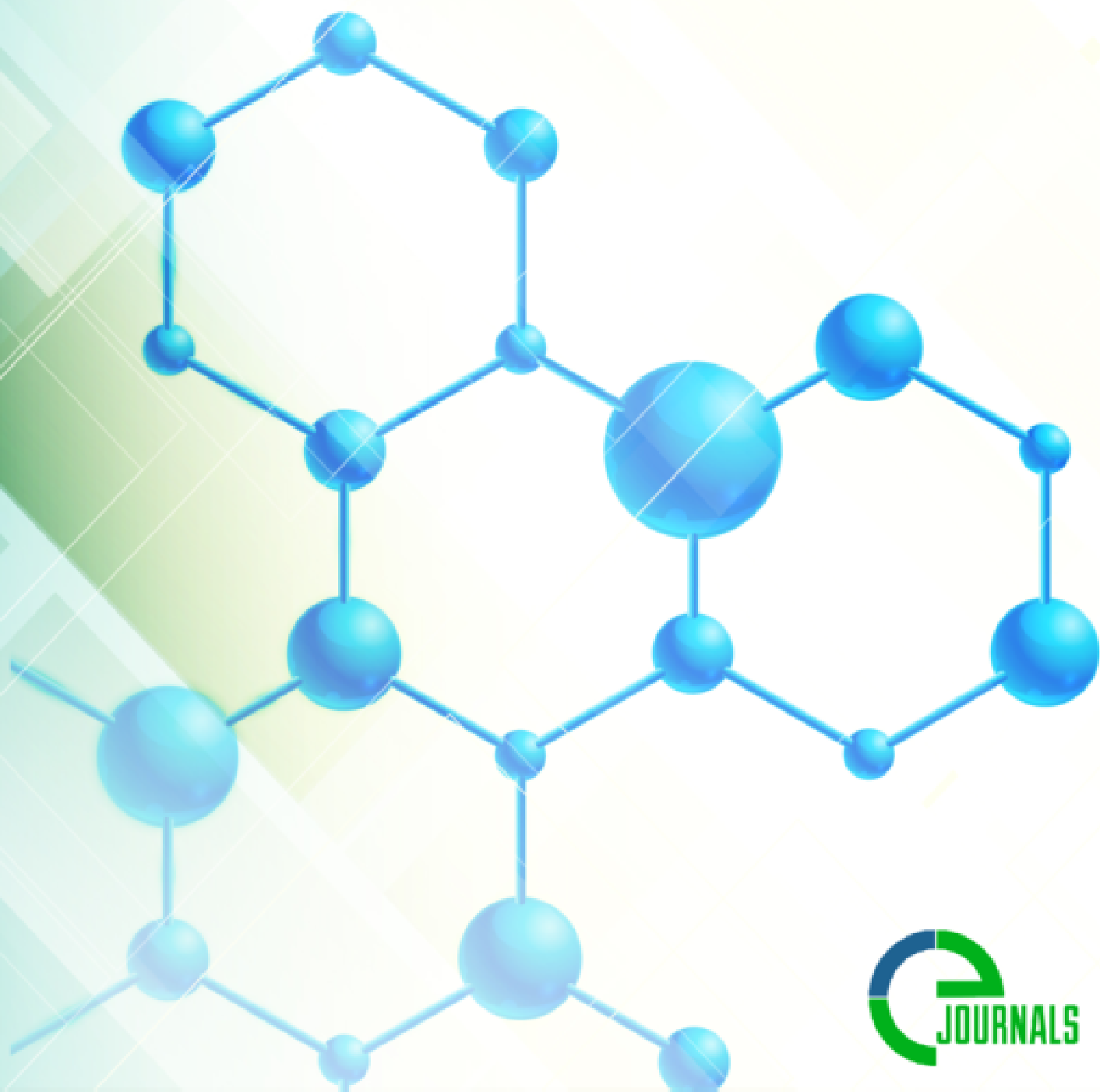


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BENIGN PROSTATIC HYPERPLASIA - MINIMALLY INVASIVE SURGICAL TREATMENT OPTIONS

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Abstract: Nowadays, the field of surgical treatment of benign prostatic hyperplasia (BPH) is flourishing - new minimally invasive methods are being improved and new ones are being developed. An article represents the main methods of endoscopic enucleation of the prostate and provides a brief comparative analysis of the effectiveness of endoscopic techniques for enucleation of the prostate. Attention is paid to the methods of minimally invasive surgical technologies in the treatment of patients with BPH.

Key words: endoscopic enucleation, prostatic hyperplasia, endoscopic enucleation of the prostate, minimally invasive surgical technologies.

Аннотация: В настоящее время сфера хирургического лечения доброкачественной гиперплазии предстательной железы (ДГПЖ) переживает расцвет - совершенствуются и появляются новые малоинвазивные методы. В статье представлены основные методы эндоскопической энуклеации простаты, проведен краткий сравнительный анализ эффективности эндоскопических методик энуклеации простаты. Уделено внимание методикам минимально инвазивных хирургических технологий в лечении пациентов с ДГПЖ.

Ключевые слова: эндоскопическая энуклеация, гиперплазия предстательной железы, эндоскопическая энуклеация простаты, минимально инвазивные хирургические технологии.

Introduction. Benign prostatic hyperplasia (BPH) is a common condition encountered in aging men and a common cause of lower urinary tract symptoms (LUTS), impairing males' quality of life. Histological prevalence is common, and disease progression is associated with bladder outlet obstruction (BOO). This may present clinically in both the emergency surgical and outpatient clinical settings. BPH is not life-threatening, but progressive disease [1, 2]. Prevalence of BPH appears to increase with age, as approximately 80% of men are affected by LUTS due to BPH at age 70. In most males, if living long enough, will develop some histologic features consistent with BPH in their lifetime [3, 4, 5].

European Association of Urology (EAU) guidelines for the treatment of non-neurogenic lower urinary tract symptoms caused by BPH presented in 2016, introduced the concept of endoscopic enucleation of the prostate (EEP) [6].

Methods: A literature review was performed in the PubMed, Science Direct, Scopus, Google scholar using the keywords: BPH, surgical treatment, endoscopic enucleation of the prostate, minimally invasive surgical technologies.

Results. In general, however, speaking of anatomical enucleation, we imply the removal of adenomas along the false capsule. Endoscopic enucleation can be carried out using both laser energy (laser methods) and electrical energy (non-laser methods). Existing EEP methods, in accordance with the recommendations of the European Association of Urology (EAU), include holmium laser enucleation of the prostate gland (HoLEP) and thulium laser enucleation of the prostate gland (ThuLEP) [7], as well as methods of monopolar and bipolar electroenucleation of the prostate gland.

For the first time holmium laser was applied by scientists from New Zealand - Peter Gilling and Mark Fraundorfer. They started working with a holmium laser in 1996 [8],

and in 1998 P.J. Gilling, M.R. Fraundorfer [9] presented preliminary results of holmium laser enucleation of prostatic hyperplasia with intravesical morcellation of removed tissue in 14 patients [10]. The creation and use of a morcellator has become a significant event in the use of a holmium laser. This fundamentally new technique pushed into the background the methods of ablation and resection. The combination of vaporizing, hemostatic capabilities of a holmium laser with transurethral morcellation allows effective surgical treatment of large adenomas with immediate improvement in urination and a decrease in the number of complications [8,11,12].

With holmium enucleation, laser energy with a power of 60-100 W, concentrated "at the tip" of the laser fiber, allows you to dissect adenomatous tissue. In this case, the adenomatous nodes are separated from the capsule in the same way as it is done with the index finger of the surgeon during an open adenectomy. Consistently enucleated middle and lateral lobes retrogradely displaced into the bladder and subsequently evacuated using a morcellator. If it is not possible to use a morcellator, the lobes of the prostate gland are partially enucleated and then the devascularized lobes are crushed using a resectoscope and removed via the tube of the latter (the "mushroom" technique). Coagulation of bleeding vessels is ensured by removing the tip of the fiber 3-4 mm from the vessel. Saline or glycine solution is used as an irrigation fluid during HoLEP [13].

The combination of the hemostatic capabilities of the holmium laser and transurethral morcellation allows for the effective treatment of even large adenomas, providing an immediate positive urodynamic effect, as with transurethral resection of the prostate (TURP), with fewer complications. The initial use of the holmium laser in the treatment of BPH was a combination of holmium and neodymium Nd:YAG lasers - endoscopic laser ablation of the prostate. A holmium laser was used to vaporize (burn) the channel before conducting a quadrant Nd:YAG with the laser. Later it became possible to vaporize the prostate only with a holmium laser wave and used an electrode with end (side) or end glow - the HoLAP technique (holmium laser ablation of the prostate) [10].

In recent years, HoLEP has become increasingly popular. HoLEP has several advantages over TURP, especially in patients with large prostate volumes [14]. According to EAU recommendations, with a prostate volume greater than 80 cm³, HoLEP is the operation of choice along with open adenectomy and bipolar enucleation [3]. Some authors have called HoLEP the new "gold standard" for the surgical treatment of prostate hyperplasia [15]. In addition, to date, holmium enucleation of prostate adenoma is positioned as a "size-independent" procedure, i.e. applicable to adenomas of any size [16]. Conducted scientific studies confirm the high efficiency of holmium enucleation in the elimination of infravesical obstruction due to prostatic hyperplasia. So, Elmansy H.M. [17] reports positive results of examination of patients even 10 years (62 months) after surgery, including patients with large prostate hyperplasia.

After HoLEP, in 2004, the method of bipolar plasmakinetic enucleation of the prostate (PkEP) appeared, then later, in the late 2000s, other transurethral methods based on laser exposure to the enucleation technique appeared: Tm:YAG (thulium laser with an aluminum yttrium garnet) vapoenucleation (TuhuEP) anatomical enucleation with support for Tm:YAG (thulium enucleation of the prostate - ThuLEP), diode laser enucleation of the prostate (DiLEP) and, finally, enucleation with a green laser "Greenlight" (GreenLEP) with lithium borate modulation (LBO). In 2010 Herrmann T.R. with colleagues were the first to propose a holmium-like technique for enucleation of an adenoma using a thulium laser called ThuLEP (thulium laser enucleation of the prostate). The pulsating radiation of a holmium laser causes a tearing effect, while the constantly generated wave of a thulium laser allows you to smoothly excise tissues and

vaporize them, achieving excellent hemostasis. Since water is found everywhere in soft tissues and is the target chromophore, this creates a constant chromophore content in laser-irradiated tissues and leads to a uniform interaction of radiation with tissues [18,19].

Discussion. As with HoLEP, a large number of studies have been conducted that confirm the effectiveness of ThuLEP [20]. Review of Barbalat et al. [21] showed that thulium laser enucleation of the prostate is a safe and effective procedure. According to the recent AUA and EAU guidelines, ThuLEP is recommended as a prostate size-independent suitable option to resolve BPH. Moreover, ThuLEP has higher intraoperative safety with regard to hemostatic properties, and its short-term results are similar to those of TURP [22]. The use of thulium laser energy for enucleation and separation of hyperplastic tissue from the capsule is accompanied by significant carbonation and leads to the fact that the operator tries to minimize the use of laser energy and carries out for the most part mechanical enucleation with a resectoscope. Modern devices for performing ThuLEP, in particular, thulium fiber laser enucleation of the prostate (ThuFLEP), devoid of such restrictions.

A number of authors analyzed the effectiveness of HoLEP in comparison with other surgical methods for treating the prostate gland: TURP [23, 24], open adenectomy [16, 25, 26], the results of HoLEP and ThuLEP were compared [11, 27]. In 2 large meta-analyses [28, 29], HoLEP and bipolar enucleation were compared with OPAE. They showed that no significant difference between EEP and OPAE was observed in the medium and long-term observation. At the same time, HoLEP is characterized by a shorter period of irrigation, catheterization, and hospitalization.

In retrospective study of Morozov A. et al. [30] assessment of EEP complications in 1413 patients has been performed. HoLEP, ThuFLEP, or monopolar enucleation of the prostate techniques were analysed. All EEP types have shown equal rates of complications intraoperatively, postoperatively, and at 6 months follow-up.

Nowadays, more and more attention is given to a minimally invasive surgical technologies (MIST) in the treatment of BPH. The following technologies can be classified as MIST:

Alternative ablative techniques

Aquablation - image guided robotic waterjet ablation: AquaBeam

AquaBeam uses the principle of hydro-dissection to ablate hyperplastic tissue while sparing collagenous structures like blood vessels and the surgical capsule. A targeted high velocity saline stream ablates hyperplastic tissue without the generation of thermal energy under real-time transrectal ultrasound guidance. Hemostasis is performed with a Foley balloon catheter on light traction or diathermy or low-powered laser if necessary. During mid-term follow-up, aquablation provides non-inferior functional outcomes compared to TURP in patients with LUTS and a prostate volume between 30-80 ml. Longer term follow-up is necessary to assess the clinical value of aquablation.

Non-ablative techniques

Prostatic urethral lift (PUL) is a minimally invasive treatment method. Enlarged lateral lobes of the prostate gland are compressed (squeezed) by small permanent suture-based implants delivered under cystoscopic guidance. It results in a widening of the prostatic urethra by forming a continuous anterior channel through the prostatic urethra.

Alternative ablative techniques under investigation

Convective water vapour energy (WAVE) ablation: The Rezum system

The Rezum system uses radiofrequency power to create thermal energy in the form of water vapour. The steam disperses through the tissue interstices and releases thermal energy onto prostatic hyperplasia tissue resulting in cell necrosis. The procedure can be performed in an office-based setting. One to three injections are needed for each lateral

lobe and one to two injections may be delivered into the median lobe.

Non-ablative techniques under investigation

iTIND (temporary implanted nitinol device)

The iTIND is a nitinol device composed of three elongated struts and an anchoring leaflet. Under direct visualisation iTIND is deployed inside the prostatic urethra in expanded configuration. The intended mode of action is to compress obstructive hyperplastic tissue by the expanded device, thereby exerting radial force leading to ischaemic necrosis. The iTIND device is left in position for five days and removed in an outpatient setting by standard urethroscopy. Randomised controlled trials comparing iTIND to a reference technique are ongoing.

Prostatic artery embolisation

Prostatic artery embolisation (PAE) can be performed as a day procedure under local anaesthesia with access through the femoral or radial arteries. Digital subtraction angiography displays arterial anatomy, and the appropriate prostatic arterial supply is selectively embolised to effect stasis in treated prostatic vessels. PAE is less effective than TURP at improving symptoms and urodynamic parameters. PAE should be performed only in units where the work up and follow-up is performed by urologists working collaboratively with trained interventional radiologists for the identification of PAE suitable patients.

HIFU (high-intensity focused ultrasound)

HIFU uses the high-intensity pulsed ultrasound energy for hyperplastic prostate tissue destruction. HIFU is divided into thermal and mechanical types, the latter is also known as histotripsy

Intra-prostatic injections

In order to improve LUTS due to BPH various substances have been injected directly into the prostate including Botulinum toxin-A (BoNT-A), fexapotide trifluate (NX-1207) and PRX302. The mechanisms of action for the injectables NX-1207 and PRX302 are not completely understood, but experimental data suggest apoptosis-induced atrophy of the prostate with both drugs. Results from clinical trials have shown no clinical benefits for BoNT-A compared to placebo for the management of LUTS due to BPH. Intraprostatic Botulinum toxin-A injection treatment should not be offered to patients with male LUTS [3].

With a large number of factors affecting the choice of method, preference is given to transurethral, and among transurethral methods, preference is given to methods of EEP. There is also a variety of MIST methods in BPH management, but all of them have certain limitations to use or still under investigation.

Thus, we can clearly say that modern trend in surgical treatment of BPH is represented by different methods of EEP and the future of the surgical treatment of BPH today determined by modern methods of endoscopic enucleation, such as holmium and thulium, as well as bipolar enucleation of the prostate gland. However, open adenectomy cannot be discounted either, since high-tech operations, such as HoLEP and ThuLEP, are not yet widely implemented and require high-level experience and endoscopic skills in many centers.

Conclusions. The radicalness of surgical treatment for BPH lies in the "anatomical enucleation" of the adenoma within its surgical capsule. Enucleation itself is of paramount importance, and not the energy source by which it is carried out, because the ultimate goal in all cases is precisely anatomical enucleation. Endoscopic adenectomy using laser or non-laser techniques confidently leads the way in the problem of surgical treatment of BPH and the future lies in the improvement of endoscopic methods.

References

1. Lokeshwar SD, Harper BT, Webb E, Jordan A, Dykes TA, Neal DE Jr, Terris MK, Klaassen Z. Epidemiology and treatment modalities for the management of benign prostatic hyperplasia. *Transl Androl Urol*. 2019 Oct;8(5):529-539. doi: 10.21037/tau.2019.10.01.
2. Sh. I. Giyasov, R. R. Gafarov, Sh. T. Mukhtarov Assessment of the Effectiveness and Safety of Different Surgical Methods for the Treatment of Benign Prostate Hyperplasia by Adaptation of the Clavien-Dindo Classification *American Journal of Medicine and Medical Sciences* 2022; 12(2): 96-103.
3. EAU Guidelines. Edn. presented at the EAU Annual Congress Milan 2023. ISBN 978-94-92671-19-6.
4. Allazov S.A., Gafarov R.R. Analysis of the effectiveness of hemostasis methods for prostate adenomectomy. Lambert Academic Publishing. Saarbrücken 2017. 62 P.
5. Гиясов, Ш.И., Гафаров, Р.Р., Шодмонова, З.Р., Мухтаров, Ш.Т., & Акилов, Ф.А. (2022). Роль систематизации послеоперационных осложнений в оценке эффективности и безопасности хирургических методов лечения доброкачественной гиперплазии предстательной железы. *Урология*, (3), 83-91.
6. Gafarov Rushen Refatovich. Minimally invasive technologies in the surgical treatment of benign prostatic hyperplasia // *Journal of Biomedicine and Practice*. 2023, vol. 8, issue 3, pp.423- 429.
7. Enikeev, D., Rapoport, L., Gazimiev, M. et al. Monopolar enucleation versus transurethral resection of the prostate for small- and medium-sized (<80 cc) benign prostate hyperplasia: a prospective analysis. *World J Urol* 38, 167-173 (2020).
8. Fraundorfer M.R., Gilling P.J. Holmium:YAG laser enucleation of the prostate combined with mechanical morcellation: preliminary results. *Eur Urol* 1998;33(1):69-72. PMID: 9471043.
9. Gilling P.J., Fraundorfer M.R. Holmium laser prostatectomy: a technique in evolution. *Curr Opin Urol* 1998;8(1):11-5. PMID: 17035836.
10. Dymov A.M. Laser (holmium) removal of prostate tissue in the treatment of patients with prostatic hyperplasia. Diss ... cand. med. sci. Moscow, 2011.
11. Enikeev D.V., Glybochko P.V., Alyaev Yu.G., Rapoport L.M. et al. Laser enucleation of prostate hyperplasia (HoLEP and ThuLEP): a comparative analysis of efficacy in the treatment of recurrence of prostatic hyperplasia. *Urology* 2017; 2: 66-70.
12. Enikeev D.V., Glybochko P.V., Alyaev Yu.G., Rapoport L.M. et al. Endoscopic enucleation of the prostate gland - a new standard in the surgical treatment of prostatic hyperplasia. *Andrology and Genital Surgery* 2017; 18(3): 83-88.
13. Гафаров Р.Р., Аллазов С.А., Гиясов Ш.И. Лазерная энуклеация - новое слово в оперативном лечении доброкачественной гиперплазии предстательной железы. *Доктор ахборотномаси* 2019;1:132-137.
14. Humphreys M.R. et al. Holmium laser enucleation of the prostate - outcomes independent of prostate size? // *J Urol* - 2008. - Vol. 180. - P. 2431-2435.
15. Tyson M.D. et al. In 2013, holmium laser enucleation of the prostate (HoLEP) may be the new 'gold standard'. *Curr Urol Rep*. 2012. Vol. 13. P. 427-432.
16. Jones P., Alzweri L., Rai B.P., Somani B.K., Bates C., Aboumarzouk O.M. Holmium laser enucleation versus simple prostatectomy for treating large prostates: Results of a systematic review and meta-analysis. *Arab J Urol*. 2015;14(1):50-8.
17. Elmansy HM., Kotb A, Elhilali MM. Holmium laser enucleation of the prostate: long-term durability of clinical outcomes and complication rates during 10 years of followup. *J Urol*. 2011. Vol. 186. P.1972-1976.

- 18.Herrmann T.R., Bach T., Imkamp F. Thulium laser enucleation of the prostate (ThuLEP): transurethral anatomical prostatectomy with laser support. Introduction of a novel technique for the treatment of benign prostatic obstruction. *World J Urol* 2010; 28: 45-51.
- 19.Herrmann T.R., Liatsikos E.N., Nagele U. et al. EAU guidelines on laser technologies. *Eur Urol* 2012;61(4):783-95. DOI: 10.1016/j.eururo.2012.01.010.
- 20.Glybochko P.V., Alyaev Yu.G., Rapoport L.M. et al. Endoscopic enucleation of the prostate: a temporary trend or a new standard of treatment? *Urology* 2018; 2: 130-134.
- 21.Barbalat Y., Velez M.C., Sayegh C.I. Evidence of the efficacy and safety of the thulium laser in the treatment of men with benign prostatic obstruction. *Ther Adv Urol* 2016; 8: 181-191.
- 22.Yuan R, Boyu Y, Fujun Z, et al. Transurethral thulium laser enucleation versus resection of the prostate for treating benign prostatic hyperplasia: a retrospective study. *Lasers Med Sci.* 2019;34(2):329-334. doi:10.1007/s10103-018-2597-3.
- 23.Eltabay M.A., Sherif H, Hussein AA. Holmium laser enucleation versus transurethral resection of the prostate. *Can J Urol* 2010;17: 5447-52.
- 24.Fayad A.S., Sheikh M.G., Zakaria T, Elfottoh HA, Alsergany R. Holmium laser enucleation versus bipolar resection of the prostate: a prospective randomized study. Which to choose? *J Endourol* 2011;25: 1347-52.
- 25.Kuntz RM, Lehrich K, Ahyai SA. Holmium laser enucleation of the prostate versus open prostatectomy for prostates greater than 100 grams: 5-year follow-up results of a randomised clinical trial. *Eur Urol* 2008;53:160-8.
- 26.Naspro R, Suardi N., Salonia A, et al. Holmium laser enucleation of the prostate versus open prostatectomy for prostates >70 g: 24-month follow-up. *Eur Urol* 2006;50:563-8.
- 27.Pirola G.M., Saredi G., Cudas Duarte R. et al. Holmium laser versus thulium laser enucleation of the prostate: a matched-pair analysis from two centers. *Ther Adv Urol.* 2018;10(8):223-233. doi:10.1177/1756287218779784.
- 28.Li M., Qiu J., Hou Q. et al. Endoscopic enucleation versus open prostatectomy for treating large benign prostatic hyperplasia: a meta-analysis of randomized controlled trials. *PLoS One* 2015;10(3):e0121265. DOI: 10.1371/journal.pone.0121265.
- 29.Lin Y., Wu X., Xu A. et al. Transurethral enucleation of the prostate versus transvesical open prostatectomy for large benign prostatic hyperplasia: a systematic review and meta-analysis of randomized controlled trials. *World J Urol.* 2016 Sep;34(9):1207-19. doi: 10.1007/s00345-015-1735-9.
- 30.Morozov A, Taratkin M, Kozlov V, et al. Retrospective Assessment of Endoscopic Enucleation of Prostate Complications: A Single-Center Experience of More Than 1400 Patients. *J Endourol.* 2020;34(2):192-197. doi:10.1089/end.2019.0630