5%), 12 (18.7%), and 5 (7.8%) patients, respectively ($p<0.05$). The distribution of the examined men according to the erection hardness scale is presented in *Table 1*. All patients underwent a pharmacological test using an oral selective 5-phosphodiesterase (PDE-5) inhibitor, sildenafil citrate (Viagra test). In 10 (15.6%) men, the test was positive, while 15 patients (23.4%) had no improvements. In the second group of men (with a negative Viagra test) a Doppler study of the penile vessels with intracavernosal administration of 2 ml of a 2% solution of vasoactive drug papaverine hydrochloride was performed. All men had a decrease in hemodynamic parameters of the cavernous arteries. A decrease in blood flow in one of the cavernous arteries was noted in 16 (25%) cases, and 9 (14%) patients had bilateral abnormalities ($p<0.05$).

Infertility, testicular hypotrophy, anejaculation. Infertility in marriage and testicular hypotrophy were noted in 31.2% and 29.6% of cases, respectively. According to the sperm analysis, oligospermia, oligozoospermia and azoospermia occurred in 13 (20.3%), 11 (17.1%) and 9 patients (14.1%), respectively. Complete impairment of the testicular functions was accompanied by an absence of ejaculate (anejaculation) during intercourse in 9 (14.1%) patients ($p<0.05$). We believe that a decrease in the number of spermatozoa, including azoospermia, and testicular hypotrophy occurred due to suppression of the secretion of gonadotropins. In addition, 14 men (29.8%) had testicular atrophy, including bilateral in 10 cases.

Lower urinary tract symptoms (LUTS). LUTS were detected in 14 (21.8%) cases. According to the IPSS questionnaire, the majority of patients ($n=10$; 15.6%) had moderate symptoms (8–19 points), while in 4 men (6.2%) mild symptoms were detected (0–7 points). In addition, the prevalence of storage symptoms was revealed. When assessing the quality of life, it was regarded as an unsatisfactory (*Table 2*).

Gynecomastia. Gynecomastia was identified in 9 (14.1%) patients (*fig. 4 A, B*). In 7 (11%) patients, gynecomastia was bilateral, and two men have unilateral growth (3.1%). Stage I (florid), stage II (intermediate) and stage III (fibrous) gynecomastia was detected in 2 (3.1%), 3 (4.6%), and 4 (6.3%) patients, respectively ($p<0.05$).

Neoplasms. Testicular tumors were detected in 3 (4.7%) men, including one Leydig cell tumor (1.6%) and two testicular cancers (3.1%) (*fig 5*).

Discussion. The use of Ts and anabolic steroids is common among men who visit gyms and fitness centers. Knowledge of the associated health risks and AEs is limited due to the lack of respective clinical studies [18, 19].

According to our results, the most common AEs in men taking Ts and anabolic steroids were ED and infertility. These problems are due to dysfunction of the hypothalamic-pituitary-

Table 1

Erection hardness scale

I grade		II grade		III grade		IV grade		*p*
Number of patients								
Abs.	%	Abs.	%	Abs.	%	Abs.	%	
–	–	11	17,1	14	21,9	–	–	0,0001

Table 2

Lower urinary tract symptoms and evaluation of the quality of life according to the IPSS

Symptoms		Number of patients	%
Weak stream		4	6,2
Increased frequency		12	18,7
Urgency		14	21,8
Nocturia		11	17,1
Quality of life			
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	Delighted	–	–
	Pleased	2	3,1
	Mostly satisfied	3	4,6
	Mixed about equally satisfied and dissatisfied	2	3,1
	Mostly dissatisfied	7	11,0
	Terrible	–	–
	Очень плохо	–	–

Fig 4. Gynecomastia.
A – Stage II in patient Ch., 28 years old. B – stage III in patient X, 27 years old

gonadal axis (HPG). The use of high doses of Ts can cause ED and infertility due to suppression of the HPG axis and a decrease in the production of FSH and LH, which leads to a decrease in spermatogenesis and steroidogenesis [20, 21].

Short-term use of TS with subsequent withdrawal can lead to the restoration of erectile and reproductive functions, but long-term administration can lead to irreversible changes in the testicles [21]. In all patients included in the study, the period of taking Ts and anabolic steroids was more than a year. In addition, 50% of men received two or more drugs in combination with other substances, which are toxic to the reproductive epithelium (growth hormone, ephedrine, insulin, thyroxine, diuretics). This combination, according to the literature, leads to a state of "persistent infertility" [22]. Also, the restoration of fertility after the use of TS and anabolic steroids for non-medical purposes is complicated by "doping polypharmacy", which leads to irreversible infertility [18]. The results of this study also indicate the presence of not only qualitative abnormalities in the ejaculate, but also quantitative ones, which is the reason for the anejaculation, which was seen in 14.1% of cases. According to a number of international studies, the average time for complete suppression of spermatogenesis after stating taking Ts is 3.5 months. [23]. At the same time, the average time for the restoration of spermatozoa concentration to 20 × 106 ml after stopping the Ts is 12–24 months. Longer-term use of these substances can lead to severe irreversible changes in spermatogenesis [24]. The majority (59.3%) of the men use Ts and anabolic steroids from 1 to 3 years.

In relation to LUTS, the majority (57.5%) of patients had storage symptoms. It is known that the functional activity of the detrusor decreases with Ts deficiency. During a long-term decrease in the Ts level, the synthesis of nitric oxide in the vascular endothelium is disrupted, which leads to a persistent spasm of the vessels in various organs and systems, in turn contributing to the development of first hypoxemic and then cellular and tissue hypoxia. Then local and systemic ischemia develops, in particular in pelvic area, leading to hypoxia in the area of the pelvic, urethra and prostate, which is considered the most important pathogenetic factor for LUTS [25, 26].

According to our data, gynecomastia developed in 14.1% of cases. This condition is caused by an increase in the level of aromatase due to supraphysiological concentrations of Ts and its conversion to estrogen as a result of exogenous use of Ts ([27, 28].

The relationship between Ts therapy and testicular tumors is not well understood, however, Ts deficiency can lead to elevated production of FSH and LH with increased stimulation of testes, which leads to hypertrophy of the testicular tissue and can possibly stimulate atypical growth and development of testicular tumors [25].

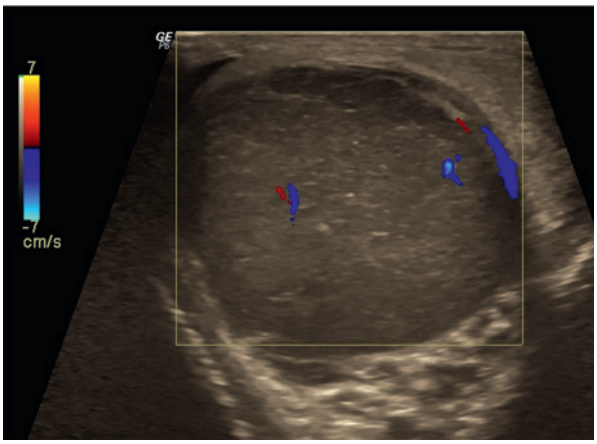

Fig 5. Ultrasound imaging of the scrotum. Testicular tumor

Conclusion. Unreasonable use of Ts and anabolic steroids can be accompanied by a wide range of AEs in the urinary tract and reproductive organs. These negative effects should be explained to men. It is important to develop a system for the treatment of AEs.

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LEVEL OF GROWTH FACTOR IN TARGETED CHEMOEMBOLIZATION OF RENAL CELL CARCINOMA

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Aim. To assess the level of vascular growth factor in the tumor tissue, peritumorous area and in the renal vein during partial nephrectomy with intra-arterial chemoembolization with a targeted drug in patients with renal cell carcinoma.

Materials and methods. The study is based on the results of partial nephrectomy with intraoperative arterial chemoembolization with the targeted drug bevacizumab in patients with clear cell renal cell carcinoma of T1aN0M0 stage. The level of vascular growth factor in the tumor tissue, parenchyma of the peritumorous area and in the renal vein before partial nephrectomy, during the compression of the renal pedicle and after intra-arterial administration of the targeted drug was evaluated.

Results. The obtained results showed that acute renal ischemia causes an increase in the level of vascular growth factor in the tumor tissue by almost twice, in the parenchyma of the peritumorous zone by more than one and a half times and in the renal vein by 2.5 times. Intra-arterial administration of the drug bevacizumab reduces the concentration of vascular growth factor in the tumor itself by a quarter, in the peritumorous zone by less than 10 percent, and in renal vein by almost 4 times.

Conclusions. The additional targeted chemoembolization prior to partial nephrectomy in renal tumors can improve recurrence-free and metastatis-free survival by inactivating vascular growth factor, a massive release of which occurs in acute kidney ischemia.

K e y w o r d s: kidney cancer, vascular endothelial growth factor, partial nephrectomy

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Introduction. The active implementation of targeted chemotherapy based on the anti-angiogenic mechanism of action into clinical practice have initiated a new era in the treatment of malignant tumors of the renal parenchyma. However, the efficiency of targeted therapy in renal cell carcinoma was not so impressive, which may be due to the presence of metastatic foci. Approximately one third of renal cell cancers are diagnosed as metastatic due to the increased potential to dissemination [1-3]. This is also proved by the fact that the systemic progression of the disease is observed after radical interventions in 20–40% of cases [4, 5], which requires systemic therapy to be prescribed in almost half of the patients [6]. Recurrence rate after partial nephrectomy is about 30% [7].

A key goal of targeted therapy based on the anti-angiogenic effect is to transform active oncological process to chronic state and to achieve a control over tumor growth, which implies a long-term therapy with its negative influence [8]. Adverse events of targeted drugs are diverse, depending on the mechanism of action, and affect many body systems. In some cases, they can be fatal [9].

All of these facts lead to the idea of creating a new method of surgical treatment of kidney tumors, aimed at eliminating even the low possibility of postoperative recurrence or metastatic progression. This method is based on the mechanism of action of an inhibitor of vascular endothelial growth factor (VEGF), which is produced due to ischemia of the tumor during partial nephrectomy. Entering the bloodstream through the renal vein, VEGF activates angiogenesis in suspected metastatic nodes. Administration into the arterial bed of the kidney at the time of ischemia of the targeted drug bevacizumab, known for its antiangiogenic activity by irreversible binding to VEGF receptors, will provide timely and targeted protection from pathological activation of metastatic foci. The release of VEGF during tumor ischemia is blocked by the targeted drug, which prevents the trigger of metastatic progression. The proposed method received the patent of the Russian Federation for the invention [10].

Aim. To assess the level of vascular growth factor in the tumor tissue, peritumorous area and in the renal vein during partial nephrectomy with intra-arterial chemoembolization with a targeted drug in patients with renal cell carcinoma.

Materials and methods. The study is based on direct measurement of the concentration of VEGF in the tumor, kidney parenchyma of the peritumorous area and in the blood of the renal vein at baseline, during acute ischemia by clamping the renal artery and after administration of the drug bevacizumab into the renal artery. To achieve this goal, 8 patients with solid renal parenchyma tumors, actively accumulating a contrast on computed tomography, were selected. The tumor size ranged

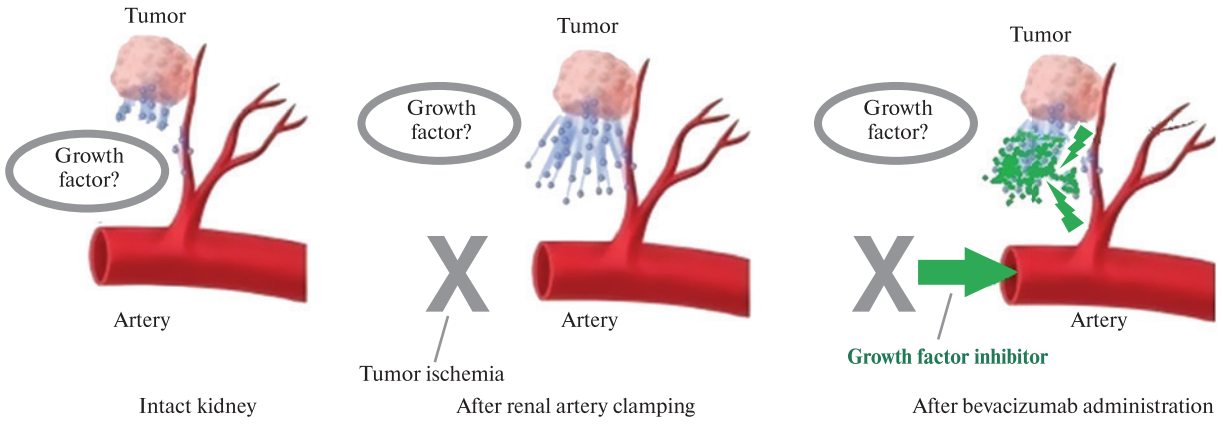

Fig 1. Study of the level of endothelial growth factor in the experiment

from 24 to 48 mm. There were no distant metastases detected by imaging studies. In all cases, aberrant renal vessels were absent, which allows to create selective renal ischemia and to administer the drug. All patients gave informed consent prior to inclusion, which was confirmed on the meeting of the Ethics Committee of the Ammosov North-Eastern Federal University Federal State Autonomous Educational Institution of Higher Education.

The design of the study is shown in *Fig. 1.* All patients underwent open partial nephrectomy using a retroperitoneal approach. After the kidney and its vessels were isolated from the paranephric fat and adjacent tissues, wedge-shaped tissue excision in the center of the tumor was done with a pointed scalpel in a volume of 0.5 cm3, as well as from parenchyma in peritumorous area adjacent to the tumor pseudocapsule. Then, aspiration of venous blood from the renal vein into a 10 ml syringe was performed. After obtaining the samples, Satinsky vascular clamps were applied selectively to the renal artery and renal vein. Five minutes after the stoppage of blood flow, the samples from the tumor and peritumorous area were taken again, as well as venous blood from the renal vein, which was punctured distal to the clamping level. Immediately after the second sampling, 2.5 mg of targeted drug bevacizumab diluted in 10 ml of saline was injected through the cannula into the lumen of the renal artery, distal to the vascular clamp, thus filling the vascular bed of the kidney. Five minutes later, the main stage of the procedure was done. The resection

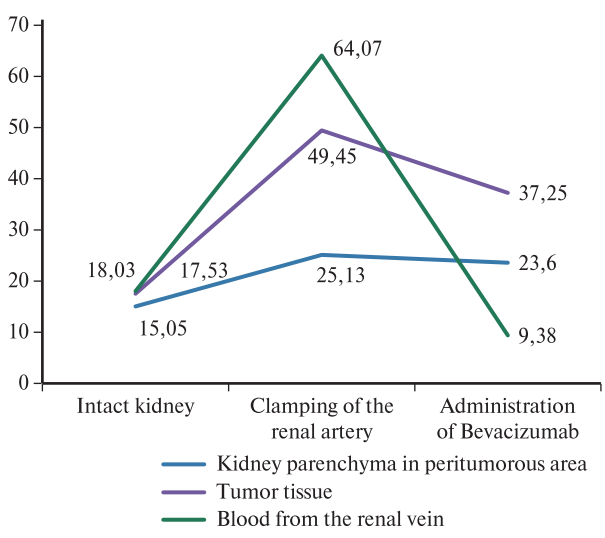

Fig 2. Dynamics of VEGF level in tissue samples during the experiment (pg/ml)

of the kidney tumor was performed with cold scissors within the healthy tissue at 5 mm distance from the tumor edge. After resection of the tumor, additional samples were obtained by excision of a fragment of the tumor and peritumorous kidney parenchyma in a volume of 0.5 cm3. Blood was taken from the renal vein by aspiration at the point distal to the level of clamping. After suturing the parenchyma wound, the blood supply to the kidney was restored by releasing the clamps; the ischemic time in all cases did not exceed 20 min. The obtained samples were placed in labeled test tubes and sent to the laboratory without any fixation for histological examination. The surgical procedure was completed by suturing the wound in the standard way.

VEGF levels were determined by enzyme immunoassay using the HEA143Hu kit (Cloud-Clone Corp., USA). The obtained samples were immediately processed. For serum preparation, the blood was centrifuged with an acceleration of 1000 G within 20 min at a temperature of - 4°C. The serum was analyzed immediately or stored at -20°C for no more than 7 days.

Tissue samples were pre-washed in cool phosphate-buffered saline (Invitrogen, USA), placed in IS007 lysis buffer (Cloud-Clone Corp., USA), and milled in a glass homogenizer on ice. The resulting suspension was processed by Qsonica Q125 ultrasonic homogenizer (Qsonica, USA) with an amplitude of 50%, a pulse duration of 5 min, a pause of 5 min, and a treatment duration of 10 min. The sample was kept on ice to avoid overheating. After ultrasonic processing, the preparation was centrifuged for 5 min with an acceleration of 1000 G at a temperature of 4°C. The supernatant was analyzed immediately or stored at -20°C for no more than 7 days.

Enzyme immunoassay was carried out in accordance with the manufacturer's instructions. The results were recorded on a plate photometer SLT Spectra II (Tecan, USA), while experimental data were analyzed using the MultiCalc software (Wallac, Finland). The statistical analysis was performed using SPSS packages (Windows, version 7.5.2). The differences between quantitative indicators were assessed by Student's t test for normally distributed samples. Differences were significant if $p<0.03$.

Results. In all cases, pathomorphological examination revealed a clear cell renal cell carcinoma with a negative surgical margin.

The concentration of VEGF in the tissue samples is presented in *Table 1.* The dynamics of changes in the concentration of VEGF during the experiment is clearly demonstrated in *Fig. 2.* The concentration of VEGF at baseline is approximately at the same level in the tumor, kidney parenchyma adjacent to the tumor, and in venous blood obtained from the renal vein. Sudden cessation of arterial blood flow in the kidney as a result of renal artery clamping causes a massive release of VEGF by tumor cells.

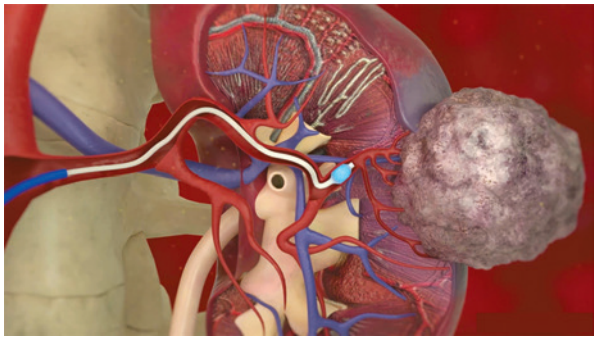

Fig 3. Superselective balloon embolization of the renal artery (computer model)

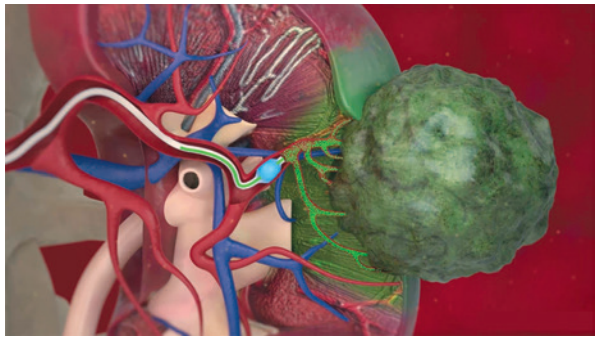

Fig 4. Introduction of a targeted drug into a renal segment with a tumor (computer model)

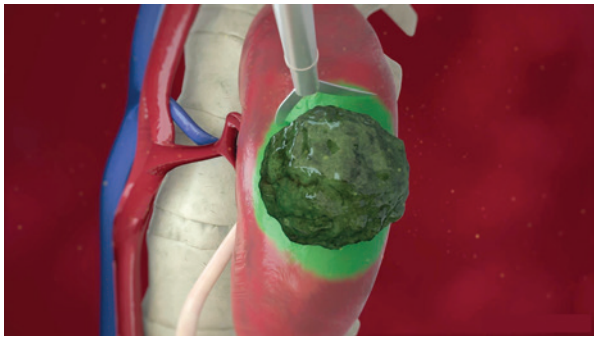

Fig 5. Resection of the kidney tumor (computer model)

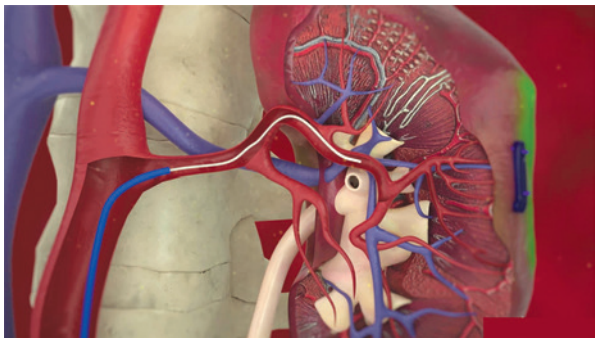

Fig 6. Removal of the balloon and restoration of blood flow (computer model)

An uneven rise in the level of VEGF occurred: the most significant change in concentration was in venous blood (more than 3.5 times, 255.35%), followed by tumor tissue (by almost 3 times, 182.08%). However, in peritumorous kidney parenchyma the smallest increase was registered, only by 66.97%, which is associated with the cessation of blood flow in the kidney and the slow diffusion of the VEGF released by the tumor. The administration of the targeted drug bevacizumab into the arterial bed of ischemic kidney leads to the binding of VEGF, which is manifested by a sharp decrease in its concentration. The most active binding occurred in the renal vein. A decrease in concentration was by almost 7 times (85.35%), compared to 24.67% and 6.08% in the tumor tissue and peritumorous kidney parenchyma, respectively.

Our data suggest the trigger phenomena of the neoangiogenesis process. A sudden cessation of blood flow in tumor immediately initiates the mechanism for the formation of new tumor vessels. Five minutes after the onset of hypoxia, the tumor releases substances aimed at restoring blood supply in an amount 3–3.5 times higher compared to baseline. Various conditions accompanied by hypoxia of a malignant tumor (fibrosis due to chronic inflammation, vascular atherosclerosis, hypertension, diabetes mellitus, traumatic injuries, etc.) lead to a release of neoangiogenesis activators and, as a result, to tumor growth. In a third of organ-preserving kidney procedures, a massive release of growth factor from the tumor occurs, which contributes to its distribution throughout the body and triggers the growth of metastases. Perhaps this explains the active growth of metastases postoperatively.

Local administration of a targeted drug that neutralizes VEGF into the blood at the time of artery clamping serves as a trap, since growth factor will not be able to realize its harmful effect. Technically, this can be done in the following way. In a hybrid operating room, selective renal angiography is performed for detecting segmental artery that feeds tumor-bearing segment of the kidney. A balloon for coronary angioplasty of the appropriate diameter, sufficient for intraluminal blockage of blood flow with a central channel for introducing solutions into the ischemic segment (*fig 3*), is advanced to corresponded branch of the renal artery. Immediately after inflation of the balloon, the targeted drug bevacizumab is injected through the central channel into the segmental artery in an amount required for reliable binding of the released VEGF (*fig. 4*). Immediately after the injection of the targeted drug, partial nephrectomy is performed using laparoscopic, robotic, or other approaches, according to the local preferences (*fig 5*). Upon completion of the main surgical stage and suturing of the parenchyma defect, the coronary balloon is deflated and blood flow in the ischemic segment of the kidney is restored (*fig 6*).

Table

VEGF levels in tissue samples (pg/ml)

	Intact kidney	After renal artery clamping	After bevacizumab administration
Kidney parenchyma in peritumorous area	15,04	25,13	23,6
Kidney tumor	17,53	49,45	37,25
Blood from the renal vein	18,03	64,07	9,38

The use of superselective balloon embolization of the renal artery, followed by targeted chemoembolization, provides reliable intraoperative hemostasis with "zero ischemia". Local administration of a small amount of a targeted drug into the tumor-bearing segment of the kidney allows to bind and inactivate the release of VEGF as a result of hypoxia. In addition, small amount of the administered drug does not have any negative effects.

The postoperative period was uneventful in all cases, and patients were discharged on time. Follow-up blood and urine tests, serum biochemical profile, ultrasound of the kidney did not show any significant abnormalities.

Conclusions. Acute hypoxia of the tumor tissue immediately triggers the formation of vascular endothelial growth factor, which is accompanied by a multiple increase in its level in the tumor and venous blood. This fact can serve as a trigger for the accelerated growth of metastases after the procedure, worsening the prognosis. Timely and local administration of a targeted drug, a growth factor inhibitor, may block the trigger and prevent dissemination of renal cell cancer metastases. As a consequence, the additional targeted chemoembolization prior to partial nephrectomy in renal tumors can improve recurrence-free and metastasis-free survival by inactivating VEGF, a massive release of which occurs in acute kidney ischemia intraoperatively.

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ENDOSCOPIC MARSUPIALIZATION OF PARAPELVIC RENAL CYSTS

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Introduction. Parapelvic renal cysts are very common. Indications for surgical treatment are upper urine tract obstruction, pain and recurrent gross hematuria.

Aim. To analyze the efficiency and safety of endoscopic transurethral and percutaneous laser marsupialization of parapelvic renal cysts.

Materials and methods. A total of 9 patients were undergone to transurethral intrarenal marsupialization of parapelvic renal cysts from March 2016 to February 2021 (4 men, 5 women, aged 42-78 years). Another 2 patients (2 men, aged 46 and 52 years) were treated by percutaneous approach. The average size of the cyst according to contrast-enhanced multi-slice computed tomography (MSCT) was 3.1±1.8 cm. In two cases, papillary tumor of the pelvis was suspected. The anteroposterior diameter of the pelvis was 2.6±1.3 cm; 9 patients had pain in the loin area, while in 7 patients recurrent gross hematuria was also an indication for surgical treatment. For marsupialization, a holmium (Ho:YAG) laser Auriga XL (Boston Scientific, USA) was used in 4 patients, and in other cases (n=7) a procedure was performed using a thulium fiber laser (Tm Fiber) Fiberlase U1 (IRE-Polus, Russia). In 3 patients, to clarify the site of incision of the cyst, intraoperative ultrasound was used. In all cases, after draining the cyst, an internal stent was placed inside the cyst for a period of 4-6 weeks.

Results. The duration of transurethral surgery was 26±11 minutes, while percutaneous marsupialization of the cyst, which was performed in combination with percutaneous nephrolithotomy, took 10 and 18 minutes, respectively. The average catheterization time was 12±8 hours. Nephrostomy tube was removed on the 2nd day. The length of stay was 4±2 days. Febrile fever was noted in 1 patient (9%), which required a change in antibiotic therapy. During ultrasound control at discharge, the dilatation of the collecting system was not detected in any cases, while the residual cavity was found in 2 patients (18%). Follow-up contrast-enhanced MSCT and ultrasound within 3-30 months in all patients (n=11) showed no dilatation of the collecting system. In 1 (9%) patient, the residual cavity was preserved with a decrease in size to 1.2 cm without signs of upper urinary tract obstruction; the initial diameter of the cyst in this patient was 4.9 cm. There was no recurrence of gross hematuria.

Conclusions. In our opinion, transurethral and percutaneous laser marsupialization of parapelvic renal cysts is an effective and safe method that allows definitive treatment for cysts up to 4 cm in size. If the cyst is larger than 4 cm, endoscopic removal should be balanced with the possibility of preserving the residual cavity. The most common complication of endoscopic treatment of intrarenal cysts is acute pyelonephritis with a rate of 9%.

K e y w o r d s: parapelvic cysts, ureterorenoscopy, laser urology

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Doi: https: //dx.doi.org/10.18565/urology.2022.1.61-66

Introduction. Kidney cysts are one of the most common benign kidney lesions. According to the literature, their incidence is up to 10% worldwide and tends to increase with age [1]. A simple renal cyst develops in 20% of the adult population by the age of 40, but a prevalence increases to 33% in those older than 60 years [1]. The vast majority of renal cysts are considered to be simple solitary lesions, which arise due to tubular obstruction, and are diagnosed incidentally. However, they can cause pain and discomfort in loin area, hematuria, urinary tract infection and renal hypertension [1].

Parapelvic cysts develop from the adjacent renal parenchyma, while peripelvic cysts arise directly from the sinus and are of

lymphatic origin [2]. Parapelvic and peripelvic cysts occur in 1.25–1.5% and 1–3% of all renal cysts, respectively [3, 4]. They are often asymptomatic, but unlike solitary cysts, even despite being small, parapelvic cysts can cause upper urinary tract obstruction [5]. Other possible manifestations of renal sinus cysts include urinary tract infection, hematuria, vasopressor-induced hypertension, and urolithiasis.

Parapelvic cysts are quite rare, which leads to certain problems associated with diagnosis [6]. Often, one can mistake a parapelvic cyst with hydronephrosis or calyx dilatation on non-contrast-enhanced computed tomography (CT) or ultrasound.

With the technical advancements, the surgical treatment of parapelvic kidney cysts have also changed from open marsupialization or nephrectomy to laparoscopic excision and ablation [7, 8]. Laparoscopic access is considered the preferred option for the treatment of renal sinus cysts [2]. However, due to the increased risk of bleeding, the possible development of adhesions and the duration of procedure, the safety profile is not so good [2]. A number of studies have described the successful treatment of parapelvic cysts using retrograde and antegrade nephroscopy [1-13]. These methods, in our opinion, are the least invasive, and therefore preferable for patients.

Our study included the results of endoscopic intrarenal marsupialization of parapelvic renal cysts in 11 patients performed by transurethral and percutaneous approaches.

Aim. To analyze the efficiency and safety of endoscopic transurethral and percutaneous laser marsupialization of parapelvic renal cysts.

Materials and methods. A total of 9 patients were undergone to transurethral intrarenal marsupialization of parapelvic renal cysts using laser energy in City clinical hospital named after D.D. Pletnev from March 2016 to February 2021 (4 men, 5 women, aged 42-78 years). Another 2 patients (2 men, aged 46 and 52 years) were treated by percutaneous approach. Percutaneous marsupialization was done during percutaneous nephrolithotomy, which was performed for pelvic stones 3.5 and 2.7 cm in size in the supine position. The chief complaint was pain in loin area, while 7 patients had recurrent gross hematuria. The average size of the parapelvic cyst according to contrast-enhanced computed tomography (CECT) was 3.1±1.8 cm. In two cases, papillary tumor of the pelvis was suspected. In 9 (81.8%) patients the anteroposterior diameter of the pelvis was 2.6±1.3 cm.

For marsupialization, a holmium (Ho: YAG) laser Auriga XL (Boston Scientific, USA) was used in 4 patients, and in other cases (n=7) a procedure was performed using a thulium fiber laser (Tm Fiber) FiberLase U1 (IRE-Polus, Russia). Laser settings were as following: 1 J, 10 Hz, 10 W. All procedures were performed in the X-ray operating room under fluoroscopic control.

A rigid ureteroscope with a diameter of 8 Fr was advanced in a retrograde fashion under general anesthesia. Ureterorenoscopy and retrograde pyelography were performed. In 3 patients, to clarify the site of incision of the cyst, intraoperative ultrasound was used. A laser fiber (365 μm) was passed through the working channel, then an incision was done along the entire length of the cyst wall protruding into the pelvis, and its cavity was carefully examined in white light, as well as using narrow-spectrum endoscopy (NBI technology, Olympus) or virtual chromoendoscopy (Image1S-technology, Karl Storz). In case of abnormalities of the inner cyst wall, a "cold" biopsy was performed. In all cases, after draining the cyst, a stent was placed inside the cyst for a period of 4-6 weeks (*figs. 1–5*). During percutaneous access, intrarenal laser marsupialization of the parapelvic cyst was done after completing lithotripsy with a use of nephroscope of 24 Fr. In addition to nephrostomy drainage, a J-J stent was placed antegradely into the cyst cavity. The nephrostomy drain was removed 2–3 days after surgery, while ureteral stent was left for 4–6 weeks.

Subsequently, all patients underwent examination during follow-up of 3–30 months, including CECT, as well as renal ultrasound. During the removal of the ureteral stent, 9 patients underwent a follow-up ureteroscopy.

Results. The duration of retrograde procedure was 26±11 minutes, while percutaneous marsupialization of the cyst, which was performed in combination with percutaneous nephrolithotomy, took 10 and 18 minutes, respectively. In one case, the so-called chocolate cyst was treated. There were no intraoperative complications, however, in three patients an intraoperative ultrasound was required in order to detect a precise location of the parapelvic cyst. After successful marsupialization and placement of JJ stent, a Foley urethral catheter was also put to prevent vesicoureteral reflux. On average, the urethral catheter was removed after 12±8 hours. In case of percutaneous marsupialization, the nephrostomy tube was removed on the 2nd day. The length of stay was 4±2 days. According to pathomorphological studies of biopsy material (6 patients), no malignant tumor was detected. Postoperatively, 1 (9%) patient with a cyst size of 4.9 cm according to CECT had febrile fever, which required a change in antibiotic therapy. All patients underwent a imaging studies before discharge. There was no dilatation of the collecting system in any patients, however, in 2 (18%) of 11 cases, the residual cavity was clearly defined. The baseline size of cysts in these patients was 4.1 and 4.9 cm, respectively. When performing a follow-up ureteroscopy during stent removal at 4–6 weeks after primary procedure, no significant residual cavity was found in any patient. The site of marsupialization was covered by fibrin.

During the follow-up period, patients underwent CECT and renal ultrasound on the 3rd and 12th months. According to ultrasound study, there was no dilatation of the collecting system in any patients, while on CT only in one patient with a baseline cyst size of 4.9 cm, a residual cavity without signs of obstruction of the collecting system was noted. Its size was 2.4 cm by the 3rd month and decrease to 1.6 cm after 12 months. Gross hematuria, which was present prior to surgery, did not recur in any case.

Discussion. Parapelvic cysts are found in 1.25-1.5% of all renal cysts [3, 4]. Currently, the gold standard for treatment in such cases is the laparoscopic unroofing. Our study demonstrated the efficacy and safety of endoscopic retrograde and percutaneous marsupialization of symptomatic parapelvic cysts. Only in one patient with a cyst size of more than 4 cm, a residual cavity was found at 3 and 12 months after marsupialization. In addition, one case of postoperative acute pyelonephritis was also documented. During the follow-up, there was no dilatation of the collecting system in other patients according to the ultrasound and the residual cavity on CECT. The baseline symptoms did not recur after treatment.

Endoscopic antegrade and retrograde treatment of parapelvic cysts was described in different publications of foreign colleagues. Kavoussi et al. were the first to perform retrograde ureteroscopy for marsupialization of a renal sinus cyst [9]. In a 60-year-old patient with acute pain in left loin area, a sinus cyst 4 cm in size was found on CECT, which caused upper urinary tract obstruction. Through a flexible ureteroscope 10.8 Fr. marsupialization of the cyst was done using fulguration. After 3 and 10 months postoperatively, the patient had no evidence of obstruction, as well as recurrence of symptoms. A similar clinical case with equivalent results were presented by

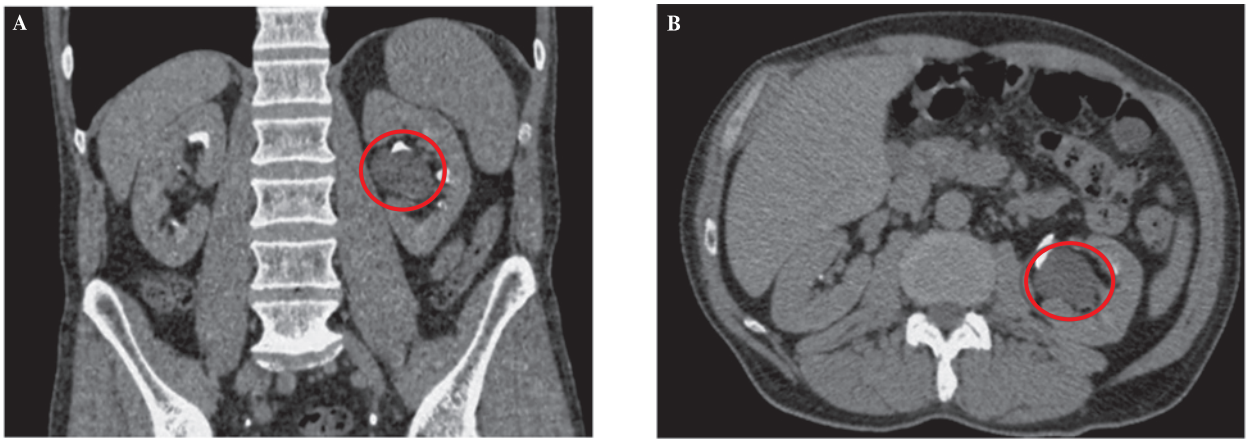

Fig 1. Patient Sh, 64 years old. Contrast-enhanced CT (A: sagittal section and B: coronal section): lesion of size 36 mm and density of 7.2 HU. Parapelvic cyst (with a suspicion of pelvis tumor) before transurethral marsupialization

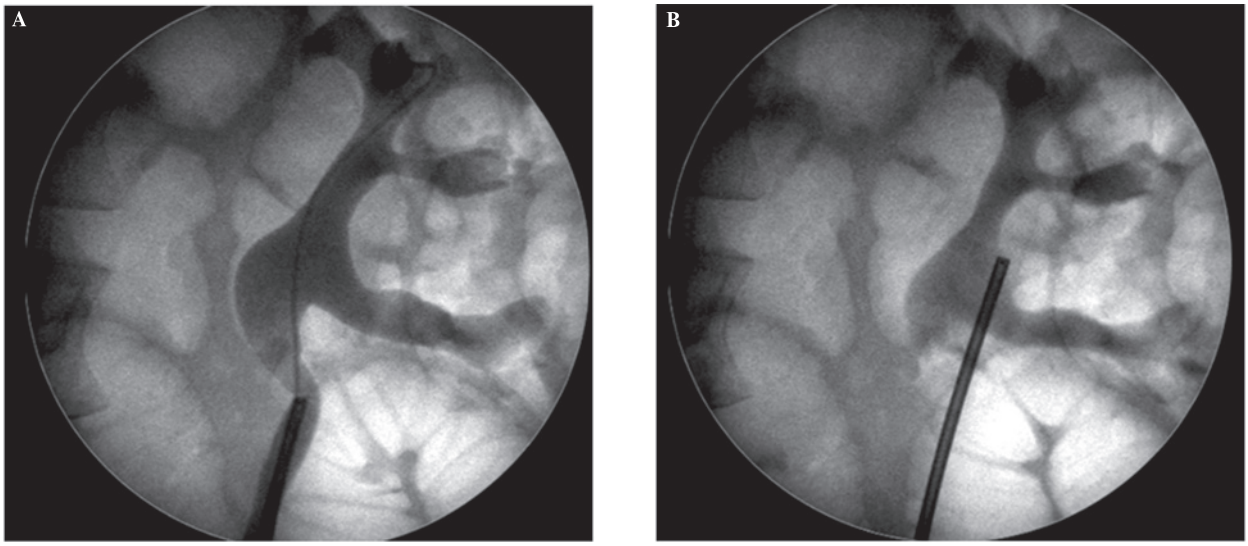

Fig 2. Retrograde pyelography of the same patient, performed during ureteroscopy (A: deformation of the renal pelvis by a cyst, B: advancement of the ureterorenoscope inside the cyst)

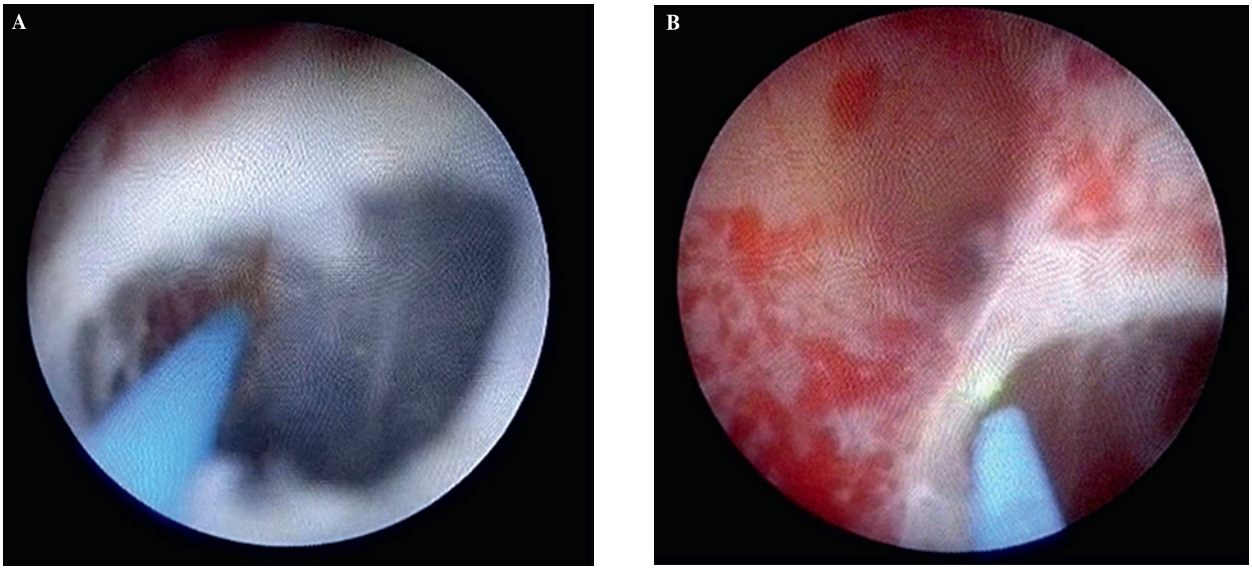

Fig 3. Laser intrarenal marsupialization of the cyst (A — opening of the cyst cavity, B — wide incision of the cyst wall)

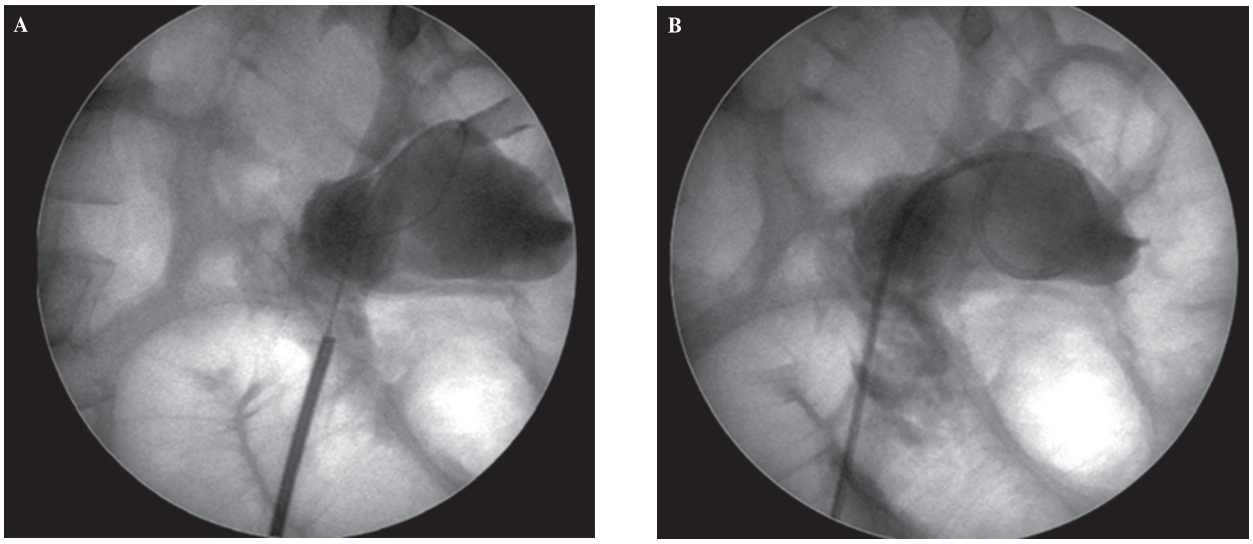

Fig 4. Follow-up pyelography: A: contrast injection through the ureterorenoscope, B: advancement of a stent into the cyst cavity

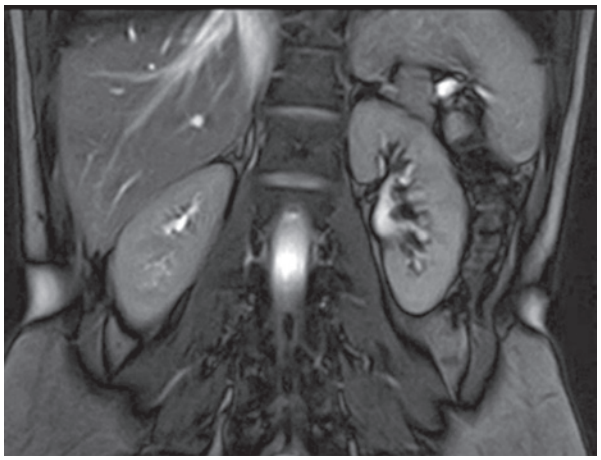

Fig 5. Follow-up contrast-enhanced CT 3 month after procedure

O'Connor et al., however, in their work, a holmium laser was chosen as the energy source [10]. In a retrospective study, Li et al. described retrograde marsupialization of parapelvic cysts in 15 patients using holmium laser [11]. The procedure was performed without complications. In 13 out of 15 patients there was no loin pain postoperatively, and its severity decreased from 6.7 to 1.1 points on average by the 6th month of follow-up. Imaging studies showed positive dynamics in 14 patients: the average size of the cysts decreased from 6.8 cm to 1.3 cm by the end of the follow-up. In one patient, a recurrent parapelvic cyst 5 cm in size was found. A same intervention was performed once again, after which residual cavity was absent, according to CECT. In a study by Luo et al. flexible ureteroscopy was performed in 15 patients with parapelvic kidney cysts [3]. Marsupialization of the cyst was performed with a holmium laser, after which J-J stent 5 Fr was put for 4 weeks in order to provide adequate drainage. The average length of stay was 3 days. The success of the surgical intervention was also evaluated using CECT or Doppler ultrasound. In 10 cases after 6 and 12 months there were no signs of cysts (recurrence). In one patient, CECT revealed that the size of the cyst decreased by less than half, and in 4 others patients it decreased by half after 6 months. Similar results were achieved by Zhao et al., who also used ureteroscopy with holmium laser [12]. Of the 27 patients undergoing marsupialization of the cyst by retrograde access, in 25 cases a rigid ureteroscope was used, while two procedures were done with a use of flexible ureterorenoscope. The average time of marsupialization was 26 min, after which a J-J-stent 5 Fr was placed in the cyst cavity for drainage. The mean follow-up period was 39 months. In 22 patients, according to CECT, there was no residual cavity, while in 4 patients the size of cysts decreased by more than half. Only 1 patient had a relapse after 60 months. Authors suggested that this could be explained by the incomplete excision of the cyst septum. The possibilities of retrograde marsupialization of intrarenal cysts using holmium laser were also assessed in the multicenter study of Mancini et al. [1]. All 14 patients had loin pain. The average size of the cyst was 53.2±14.23 mm. There were no intraoperative complications, however, two patients experienced pain in loin area and dysuria postoperatively. The average length of stay was 3.5 days. During the follow-up period of 44±17.24 months, no patients have any symptomatic manifestations of intrarenal cysts. By the 12th month, according to CECT, 13 patients had no signs of cysts, while one patient with an initial cyst size of 60 mm had a 10 mm fluid lesion.

Despite the good results demonstrated in the studies above, it should be noted that the retrograde endoscopic method has its limitations. For example, in all publications, retrograde marsupialization was more effective in patients with small cysts. In addition, there is a certain risk of injury to the renal vessels if a cyst is centrally located [13], which must be considered when choosing a treatment method. Percutaneous marsupialization of a peripelvic cyst was reviewed by Shao et al. [4].

In contrast to those publications, we used a thulium solid-state laser (Tm: Yag) as the energy source as well. After marsupialization, in addition to nephrostomy drainage 18–20 Fr, in all cases (n=31) a double J-J stent 6 Fr was put with a positioning of the proximal pigtail into the cyst cavity for drainage. The nephrostomy tube was removed 3–5 days after the procedure, while stenting time was 2–3 months. Patients underwent follow-up examinations every 3 months during the first year, then once a year. There were no intra- or postoperative surgical complications. All patients experienced a resolution of loin pain and recurrent infections. According

to imaging studies, in 18 patients there was no residual cyst, while in the remaining 13 cases a decrease in cyst size by more than a third was seen. In our study, we used both holmium and thulium fiber lasers. We did not note any specific advantages of one laser over another.

Conclusions. Transurethral and percutaneous laser marsupialization of parapelvic renal cysts is an effective and safe method that allows definitive treatment for cysts up to 4 cm in size. If the cyst is larger than 4 cm, endoscopic removal should be balanced with the possibility of preserving the residual cavity.

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OUR EXPERIENCE OF HOLMIUM LASER ENUCLEATION OF THE PROSTATE

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Introduction. Surgical treatment of benign prostatic hyperplasia (BPH) is influenced by a rapidly growing number of technologies.
Aim. To determine the surgical potential of holmium laser enucleation of the prostate (HoLEP) and the rate of postoperative complications during the learning curve.
Materials and methods. A total of 98 patients undergoing HoLEP in the surgical department of the Clinical Hospital "Mother & Child" during the period from January 2018 to May 2020 were included in the study. HoLEP was performed by a single surgeon with previous experience in transurethral procedures. The criteria for inclusion in the study group were as follows: moderate-to-severe lower urinary tract symptoms, prostate volume > 40 cm3, maximum flow <15 ml/sec, the volume of residual urine > 50 ml. The exclusion criteria were the following: inflammatory process in the lower urinary tract, genitourinary malignancy, previous urinary tract interventions. The evaluated criteria included age, prostate size, International Prostate Symptoms Score (IPSS and QoL), bladder diary, PSA, uroflowmetry, total operative time, length of catheterization, complications according to the Clavien-Dindo Classification, and length of stay.
Results. During pathologic study, two cases of incidental prostate cancer (2.1%) were detected. The relationships between the prostate size and operative time ($p<0.05$), operative time and length of stay ($p<0.05$) were found. The total rate of complications was 16.3%. There were no complications ⩾IIIb according to the Clavien-Dindo Classification. The most dangerous complications were injuries of the bladder wall and ureteral orifice (31.25% and 18.75% among all complications, respectively).
Discussion. It should be considered that a large "middle lobe" is associated with a high risk of injury of the ureteral orifices. In our series, there were 5 cases of bladder tamponade, while bladder injuries during the morcellation developed in the first 10 patients.
Conclusion. HoLEP is a reasonable alternative to TURP for surgical treatment of BPH and is considered a safe procedure for patients taking anticoagulant and antiplatelet drugs. Past experience of TURP allows to learn the technique faster and to reduce the number of complications.

K e y w o r d s: *benign prostatic hyperplasia, holmium laser enucleation of the prostate, the learning curve*

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Doi: https: //dx.doi.org/10.18565/urology.2022.1.67-71

Introduction. Surgical treatment of benign prostatic hyperplasia (BPH) is characterized by a rapidly growing number of technologies. The minimally invasive methods have been actively introduced in the routine urological practice. At the same time, novel drug therapy leads to an increase in the age of patients requiring surgical intervention. Laser technologies in the treatment of BPH are proved to be a safe, and the average enucleation time during holmium laser enucleation of the prostate (HoLEP) is about 0.28 min/g, which allows to perform it, independent of the prostate volume [1]. The total number of early postoperative complications does not exceed 19% and depends on both preoperative (use of antiplatelet agents and anticoagulants, age, body mass index, ASA score, prostate volume) and operative factors (duration of surgery and catheterization, blood transfusion, pathomorphological data, surgeon experience) [2]. With an increase in the experience, the number of peri- and postoperative complications decreases. On average, the learning curve can be completed after 25–50 procedures, and the surgeon reaches a plateau after 60 procedures [3, 4].

Significant risks of complications of traditional methods, dissatisfaction of elderly patients with the surgical results, persistence of bothering symptoms, as well as the problem of polydrug use dictate the need to search for safe, effective, minimally invasive methods of surgical treatment of BPH [5].

Aim. To determine the surgical potential of holmium laser enucleation of the prostate (HoLEP) and the rate of postoperative complications during the learning curve.

Materials and methods. A randomized retrospective study of HoLEP in men with BPH was carried out. A total of 98 patients were undergone to HoLEP in the surgical department of the Clinical Hospital "Mother & Child", Ufa, during the period from January 2018 to May 2020. HoLEP was performed by a single surgeon with previous experience in transurethral procedures. The criteria for inclusion in the study group were as following: moderate-to-severe lower urinary tract symptoms, prostate volume > 40 cm^3, maximum flow rate (Qmax) <15 ml/sec, postvoid residual volume (PVR) > 50 ml. The exclusion criteria were inflammatory process in the lower urinary tract, genitourinary malignancy, previous urinary tract interventions.

In case of suspicion of prostate cancer, a multifocal prostate biopsy was done 4 weeks prior to HoLEP. Surgical treatment was performed using a Lumenis 100H holmium laser (Israel) with 12° optics and end-fire laser fiber 550 nm. For enucleation,

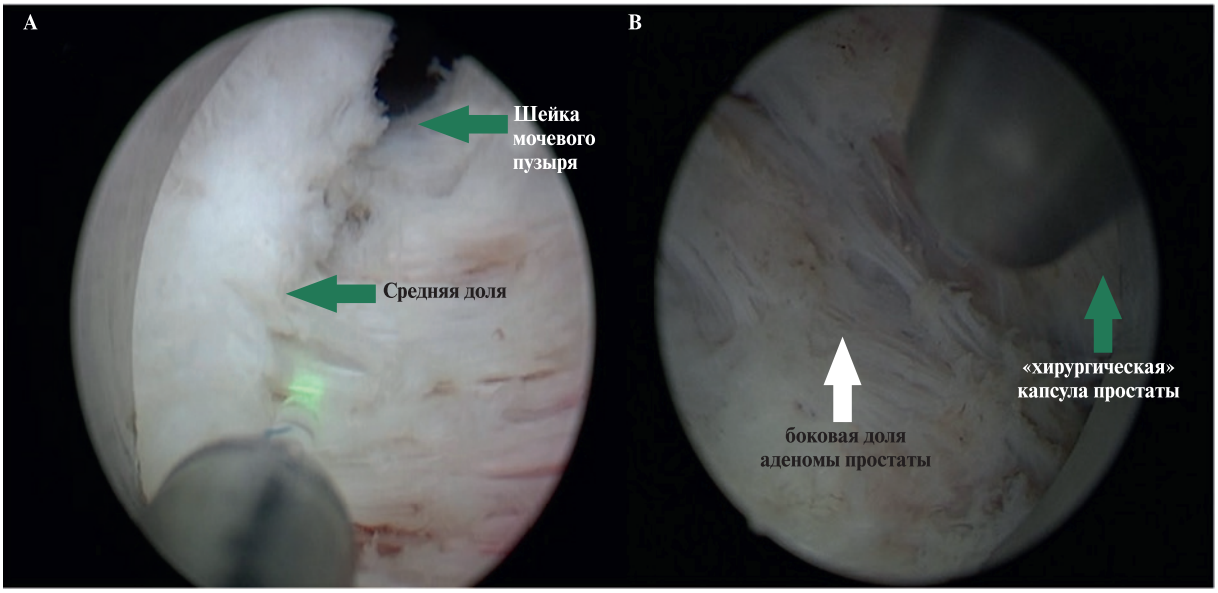

Fig 1. Stages of HoLEP: A — enucleation of the middle lobe of the prostate, B — enucleation of the lateral lobe of the prostate

energy level of 1.4 J with a frequency of 53 Hz was used, and in the coagulation mode, energy level was the same, while a frequency was reduced to 40 Hz. Tissue morcellation was performed using a Unidrive SIII SCB morcellator, a Drillcut-X II URO Karl Storz (Germany) morcellator handle, and a nephroscope 0° at 900–1200 rpm. In patients with a large "middle lobe", a "three-lobe" technique was used, while in other cases, a "two-lobe" technique was chosen (*figs 1, 2*).

The evaluated criteria included age, prostate size, International Prostate Symptom Score (IPSS) and quality of life (QoL) score, bladder diary, prostate-specific antigen (PSA), Qmax, total operative time, length of catheterization, complications according to the Clavien-Dindo classification, and length of stay. A histological examination of the adenomatous tissue was performed in all patients. Statistical analysis was carried out using Microsoft Office Excel, 2010, Statistica, 2010. Data are presented as M + m, where M is the arithmetic mean, and m is the statistical error of the arithmetic mean. Significance of differences was calculated using analysis of variance with T-test for dependent variables. Data were significant if $p<0.05$.

Results. All patients received drug therapy prior to HoLEP, including alpha-blocker and 5-alpha reductase inhibitors. Men receiving anticoagulants stopped them 7 days before procedure. Twenty-six patients underwent prostate biopsy prior to HoLEP due to PSA elevation above 4 ng/mL or abnormalities on transrectal ultrasound or digital rectal examination. Patient's age, prostate volume, IPSS and QoL score, bladder diary, PSA level, Qmax, PVR, the total operative time, duration of the catheterization and hospitalization were presented in the *Table 1.*

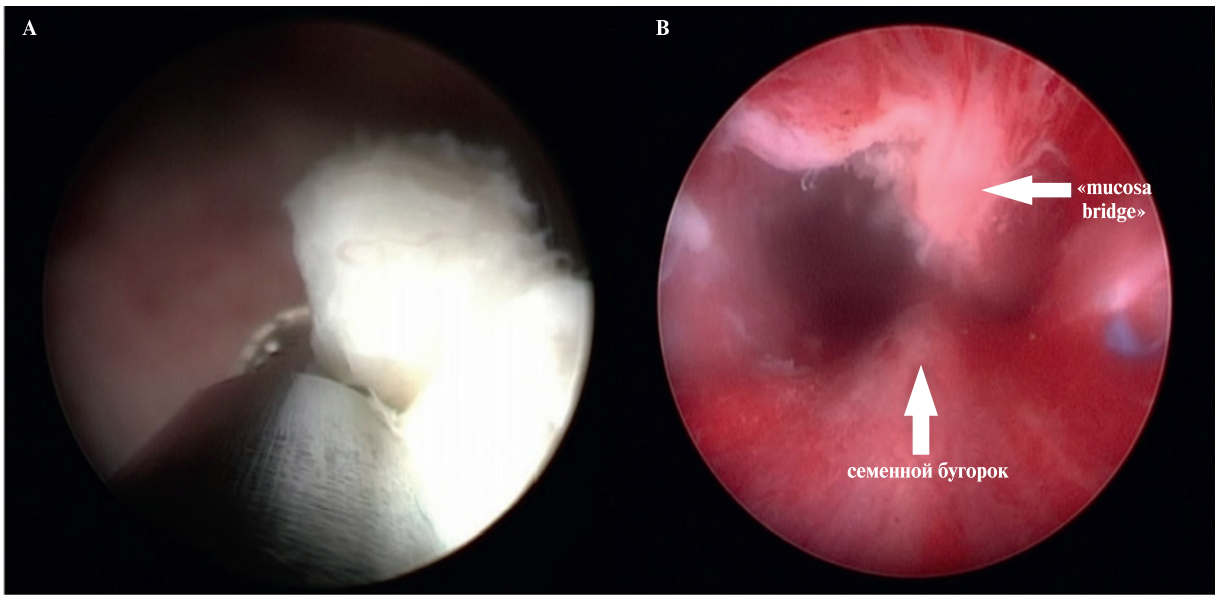

Fig 2. Stages of HoLEP: A — tissue morcellation, B — view of the external sphincter (the verumontanum and preserved "mucosal bridge" are presented on the figure)

Table 2

Characteristics of baseline and perioperative factors

Indicator	Value
Number, *n*	98
Age, years	64,6±8,3
Prostate volume, cm^3	61,9±20,4
Minimal prostate volume, cm^3	40
Maximum prostate volume, cm^3	150
PSA, ng/ml	2,9±1,9
IPSS score	21,6±1,6
QoL score	4,2±0,7
Residual volume, ml	105±54,5
Qmax, ml/s	5,2±1,8
Number of nocturia episodes	3,1±0,9
Operation time, min	98,3±47,04
Length of catheterization, days	2,2±0,8
Length of stay, days	3,6±0,7

Note. PSA - prostate-specific antigen, Qmax – maximum urine flow rate.

The operation time was measured from the insertion of the resectoscope into the urethra until the catheterization. After surgical treatment, the irrigation system was continued up the next morning. The urethral catheter was removed after normalization of urine color (to pink or yellow). Histological examination revealed two cases of incidental prostate cancer, which accounted for 2.1% and required further follow-up. When assessing the main outcomes, a significant association between the prostate size and operative time ($p<0.05$), as well as between the operation time and the duration of hospitalization ($p<0.05$) was found. In our study, the operation time increased due to intraoperative complications, including bladder perforation, trauma to the ureter orifice, severe intraoperative bleeding.

In-hospital complications occurred in 16 patients (16.3%). However, there were no complications ⩾IIIb grade, according to the Clavien–Dindo classification (*Table 2*).

Eleven patients had increased frequency and urgency in the first 2 days after catheter removal, which resolved spontaneously. In our opinion, these symptoms are associated to normal course of postoperative period and were not considered as complications. The most dangerous complications included injuries of the bladder wall and the ureteral orifices (31.25 and 18.75%, respectively, of the total number of complications that required repeated interventions). Injuries of the ureteral orifices occurred in patients with a large middle lobe and required ureteral stenting in the postoperative period. In all cases of ureteral stenting, bladder catheterization was prolonged for 3 days in order to reduce vesicoureteral reflux during urination. There were no typical complications for transurethral resection of the prostate (TURP), such as epididymo-orchitis. Injury to the bladder wall required a longer catheterization. In one patient, open revision with bladder suturing was required.

Clot retention was usually associated with unrecognized perforation of the bladder during morcellation of adenomatous tissue or bleeding from the bladder neck. Patients taking anticoagulants preoperatively have a greater risk of this complication. All patients with clot retention (n=5) in our study received anticoagulant therapy (total number was 28) and were switched to low-molecular-weight heparin. In one case, fresh frozen plasma was administered, but no blood transfusion was required.

Discussion. Currently, the "gold" standard for the treatment of BPH in patients with a prostate volume of 30 to 80 cm^3 remains TURP [6]. However, techniques for laser enucleation of the prostate, such as HoLEP, thulium laser enucleation of the prostate (ThuLEP), etc., are considered as an alternative not only to simple prostatectomy, but also to TURP [7, 8]. According to the results of numerous studies, endoscopic enucleation using holmium, thulium and "green" (GreenLight) lasers shows the best results [9]. In many publications it has been proved that HoLEP is characterized by the lowest rates of re-catheterization, acute urinary retention, inflammatory and infectious complications, stress urinary incontinence, and retrograde ejaculation [10]. Despite the its advantages, HoLEP is not currently routine procedure. The main reasons are the high cost of laser equipment, the need for morcellation, the technical complexity, and a long learning curve [11]. It is believed that minimal number of procedures to achieve the sufficient experience of the surgeon ranges between 30 and 50 [12]. In recent meta-analyses and clinical studies, it was confirmed that all techniques of endoscopic enucleation are quite highly effective and have similar intraoperative and postoperative results [14, 15].

It should be noted that in patients with a large middle lobe there is a high risk of injury to the ureter orifices. Due to the coagulation of vessels near the prostate capsule, the risk of intraoperative bleeding is significantly reduced. HoLEP has advantages over other surgical interventions in terms of blood loss, catheterization, and hospitalization time [15, 16] and is recommended for patients who cannot stop anticoagulant and antiplatelet therapy [17]. In our study, five patients had a clot retention, which required endoscopic evacuation. To reduce the likelihood of leaving residual tissue, careful examination of the prostate capsule for achieving hemostasis is required. Bladder injuries at the stage of morcellation occurred during the first 10 procedures. In our opinion, it is necessary to learn this manipulation as separate procedure. The possibility of histological examination of tissue after surgical treatment is

Table 2

Assessment of complications according to the Clavien–Dindo classification

Grade	Description	Number, *n*	Percentage of all complications, %
II	Acute urinary retention	3	18,75
	Prostatitis	3	18,75
IIIa	Bladder injury with clot retention requiring endoscopic evacuation	5	31,25
	Residual tissue requiring endoscopic resection	1	6,25
	Injury to the ureteral orifice requiring stenting	3	18,75
IIIb	Injury to the bladder wall requiring open revision	1	6,25

one of the necessary criteria in patients with BPH. The rate of incidental prostate cancer after BPH procedures ranges from 5 to 14% and requires careful preparation of patients of older age groups [18]. According to our results, prostate cancer was diagnosed in 2% of cases.

Conclusions. HoLEP is a reasonable alternative to TURP for surgical treatment of BPH and is considered a safe procedure for patients taking anticoagulant and antiplatelet drugs. Past experience of TURP allows to learn the technique faster and to reduce the number of complications.

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CASE REPORT

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OVERACTIVE BLADDER IN THE STRUCTURE OF SOMATIZATION DEPRESSION

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In everyday practice, urologists often encounter clinical manifestations of overactive bladder (OAB), without of organic or infectious disease. In such cases, OAB may appears in the structure of a somatization (more often depressive) disorder, and therefore an integrated psychosomatic approach to such patient management is becoming increasingly relevant. The importance of studying the topic is due to the high prevalence of OAB symptoms, its recurrent course, insufficient treatment efficiency, a significant decrease in the quality of life and working capacity of the socially active part of the adult population. Our clinical case illustrates the development of symptoms of OAB with massive «pseudo-urological» symptoms due to recurrent somatization depression in a woman of postmenopausal age.

K e y w o r d s: *overactive bladder, psychosomatics, somatization depression*

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Overactive bladder (OAB) is a syndrome manifested by urgency, increased frequency (more than 8 times a day) and/or nocturia, which can be accompanied with urge urinary incontinence [1]. The prevalence of OAB in the general population ranges from 11 to 16% among both men and women [2]. The current episode of depression was detected in almost a third of patients with OAB, and it is associated with more pronounced urinary disturbances than in the control group with negative impact on quality of life; 32% of patients with OAB had a history of depressive episodes [3]. N.Y. Siddiqui et al. (2018) in a series of 545 women found a significant association between the severity of urgency and urinary incontinence with the level of anxiety and depression [4]. According to IGR Melotti et al. (2018), the severity of OAB symptoms was directly related to the age of the patients, the severity of anxiety and depression [5]. T. Kawahara et al. (2021), using a screening questionnaire among 509 patients with OAB, found depression in 44% of men and women in approximately equal proportions. Considering the lack of a thorough understanding of the relationship between OAB and depression, the authors suggest an increase in sensations in the bladder as a result of biological changes both in the areas of the brain responsible for the affective sphere and in the neural pathways that regulate the process of urination, as a pathogenetic link [6]. According to J. Gross et al. (2021), the symptoms of OAB may have "descending" mechanisms due to sensitization, systemic inflammation, or mental disorders [7].

The following clinical case illustrates the development of OAB symptoms with massive "pseudo-urological" symptoms as part of recurrent somatic depression in an older woman.

Female M., 55 years old, is an accountant. Her youngest daughter (24 years old) is followed by a psychiatrist for depression. The patient was born in the Oryol region. She grew up as a quiet, uncommunicative, shy child and studied at school satisfactorily. Answering at the blackboard, she experienced anxiety because of everyone's attention, was afraid to make a mistake. In addition, she felt chills, sweating of the limbs, and discomfort in the stomach. Menarche was at the age of 13. After graduation, she went to a technical university with a low passing score. In the fourth year, due to the moving of her parents to Europe, the patient started living in a hostel, working as a cleaner. In the friend company, she often remained silent. After graduating from the institute, she moved to her in Moscow at the invitation of her sister. Under her patronage of her sister, she got a job in a bank. Her sister also introduced her to the future husband.

In family life, the patient was flexible, compliant. At 23, she had a pregnancy with toxicosis in the first trimester and the threat of miscarriage. She had premature, complicated birth. For the first time, her mood steadily decreased, sleep was disturbed, and appetite disappeared. Having read in the newspaper about the stolen child, she was afraid to leave the stroller with the child unattended. Six months later, the mood leveled off, anxiety was improved. She was on maternity leave for 2.5 years, after which returned to work in a bank.

At the age of 25, with increased workload, her mood again steadily decreased. She bothered from depression, tearfulness, weakness, and lethargy. Other manifestations included decreased appetite, which results in weight loss of 8 kg in 2 weeks, decreased concentration of attention and bad memory. She made mistakes in documents, which caused dissatisfaction of her supervisor. There was a pressing pain in the hypochondrium, which was improved as the mood returned to normal after 3 months, when she visited her parents

at vacation for two weeks. At 31, she gave birth to her second child. Pregnancy and childbirth were without complications.

At the age of 34, due to industrial stress, mood again sharply decreased, sleep and appetite were disturbed. The patient began to feel a progressive asymmetry of the face despite the absence of any objective changes. She felt hoarseness (up to complete loss) of the voice, numbness of the arms and legs, a "lump" in the left hypochondrium, from which the pain irradiate to other internal organs. During consultation with a neurologist, impaired superficial sensitivity in hands and feet was revealed. She visited specialists of various profiles, underwent expensive examinations, but the reasons for these symptoms were not identified. She changed her work to more relaxed one, getting a position of an accountant in a flower shop. New job contributes to an improvement of the condition, and previously bothering complaints were resolved.

At the age of 42, during the next persistent decline in mood, neurodermatitis was diagnosed. There was a connection of skin manifestations with an increase in the workload. She had transient widespread pruritus.

Within six months, the symptoms completely resolved. From the age of 42 to 52, she suffered several episodes of low mood lasting up to several months. Deterioration of well-being occurred both autochthonously and with increased professional loads or other stress factors. At the age of 47, she fired from her last permanent job due to health reasons, after which she worked part-time as a cleaner, working by appointment.

At the age of 52, when, family conflicts and a serious illness of her father occurred, she was in a persistently decreased mood, felt a pressing pain in the left hypochondrium, as well as had problems with urination. She began to notice the impossibility of complete bladder emptying. The patient noted an urgent need to "urinate" until she felt completely emptied. In addition, there were "false" urge to urinate, which became more frequent and severe in stressful situations. Within six months, she had an "exacerbation" and worsening of symptoms. She also started feeling of "pressure" in the bladder area.

The patient visited various urologists many times due to persistent discomfort in the bladder area, frequent episodes of urgency. Although she repeatedly underwent examinations, there were no abnormalities in the urinary system, explaining the condition. Antibiotics were recommended. Every 2-3 months she experienced exacerbation of symptoms, which she partially resolved by taking antibiotics without prescriptions.

In June 2021 (aged 55), a menopause occurred. The clinical manifestations included hot flashes, followed by chills, the feeling of “pressure” in the bladder area became more pronounced, number of urgency episodes increased and blood pressure rarely elevated up to 150/100 mm Hg. The woman was consulted by a gynecologist. A diagnosis of uterine fibroids, which did not require surgical treatment, and menopausal syndrome was made; hormone replacement therapy was prescribed (femoston conti). In the same period, the patient's depressive mood exacerbated, sleep disturbances developed. She began to notice a decrease in concentration, memory impairment, and became more distracted. She was weary of communication and narrowed her circle of communication. On the recommendation of one of the doctors (urologist), every other day she performed bladder catheterization due to incomplete emptying. She felt a change in symptoms, since rare urge urinary incontinence developed (she did not have time to find a toilet). The woman had thoughts about unwillingness to live, but she didn’t have specific suicidal intentions. She first visited a psychiatrist on the urgent recommendation of urologists.

Urological status. The woman complaints about increase frequency, including “false” urge to urinate, mainly disturbing at night with up to 3-4 episodes of nocturia; episodic urge urinary incontinence, difficulty starting urination, feeling of incomplete bladder emptying, two-staged urination, recurrent urinary tract infection (UTI).

History: for the past 2 years, she noted periodic pain when urinating (in some urine tests, UTI was confirmed). Repeated courses of antibiotics had modest effect, as well as an incomplete course of Uro-Vaxom.

On examination, she had satisfactory condition, was in active position with clear consciousness. During a pelvic exam it was found that the urethra was located in a typical place, and there was no vaginal vault prolapse. Deep tendon, anal and bulbocavernosus reflexes were preserved. Urine leakage during the cough test was not observed. Urine tests revealed no abnormalities. According to bacteriological examination of urine, E. coli in a concentration of 102 was isolated. Ultrasound study of kidneys demonstrated no pathological changes; postvoid residual volume was from 110 to 178 ml. Uroflowmetry showed normal type of curve, with a volume of urine excreted of 240 ml, the maximum urine flow rate of 25 ml/s, the urination time of 19 s. There were no signs of obstructive urination.

Urodynamic study revealed phase detrusor hyperactivity (provoked), normal detrusor contractility, absence of signs of bladder outlet obstruction and detrusor sphincter dyssynergia. On MRI of the lumbosacral spine, signs of static disturbance, dextroscoliosis, osteochondrosis of stage 1-3, in L4-5 and L5-S1, spondylarthrosis of the lumbosacral spine and right lateral spondylolisthesis at the level L4 were found.

Cystoscopy: bladder capacity was 250 ml. The slit-shaped ureteral orifices are located typically on the ridges, rhythmically contracting. The mucosa of the bladder neck was somewhat hyperemic, loose, no pathological lesions were detected.

Contrast-enhanced computed tomography showed that the urinary bladder had round shape, sufficiently filled, measuring 75x93x85 mm, with thin walls and smooth contours. The pelvis fat was without abnormalities. There was no regional lymphadenopathy.

Conclusion: the results of the clinical examination suggest neuromuscular bladder dysfunction, unclassified in other rubrics, in combination with somatoform disorders. Recommendations included biofeedback therapy and psychiatric consultation followed by therapy.

Psychosomatic status: the patient looked appropriate for her age, had normosthenic body. She was dressed casually. Her hair was clean, combed, she didn’t use decorative cosmetics. She looked outwardly tense. The facial expression was disturbing. Her complains included discomfort in the form of painful tension and pressure in the left hypochondrium and lower abdomen, frequent daily, including "false", urges to urinate, nocturia (up to 3-4 episodes), a feeling of incomplete bladder emptying, which made her to return to the toilet 2-3 times. Occasionally she noted urge urinary incontinence.

The woman noted persistently reduced mood with situational fluctuations, lethargy, apathy. At the same time, she experienced anxiety, which might progress to feeling of a lump in the throat, weakness in the upper and lower extremities, hoarseness or complete loss of voice, which was why she was not able to answer calls. Before going to bed, she scrolls thoughts about the future of gloomy content. Sleep was disturbed due to nocturnal and early awakenings. Appetite and libido were severely decreased. A woman was fixed on urological symptoms and the results of numerous examinations in order to determine

their cause. Not having received a specific diagnosis at the next visit to the doctor, she felt despair. The patient thought about leaving life as getting rid of bodily and mental suffering, but didn't not show any tendency to implement suicidal ideas. Due to frequent urges, she was not able to work full-time.

The woman treats her condition with criticism, admits a possible psychosomatic disorder. She agreed for examination and treatment by a psychiatrist.

Clinical review. Psychosomatic status was determined by prolonged somatization depression at menopausal age in an avoidant (cluster C) personality with neuropathic somatoperceptual accentuation in the absence of organic bladder pathology. Somatic symptoms of depression (including in the bladder area) were represented by conversions, hysterical algia, bodily fantasies, functional dysuria and aphonia (dissociative disorders). Vital manifestations included early and moderate insomnia, decreased appetite and libido. Among the symptoms of depression, disturbing fears associated with the suggested bladder dysfunction, the possibility of progression of the urological disease and failed treatment, along with exaggerated hypochondriacal fixation, and the desire for a diagnostic search were predominated.

The dynamics of the current depressive episode is typical for older patients. The history includes repeated depressive episodes with anxiety-hypochondriac, dissociative and somatic symptoms. The affective nature of the mental disorder is additionally proved by a family history (depression in the daughter), personal and somatopsychic accentuation, as well as the absence of negative personality changes.

A diagnosis of recurrent depressive disorder with a prolonged depressive episode of a moderate degree with somatic symptoms predominant in the urological sphere (like an OAB) was made.

After outpatient administration of paroxetine, nausea and vomiting developed. The therapeutic response was obtained on the following scheme: trazodone 150 mg/day, tiapride 50 mg/day. In addition, cognitive-behavioral therapy was used. Within a month, the condition improved significantly: mood, sleep and appetite improved, polymorphic anxious physical symptoms resolved, as well as pathological sensations in the form of painful tension and pressure in the left hypochondrium and lower abdomen, frequent episodes of urgency with a feeling of incomplete bladder emptying didn't bother anymore, urge episodes of urinary incontinence completely disappeared. Within 2 months, there were fears of the recurrence of typical urological symptoms ("anxiety of anticipation") with excessive emphasis on the urination. The patient returned to a normal lifestyle and got a permanent job in her specialty.

This clinical case is consistent with the results of a number of modern publications indicating a close relationship between depression, high levels of anxiety and stress and the severity of urination disorders. A comprehensive interdisciplinary approach in the current and similar cases contributes to adequate referral, reducing the burden for healthcare, providing effective treatment and improving the quality of life in patients with OAB symptoms.

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LITERATURE REVIEWS

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MALE REPRODUCTIVE HEALTH AND COVID-19

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The SARS-CoV-2 pandemic has brought serious economic and social problems worldwide`. Due to its medical consequences, it is of importance to study the mechanisms of the disease and new therapeutic interventions, as well as rehabilitation processes. Despite the fact that the genome of the new coronavirus has been sequenced and studied, clinical and epidemiological data are constantly updated and analyzed, and exact pathogenesis has not yet been understood. At the same time, domestic and foreign studies suggest that the virus is an agent that affects not only the lungs, vascular wall, hemostasis, but also the reproductive system. The aim of the review is to summarize the current knowledge about novel SARS-CoV-2, including its pathophysiology and potential impact on male reproductive function.

K e y w o r d s: *reproduction, men's health, SARS-CoV-2, COVID-19, oxidative stress, spermatogenesis, antioxidants*

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Of all the physiological systems of the body, the reproductive system of men is the most important and least studied in terms of adaptive responses (WHO, 2010). Infertility in marriage is one of the serious and complex medical, as well as socio-demographic problems [1-4]. Over the past 20 years, there has been a persistent trend towards an increase in the proportion of male factor in infertile couples from 30 to 50% [5, 6].

The causes of reproductive disorders in men are very diverse, including varicocele, diabetes mellitus, decreased function of testis, pituitary gland and hypothalamus; congenital anomalies or disorders resulting from injuries, surgeries or inflammation; occupational hazards and certainly viruses and infections.

The outbreak of the COVID-19, caused by the SARS-CoV-2, has posed a serious threat to public safety, and its rapid spread has caused a global health emergency [1, 7]. The World Health Organization (WHO) has classified COVID-19 as a pandemic of a new coronavirus infection, which has changed the usual work of healthcare systems in countries that have faced this problem, including the andrologists [8, 9]. The aim of the review is to summarize the current knowledge about novel SARS-CoV-2, including its pathophysiology and potential impact on male reproductive function.

An in-depth analysis of foreign and domestic publications using the Scopus, Web of Science, eLIBRARY, PubMed, Wiley Online Library, EMBASE, Google Scholar, and Research Gate databases was carried out. The search included original articles, reviews, guidelines, letters to the editor, guidelines comments, and editorials regarding the impact of the SARS-CoV-2 on the male reproductive system. The study was reviewed and approved at a meeting of the Biomedical Ethics Committee at the Research Center for Family Health and Human Reproduction (extract from the meeting No. 2/1 dated February 18, 2020).

The reproductive health of a man is a very delicate area that does not deserve a dismissive, superficial attitude. The infectious and inflammatory process in the reproductive tract can have a negative effect on the germinal epithelium, disrupt the secretion of the male sex hormones, change the composition and rheological properties of the seminal fluid, affect the blood-testis barrier and lead to the formation of antisperm antibodies and sclerosis in the tissues where spermatozoa are formed and transported [4, 10]. Along with this, inflammation in the mucosa of genital tract, induced by infectious agents, activates the generation of reactive oxygen species (ROS) by leukocytes with the further development of oxidative stress [10]. More than 25 viruses can enter the ejaculate and adversely affect male fertility, such as human immunodeficiency virus, hepatitis B and C, human papillomavirus, herpes, mumps, Epstein-Barr virus, EBOLA, and probably many others. They cause viral orchitis, male germ cells apoptosis, disturbances in spermatogenesis, a decrease in the number and motility of spermatozoa, changes in hormonal levels, inflammation and destruction of germ cells with concomitant development of infertility and tumors. In this regard, many questions arise regarding the impact of a new coronavirus infection on spermatogenesis.

Published data suggest a much higher than expected prevalence of SARS-CoV-2 with severe consequences in men in various parts of the world [11–13]. In addition, men are not only more susceptible to SARS-CoV-2 compared to women, at least in Western countries, but also have a higher mortality rate associated with COVID-19 [14]. Hormonal levels may play a profound pathophysiological role in the pathogenesis of SARS-CoV-2, as endogenous testosterone (Ts) contributes to development of more serious complications associated with SARS-CoV-2. Moreover, decreased androgen reserve and hypogonadism are associated with a serious or even fatal course of the disease [15–17].

A significant increase in the level of luteinizing hormone (LH) and a concomitant decrease in the ratio of total testosterone to luteinizing hormone (Ts/LH) in the serum of men with COVID-19 was shown, which points to the early stage of hypogonadism [16]. Therefore, special attention should be paid to the hormonal levels in men recovering from COVID-19, as well as to the study of possible long-term consequences of SARS-CoV-2.

Studies show that angiotensin-converting enzyme-2 (ACE2), as the main cellular receptor for the SARS-CoV-2, may be a mechanism for invading the male reproductive organs [18, 19]. ACE2 is highly expressed not only in the airway mucosa and alveolar epithelial cells, but also in renal tubule cells, testicular Leydig cells, and seminiferous tubule cells, and ensures the formation of tight junctions between spermatogenic epithelial cells [20, 21]. Strong influence of ACE2 receptors on the male reproductive tract is proved by the fact that infertile men with severe impairment of spermatogenesis have lower levels of ACE2 compared to fertile subjects. Definitely, ACE2 is recognized as a physiological modulator of the male reproductive system, which plays a regulatory role in steroidogenesis and affects germ cells [22, 23]. It has been suggested that the distribution of these receptors in testicular tissue depends on age and decreases with time, and therefore it is assumed that SARS-CoV-2 may cause long-term consequences with impairment of reproductive function in young men and adolescents [24, 25].

Researchers found that some males with COVID-19 had impaired renal function [26, 27]. This fact, as well as the detection of SARS-CoV-2 in the semen, indicate that the virus can affect the male reproductive system [28, 29].

When analyzing the sperm quality in men with mild to moderate COVID-19, who recover from the disease, lymphocytic inflammation and a decrease in the level of germ cells up to oligospermia was noted [30]. Fever due to infection disrupts the blood-testis barrier and promotes the penetration of macromolecular substances into the testicles; therefore, some parameters such as sperm concentration and motility may decrease within 72–90 days after infection [27, 31]. A high inflammatory response with fever, activation of the immune cells, and inflammatory mediators such as interferons and cytokines inhibiting steroidogenesis and spermatogenesis have a negative impact on the reproductive system [31-34].

Histological examination of testicular samples from men who died from COVID-19 revealed thinning of the seminal epithelium (decrease in the number of cell layers) and massive destruction of spermatozoa in the seminiferous tubules. Also, in all specimens the signs of inflammation of the testicles (orchitis) and epididymis (epididymitis) were seen [35].

Inflammatory response during COVID-19 infection is accompanied by increased production of pro-inflammatory cytokines and chemokines in the serum. As the cytokine release syndrome develops, disturbances in coagulation, immune system functions, and oxidative stress all cause mitochondrial dysfunction [36–38]. Increased formation of ROS and inhibition of antioxidant defense are crucial for viral replication and subsequent disorders [37]. In the presence of a SARS-CoV-2, mitochondria, as well as activated phagocytes, neutrophils, monocytes, and macrophages, actively generate free radicals [36, 38]. Along with high levels of ROS, there is an increase in nitric oxide production and accumulation of nitroguanidine [36]. An important factor that enhances oxidative stress reactions in SARS-CoV-2 is a disturbance of the antioxidant defense system. An association has been found between decreased expression of the antioxidant enzyme superoxide dismutase in lungs of patients with COVID-19 and disease severity [39]. Reduced glutathione levels seem to be lower in men than in women, which may also be the reason why formers are more susceptible to COVID-19, its severe course and complications [40]. Experimental studies have shown that a sufficient level of ACE2 prevents the formation of ROS [29, 36].

The presented data support the hypothesis that in patients with severe symptoms, a high viral load can reach the threshold for crossing the blood-testis barrier. It is clear that COVID-19 may be more likely to affect the reproductive tract in patients with more severe disease, however, the clinical studies have demonstrated that SARS-CoV-2 can be present in the male genital tract at a relatively early stage, within about 2 weeks. It should also be considered that in the first months of the pandemic, patients, including men, receive very aggressive treatment (cytostatics, hydroxychloroquine and other drugs), so whether the abnormalities in sperm analysis are associated with the SARS-CoV-2 or with the therapy is quite controversial.

As treatment regimens are changing and becoming less aggressive, it is necessary to carry out the comparative analysis during the first six months and later for the studying the effect of therapy on sperm production. The process of spermatogenesis lasts 72–74 days, and in order to understand how and what is affected, long-term follow-up is needed.

Currently, there are also insufficient evidences that SARS-CoV-2 persists in the male genital tract after recovery, suggesting that the testes cannot be a reservoir for virus and the risk of sexual transmission of SARS-CoV-2 is low. However, some researchers do not exclude this possibility [13, 16]. As a consequence, the potential impact of SARS-CoV-2 on male fertility remains poorly understood. The results of the clinical studies are very contradictory. Expression of ACE2 in male reproductive organs suggests possible damage to the testicles during infection, accompanied by local and/or systemic inflammation, which, due to the activation of ROS and increased cell membrane permeability, can contribute to the penetration of a virus at high concentrations through the blood-testis barrier.

Accumulation of scientific data is needed to fill a gap in current knowledge on this issue, which could have serious consequences to the millions of men. It is extremely important to elucidate the mechanisms of damage to the urogenital tract and their association with cytokine storm, oxidative stress, and other factors.

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LECTURES

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URINARY INCONTINENCE IN WOMEN AND ITS IMPACT ON QUALITY OF LIFE

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The prevalence of urinary incontinence at a young age is 20-30%, gradually increasing to 40% among older women. Urinary incontinence affects many areas of the patient's life, including social, psychological, work, sexual, etc. The main causative factors, which also influence on its severity, include age, pregnancy, childbirth and obesity.
To date, there are many treatment methods for stress urinary incontinence. However, more preference is given to the sling procedures, in which mesh is placed under the middle part of the urethra. Despite being the "gold" standard for the treatment of stress urinary incontinence, it is difficult to determine indications for surgical treatment, since "non-medical" view of the patient's problem is often required.
The low awareness of primary care physicians about the possibilities of treating urinary incontinence often leads to an erroneous opinion in patients about their disease and methods of treatment. Many patients regard this condition as an integral part of aging, avoid situations in which urinary incontinence is possible, which limits daily activities, sexual activity, sports and other areas of life.
Based on the latest data, a review of the literature on urinary incontinence in women, risk factors, as well as existing methods of surgical correction are presented in the lecture. Particular attention is paid to the impact of urinary incontinence on the quality of life of patients and current methods for its assessment.

Key words: *urinary incontinence in women, quality of life, suburethral slings, risk factors for urinary incontinence*

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There are three main types of urinary incontinence: (1) stress urinary incontinence resulting from increased intra-abdominal pressure; (2) urge incontinence associated with an urgent desire to urinate; (3) mixed, representing a combination of the first two types. According to current literature, the prevalence of urinary incontinence in women ranges from 5.2 to 36% [1-4].

However, it is difficult to estimate the true prevalence of urinary incontinence, since many patients do not seek medical help because of embarrassment, misperception of their condition, as well as an ignorance of the possibilities and treatment methods. The duration of the disease at the moment of first admission is often years and even decades. Patients usually consider involuntary loss of urine as a normal part of life and do not perceive it as a problem. Therefore, urinary incontinence requires active detection by clinicians, including primary care professionals, through interviewing.

The prevalence of urinary incontinence increases with age. According to the National Health and Nutrition Examination Survey (NHANES), prevalence of urinary incontinence in women aged 20 to 39, who visit a doctor, is 6.9%, compared to 17.2% and 23.3% in those of age 40 to 59 and 60-79 years old, respectively. In the age group over 80 years, 31.7% of patients reported involuntary loss of urine ($p<0.001$) [5]. An increase in life expectancy is believed to result in raising the number of patients with urinary incontinence.

Despite the multifactorial nature of this condition, traumatic childbirth is one of the most significant risk factors; in most cases, a stress urinary incontinence develops [6]. Compared with caesarean section, vaginal delivery is associated with increased risk of stress urinary incontinence by almost 2 times [7].

Other risk factors include being overweight and obese. In was estimated that during the period from 2011 to 2014, 38.6% of the female population in USA was obese [8]. In Louisiana, 69% of residents were found to be overweight or obese in 2016 [9]. Among Russians, these values are not so high. A study carried out by Rosstat in 2018 showed that 24.5% of women had some degree of obesity, and 34.7% were overweight. Only 38.1% of Russian women had weight in normal range [10]. Subak et al. showed the association of urinary incontinence with obesity. An increase in body mass index by 5 raises the risk of stress urinary incontinence by 20–70% [11]. A meta-analysis confirmed the role of obesity as risk factor for failed treatment of stress urinary incontinence using suburethral slings [12].

Treatment of stress urinary incontinence should include lifestyle interventions to prevent or decrease an influence of risk factors.

Urinary incontinence and sports

Given the many facets of the causes of incontinence, Hagovska et al. assessed the risk of developing urinary incontinence depending on the sport. The analysis of 10 types of sports activities was carried out, including athletics, fitness, basketball, volleyball, football, handball, tennis, indoor bandy (floorball), skating and dancing. The highest prevalence of urinary incontinence was found among patients who were involved in athletics (23.8%), followed by volleyball (19.6%). The "safest" types of sport were skating and hockey in the hall, since the risk of development of stress urinary incontinence was 0.

The authors suggest that the prevalence of urinary incontinence depends on jumping during exercise [13]. A negative effect on the pelvic floor is exerted by constantly increased intra-abdominal pressure that occurs during high-intensity exercise. The muscles and ligaments are gradually stretched, leading to irreversible deformation [14].

A study of Elks et al. also showed a greater prevalence and severity of symptoms in patients who were engaged in CrossFit, compared with women who did not train [15]. Although urinary incontinence can be severe, only a small number of patients seek medical help [16].

Successful primary prevention of urinary incontinence has positive outcomes in high-risk women. In case of inefficiency of preventive measures and the development of incontinence, behavioral and conservative therapy may be recommended. Women who persist with symptoms of stress urinary incontinence despite conservative treatment may be candidates for surgical treatment. Suburethral sling is an effective method for treatment of stress urinary incontinence. In a large systematic review and meta-analysis, objective cure rates ranged from 62% to 98% for transobturator slings and from 71% to 97% for retropubic slings [17]. At the same time, in foreign literature, this intervention is described as a “30-minute outpatient procedure” [18].

The quality of life

Traditionally, biomedical results are the final stage in medical research, but over the past decade, more and more work has appeared on the quality of life (QoL).

Despite the importance of QoL for health and medicine, there is an ongoing conceptual and methodological discussion about what it is and how it can be measured. WHO defines QoL as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. The quality of life is determined by the physical, social and emotional factors of a person's life that are important to him and affect him.

Usually, the assessment of the QoL is carried out using special questionnaires, among which there are “general”, allowing to understand the level of well-being, as well as “disease-specific”, questions in which are aimed at a more thorough understanding of each individual nosology and its impact on the QoL. Disease-specific questionnaires allow to understand not the severity of the disease, but its impact on a particular patient, the patient's attitude to the disease and the medical care provided to him.

Patient-reported outcomes provide an objective assessment of symptoms that can help determine treatment goals and success. Several questionnaires have been developed over the years, but none of them has been validated to measure all possible outcomes associated with urinary incontinence, and none of the proposed questionnaires is used universally to assess QoL [19].

A clinician's understanding of a patient's QoL can have a positive impact on symptom improvement, care and rehabilitation. It is also important to determine the range of concomitant problems, which can affect the treatment or show the inefficiency of some methods on individual basis. In addition, an insufficient assessment of the QoL can adversely affect the outcomes and contribute to the persistence of complaints after therapy [20]. It has been established that QoL is a strong predictor of survival, therefore it is necessary to study this factor in clinical trials [21].

The studies dedicated to the QoL have been carried out worldwide, with the largest number of articles published in the United States, followed by China and European countries. Fewer publications have been prepared on the African continent. This trend indicates that such an analysis is more typical for developed countries [5]. Shek explained this feature by socio-economic and political circumstances in combination with cultural and philosophical features [22].

Despite the high prevalence of urinary incontinence among women, its effect on QoL is not studied well. QoL is multifaceted and may include satisfaction with financial condition, intimate relationships, family life, well-being, work and leisure, and physical health. Stress urinary incontinence affects all of these domains, but for some patients, even one parameter can have a significant influence on daily life, leading to a decrease in QoL.

In a study by Krhut et al. there was no correlation between the severity of urinary incontinence and QoL [23]. A total of 391 women with urinary incontinence were interviewed. The severity of symptoms was assessed by weighing pads at the end of the day. The average urine loss was 74.8 ml $\pm$ 219.72 ml. Patients also completed the International Consultation on Incontinence questionnaire Short Form (ICIQ-SF), and the King’s Health questionnaire (KHQ) for assessing QoL. The authors highlighted the need for adequate evaluation and treatment of patients with any degree of urinary incontinence.

In another study by Sawaqed et al., 200 Jordanian women with urinary incontinence were interviewed, among whom 47% reported mild incontinence, 37% reported moderate incontinence, while 16% of the respondents reported severe incontinence. The severity of symptoms was not objectified. It is worth noting that in Jordan there is a lower rate of seeking medical help among women with urinary incontinence, as they are embarrassed to talk about the problem or believe that this condition is incurable [24]. Respondents were asked to note how strongly urinary incontinence affects the listed activities: prayer, household chores, social activities, recreational activities, the ability to travel by car. In addition, the degree of nervousness and disappointment due to their condition was considered. According to results, in the majority of the participants, urinary incontinence had a pronounced negative impact on the performance of prayer (31.2%), which in a country where the main population is Muslim, strongly affects the practice of religious rites.

In 2015, P. Abrams et al. published an article on the impact of urinary incontinence on QoL. Their study included 1203 patients aged 45 to 60 years and showed a positive correlation between the severity of incontinence and its impact on various daily tasks. A distinct feature of this work is the young age of the participants, whose life activity is associated with intensive work, family and social affairs. In addition, the results showed that urinary incontinence is caused by feelings of humiliation and stigmatization [25].

Like any chronic disease, urinary incontinence has an impact on the psycho-emotional state of a woman. The pathogenesis can be represented as following. A psycho-traumatic factor (stress due to constant urine leakage) of varying severity, combined with the psychosexual characteristics of each individual woman, causes psycho-neurological symptoms, which in most cases is of psychosomatic type. It is not difficult to imagine that urinary incontinence causes frequent conflicts in relationships and families, tension in society, and as a result, gradually leads to the

social isolation of women, the consequence of which is physical isolation from society.

Thus, the assessment of the quality of life can be considered a highly informative, reliable, sensitive and cost-efficient tool for examining of patients with urinary incontinence. Determination of QoL plays an important role in quality control of care and evaluation of the efficiency of new organizational and medical treatment methods.

There are no articles, published in Russian, devoted to the QoL of women with urinary incontinence. This problem doesn't have enough attention. The lack of methods and criteria for assessing the impact of incontinence makes it difficult to choose an appropriate surgical treatment.

Urinary incontinence remains an urgent problem in modern clinical practice. The risk factors for incontinence are well understood, which allows to begin prophylaxis before symptoms develop. However, there are also non-modifiable risk factors, such as age and the onset of menopause. Being a non-life-threatening condition, however, incontinence negatively affects daily life, professional activities, intimate relationships, which has an impact on the QoL. Insufficient awareness of primary care specialists precludes a formation of the correct knowledge, as well as a ensuring of specialized care. The lack of information available to patients in Russian-language sources leads to an erroneous perception of their disease.

Urinary incontinence is associated with a sense of shame, fear, embarrassment, which leads to negative consequences for self-esteem and, as a result, disturbances in personal, sexual and social life. To date, specialists dealing with urinary incontinence do not have a universal tool for choosing surgical treatment. It is difficult to overestimate the role of psychologists for patients with urinary incontinence. "Non-medical" consultation can be a predetermining factor regarding surgical treatment, since it allows to form the correct expectations of the patient and to have greater satisfaction after treatment.

Knowledge about QoL is important for understanding the consequences of the disease and its treatment. For clinical trials, QoL evaluation is as important parameter as medical outcomes. The terms "quality of life" and "health" are often used in the literature as identical, but they have different meanings.

Urinary incontinence is a major concern for women. Treatment should begin with a discussion of current methods, including their benefits, risks, and complications. Currently, the evaluation of the QoL has become an integral part of determining the impaction of the disease, which is important for the efficient treatment. For women with urinary incontinence, multidisciplinary care, including counseling not only by medical providers, but also by psychologists, is of importance.

The growth of requirements and expectations from medical care at all stages makes it obligatory to consider the preferences of the patient when evaluating complaints and choosing a treatment method. As a result, the decision on surgical procedures should be made in coordination with other specialists, if necessary, with the involvement of a psychologist. In addition, to provide objective assessment of complaints, the special questionnaires should be developed.

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