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### Prostatic Hyperplasia and Urethral Stricture as Comorbid Factors of Infravesical Obstruction

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#### **ABSTRACT**

Prostatic hyperplasia and urethral strictures are the most common causes of infravesical obstruction. These disorders are typically studied in isolation, without consideration of their potential coexistence in a single patient, which leads to insufficient awareness of the combined condition of the urethra, prostate, and bladder. This review analyzes the scientific data published between 2020 and 2024 that addresses infravesical obstruction caused by the combination of prostatic hyperplasia and urethral stricture. Scientific sources were searched in both Russian (eLibrary) and international (PubMed, Embase, Cochrane Library, Web of Science, Scopus) databases. The following keywords were used: *стриктура уретры (urethral stricture)*, доброкачественная гиперплазия предстательной железы (benign prostatic hyperplasia), инфравезикальная обструкция (infravesical obstruction), симптомы нижних мочевых путей (lower urinary tract symptoms), хроническая задержка мочи (chronic urinary retention), хирургическое лечение (surgical treatment), and послеоперационные осложнения (postoperative complications). Only a limited number of publications were found that discuss clinical scenarios where infravesical obstruction is simultaneously caused by both prostatic hyperplasia and urethral stricture. Treatment strategies for such patients should be based on a functional and anatomical assessment of the lower urinary tract, which may vary significantly in each case. An individualized approach is required when managing patients with this comorbidity. The lack of large-scale studies limits the ability to obtain meaningful data necessary for developing treatment guidelines for the concurrent management of both conditions.

Keywords: infravesical obstruction; benign prostatic hyperplasia; urethral stricture; surgical treatment.

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# Гиперплазия предстательной железы и стриктура уретры как коморбидные факторы инфравезикальной обструкции

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#### *RNПАТОННА*

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Гиперплазия предстательной железы и стриктуры уретры — наиболее частые причины инфравезикальной обструкции. Данные заболевания, как правило, изучаются без учета их возможного сочетания у одного больного, что приводит к недостаточной осведомленности о совокупном состоянии уретры, простаты и мочевого пузыря. Проведен обзор литературы, посвященной оценке инфравезикальной обструкции, обусловленной сочетанием гиперплазии предстательной железы и стриктуры уретры, опубликованной в период 2020–2024 гг. Поиск источников литературы производили в отечественных (eLibrary) и иностранных (PubMed, Embase, Cochrane Library, Web of Science, Scopus) базах данных. В качестве поисковых запросов использовали следующие ключевые слова: «стриктура уретры», «доброкачественная гиперплазия предстательной железы», «инфравезикальная обструкция», «симптомы нижних мочевых путей», «хроническая задержка мочи», «хирургическое лечение», «послеоперационные осложнения». Найдено крайне ограниченное число публикаций, касающихся клинических ситуаций, при которых причинами инфравезикальной обструкции одновременно выступают гиперплазия предстательной железы и стриктуры уретры. Подходы к тактике лечения таких пациентов должны основываться на функциональной и анатомической оценке состояния нижних мочевых путей, отличающихся особенностями в каждом случае. Требуется поиск индивидуальных решений при лечении пациентов с данными заболеваниями. Нехватка крупных исследований ограничивает возможность получения значимых данных, необходимых для формирования рекомендаций по тактике лечения обоих заболеваний при их сочетании.

**Ключевые слова:** инфравезикальная обструкция; гиперплазия предстательной железы; стриктура уретры; хирургическое лечение.

#### Как цитировать

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#### INTRODUCTION

Advancements in medical research and clinical urological practice over the past decades have contributed to a more profound understanding of the multifaceted nature of infravesical obstruction (IVO) [1]. The most common causes of non-malignant IVO are benign prostatic hyperplasia (BPH), bladder neck stenosis, and urethral strictures (USs) [2]. Studying the heterogeneity of conditions associated with IVO is highly relevant for several reasons. Firstly, IVO significantly impacts the patient's quality of life. The debilitating symptoms of lower urinary tract symptoms (LUTS) negatively affect daily activities, sleep patterns, and psychosocial well-being [3, 4]. Secondly, symptoms such as urgent and frequent urination, as well as incomplete bladder emptying, not only bother patients, but may also lead to serious complications, including recurrent urinary tract infections, secondary stone formation, and renal failure [1]. Finally, the growing prevalence of IVO-associated conditions, particularly BPH and USs, highlights the need for comprehensive research in this field. The current demographic landscape reveals a growing proportion of older individuals worldwide. Consequently, healthcare professionals must employ the latest knowledge and tools to effectively address the increasing burden of LUTS associated with IVO [5].

Obviously, IVO-associated conditions require an indepth understanding of the pathophysiology, diagnosis, and treatment of each case. Moreover, diseases such as BPH and US are usually considered separately without taking into account the possibility of their combination in one patient. This leads to an underestimation of the functional and anatomical condition of the lower urinary tract

#### SEARCH STRATEGY

A review was conducted to assess benign urinary tract obstruction caused by US and BPH, with a particular focus on clinical scenarios where these pathologies coexist. The search strategy aimed to identify relevant articles published in leading, global, peer-reviewed journals.

The following keywords in various combinations were used: стриктура уретры (urethral stricture), доброкачественная гиперплазия предстательной железы (benign prostatic hyperplasia), инфравезикальная обструкция (infravesical obstruction), симптомы нижних мочевых путей (lower urinary tract symptoms), хроническая задержка мочи (chronic urinary retention), хирургическое лечение стриктур уретры (surgical treatment of urethral strictures), and послеоперационные осложнения (postoperative complications).

#### Medical Journal Databases

The search for relevant data was conducted using a variety of electronic databases to ensure comprehensive coverage of publications. The following databases were used:

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- eLibrary is an online database of Russian-language publications offering access to a wide range of academic literature, including journals, dissertations, and conference materials.
- PubMed is an open-access resource developed and maintained by the National Center for Biotechnology Information that provides access to MEDLINE and other natural science journals.
- Embase is a biomedical and pharmacological database that includes published papers from journals and conference abstracts worldwide.
- Cochrane Library is a collection of high-quality systematic reviews and randomized controlled trials related to healthcare.
- Web of Science is a multidisciplinary citation database that provides access to scientific papers across various disciplines.
- Scopus is a comprehensive database with abstracts and citations covering a wide range of scientific, technical, and medical disciplines.

#### Inclusion and Exclusion Criteria

Inclusion criteria:

- 1. Papers published between January 2000 and October 2024
- 2. Peer-reviewed studies concerning the role of USs and/or BPH in the development of urinary tract obstruction
  - 3. Studies involving patients over 18 years of age.
- 4. Original studies, systematic reviews, and clinical quidelines.

Exclusion criteria: studies including patients with genitourinary malignancies and non-compliance with the inclusion criteria.

#### Search Algorithm

The search algorithm was structured as follows:

- 1. Selection of keywords related to benign urinary obstruction using operators and/or advanced search tools in the specified publication databases.
  - 2. Using inclusion criteria and filtering results.
  - 3. Removing duplicate entries.
- 4. Search for titles and abstracts to identify relevant papers. A full-text search was conducted among papers that met the initial search criteria. During the search, studies addressing the complex genesis of IVO associated with BPH and USs were selected from the publications.
- 5. Findings on the causes, diagnostic approaches, treatment options, and outcomes related to BPH and USs were summarized by extracting data from selected papers.

#### **Data Aggregation**

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We analyzed the data from the included studies in detail and identified key issues in the epidemiology, etiology, diagnosis, and treatment strategies of urinary tract obstruction associated with BPH and USs. Statistical analysis was not used due to the heterogeneity of the papers.

#### PREVALENCE OF BENIGN PROSTATE HYPERPLASIA AND URETHRAL STRICTURES

BPH is one of the most common diseases in men over 50 years of age. It affects approximately 50% of men over 50 years of age and up to 90% of men over 80 years of age [6, 7]. LUTS associated with BPH most frequently occur in men around 40 years of age, and their severity correlates with an increase in prostate volume. The overall prevalence of LUTS associated with BPH, as reported in the Triumph retrospective cohort study based on the Integrated Primary Care Information database of general practitioners in the Netherlands, was 10.3%. Moreover, the lowest prevalence was among men aged 45-49 years (2.7%) and increased with age, reaching a maximum at 80 years (24.9%) [8]. These data are considerably lower than the overall prevalence indicated in the SNAPSHOT report for Egypt and the Gulf countries and are analogous to those observed in Turkey [9]. However, the Triumph study was conducted using a primary care database, whereas SNAPSHOT was a prospective population-based study.

LUTS/BPH are known to have a negative impact on health-related quality of life. Their impact on work productivity, social and family life, mental health and sleep quality was described. A study conducted in the UK showed that quality of life (assessed using the EQ5D questionnaire) decreases as the severity of LUTS increases [10]. One of the most debilitating symptoms is nocturia. Frequent urination at night may have an extremely negative impact on a person's perception of their quality of life by affecting the quality of sleep [11].

Although significantly less common, USs are still widespread among men, being one of the leading causes of obstructive uropathy. The prevalence rate ranges from two to six cases per 1000 men, representing 0.6% of the risk population, which is mainly older men [12]. The incidence of USs increases significantly among men over 65 years of age. Previous pelvic surgeries, trauma, sexually transmitted infections, and inflammatory conditions are all factors associated with an increased risk of USs.

A retrospective observational study conducted in China from 2000 to 2020 found that the incidence of bulbar urethral strictures and multifocal strictures increased (14.8% vs 18.4% and 5.4% vs 9% before and

after 2010, respectively) [13]. However, the incidence of post-traumatic and post-infectious USs decreased (54.2% vs 34.3% and 6.3% vs 4.2% before and after 2010, respectively), whereas the prevalence of USs associated with transurethral interventions and of unknown etiology increased after 2010 (17.1% vs 30.5% and 2.8% vs 5.4%, respectively). Additionally, the authors reported changes in the approach to treating USs. Between 2010 and 2020, the frequency of internal optical urethrotomy and anastomotic urethroplasty decreased compared with the previous decade (40.9% vs 22.5% and 32.4% vs 28.3%, respectively), whereas the frequency of non-anastomotic urethroplasty increased (23.6% vs 46.0%, respectively).

There is little epidemiological data on the prevalence of BPH and USs as comorbidities. There are several reasons for this. First, research in this area focuses on specific diseases individually, without considering their possible interactions. This results in inadequate attention to the issue of managing patients with IVO of complex genesis, which complicates the collection of data on the comorbid progression of these conditions. Second, inconsistencies in identifying and recording patients with these conditions may result from differences in diagnostic and treatment methods across healthcare settings. For example, more in-depth diagnosis may be used when symptoms are ambiguous, whereas a less thorough approach may be applied in other cases. Additionally, these topics remain understudied due to insufficient funding, a lack of interest in studying this issue by the research community, and numerous iatrogenic factors contributing to the formation of USs [14-19]. These factors explain the lack of epidemiological data on the coexistence of BPH and USs and highlight the need for further research

## SIMULTANEOUS TREATMENT OF BENIGN PROSTATE HYPERPLASIA AND URETHRAL STRICTURES

When the anterior urethra is compromised, one option for endoscopic removal of adenomatous tissue is urethrostomy. The endoscopic resection of the prostate, or enucleation through temporary perineal urethrostomy, has been described for a long time. For example, Melchior et al. described transurethral resection of the prostate (TURP) via perineal urethrostomy in 676 patients over seven years in 1974 [20]. Three years later, Bissada published a controlled prospective clinical study justifying the use of this approach by citing a reduction in the US incidence [21]. Patients who underwent TURP with perineal urethrostomy were shown to have a lower risk of USs than patients who underwent traditional TURP (2.27% vs 16.4%; p < 0.01) [21]. In 2020, Krambeck et al.

reported on a similar technique for performing the intervention through a perineal urethrostomy. This technique was used on a small cohort of patients with significant anatomical limitations, such as extremely large prostate volumes, the presence of a penile prosthesis, and morbid obesity. The only difference was the use of holmium laser enucleation of the prostate (HoLEP) instead of TURP [22].

Garabed et al. [23] described the case of a 75-yearold man with severe prostatic obstruction associated with large-volume (200 cm<sup>3</sup>) BPH and concomitant clinically significant bulbar US [23]. The patient had undergone TURP more than 10 years prior to the detection of recurrent prostatic obstruction and had a history of false passage during urethral catheterization. A preoperative evaluation that included retrograde and antegrade urethroscopy, antegrade cystoscopy, and urethrography revealed an obliterating proximal bulbar stricture, several other strictures, and significant growth of trilobar adenomatous prostatic tissue. Prostatic enucleation prior to urethroplasty was not possible due to obliterative US. Furthermore, urethroplasty performed before enucleation would greatly increase the risk of US recurrence. After discussing treatment options with the patient, a decision was made to perform both HoLEP and buccal graft urethroplasty in a single operation. A HoLEP procedure was performed via a dorsal urethrotomy using a 26-Fr resectoscope. Enucleation was performed using the standard bilobar technique. Another surgeon simultaneously performed buccal urethroplasty and harvested a  $2.5 \times 5.0$  cm oral mucosa graft from the left cheek using standard technique during the HoLEP procedure [23]. The technique described by Garabed resulted in complications. In the presented clinical case, the patient underwent revision cystoscopy one month after surgery to remove a residual prostate fragment.

In 2024, Katibov et al. presented the results of the simultaneous treatment of anterior USs and BPH in four men who underwent perineal/penile urethrostomy and thulium laser enucleation of the prostate (ThuLEP) [24]. The study endpoints were to evaluate the efficacy and safety of ThuLEP performed through urethrostomy. Treatment was considered successful in all four patients, with a mean follow-up period of 11.3 months. For half (50%) of the patients who underwent single-stage surgery, urethrostomy closure was performed via urethral tubulization after three months. Two patients (50%) retained the urethrostoma for a prolonged period.

Chong et al. [25] reported on the simultaneous treatment of patients with BPH and USs. The authors described 25 cases of internal optical urethrotomy followed by prostatic hyperplasia surgery in a single procedure. The authors concluded that, in some cases, treating BPH and USs simultaneously within a single intervention may be an effective approach.

# TREATMENT OF BENIGN PROSTATE HYPERPLASIA WITH A HISTORY OF URETHRAL INJURY

Managing patients with complicated BPH who have a history of urethral injury is challenging for several reasons. It is known that direct exposure of the urethra to mechanical, infectious-inflammatory, and other traumatic factors associated with the surgical treatment of BPH may lead to USs [26, 27]. In patients who have undergone surgical treatment of USs, the urethral lumen in the reconstruction area often exceeds 16 Fr, and the periurethral tissues are characterized by minimal elasticity and an impaired blood supply. A history of USs increases the risk of urinary tract infections, which requires a heightened focus on prevention and treatment. Research shows that prostate surgery in these situations is often accompanied by an elevated risk of complications and less predictable results. Additionally, comorbidity and psychological factors, considering the effect of health status on patients' quality of life after repeated treatment, often necessitate a personalized approach.

A retrospective analysis of clinical data from 39 patients with a history of reconstructive interventions on the urethra is worth highlighting. These patients were asymptomatic following primary surgical treatment for USs and underwent urethra-sparing laparoscopic adenomectomy for large-volume BPH (>80 cm³) from January 2016 to October 2021 [28]. Following successful primary surgery for USs, including anastomotic urethroplasty, substitution urethroplasty, and internal urethrotomy under visual control, all patients exhibited satisfactory urodynamic parameters (maximum urinary flow rate  $[Q_{max}]$ ) >15 mL/s and a residual urine volume <50 mL). The urethra was passable for urethroscopy with a 16 Fr flexible urethrocystoscope. However, 24 Fr and 26 Fr resectoscopes could not pass through the narrowed area. Because of the development of severe BPH-associated LUTS, the patients underwent urethrasparing laparoscopic adenomectomy. During the sixmonth postoperative follow-up, there were no cases of stress urinary incontinence, and there was no progression of clinical symptoms of US. At the postoperative follow-up checkpoints, there was a significant improvement in International Prostate Symptom Score (IPSS) and Quality of Life Scale scores, as well as an increase in  $Q_{\text{max}}$  and a decrease in residual urine, compared with baseline [28].

A complex patient category with USs includes those whose condition is caused by urethral damage resulting from pelvic bone fractures [29]. Over time, patients who have undergone urethral reconstructions may develop BPH-associated LUTS. The treatment of BPH in these patients poses significant challenges, as the function of

the external sphincter is frequently compromised due to trauma and/or urethroplasty, with urine retention being maintained by the internal sphincter located in the bladder neck [30-32]. Mishra et al. [33] presented data from a cohort of five such patients. All patients had a history of pelvic bone injury, followed by successful urethral reconstruction and satisfactory urination. They subsequently developed progressive, severe LUTS. The average prostate size was 67.2 ± 21.1 cm<sup>3</sup>. Treating LUTS secondary to BPH in patients who have undergone reconstructive urethral surgery for pelvic bone fractures presents a unique challenge. The urologist must eliminate urethral obstruction while preserving urinary continence. Mishra et al. proposed a modified TURP technique that involves the isolated resection of either the middle lobe or one of the lateral lobes, if the middle lobe is absent. Additionally, the authors recommended making every possible effort to avoid crossing the circular fibers in the bladder neck area. The IPSS questionnaire results demonstrated a significant reduction in symptom severity of 16  $\pm$  5.8 points (p = 0.002). Additionally, objective assessment of postvoid residual urine revealed significant improvement in bladder emptying parameters. Furthermore, the authors did not observe any significant differences in the  $Q_{\max}$ rate between preoperative and postoperative uroflowmetry. All patients retained complete urinary continence. The main limitation of this study was its small sample size.

Another study, conducted by Berger et al. [34], evaluated the use of transurethral resection of the prostate via cystostomy in patients with severe symptoms of obstruction caused by BPH who had a history of reconstructive surgery for extensive USs. All three patients in the study had undergone dorsal onlay urethroplasty for extensive USs prior to prostate resection. The strictures measured 9, 7, and 6 cm long. The authors concluded that prostate resection performed through an extended cystostomy approach appears to be a safe and effective treatment option in a selected group of patients who have undergone surgery for extensive USs, with a small prostate volume (<50 cm³) and LUTS refractory to conservative therapy.

#### DISCUSSION

Currently, there are no publications addressing clinical situations in which both BPH and USs are simultaneous causes of IVO. This may be related to the fact that research on this issue requires a complex diagnostic approach, which complicates scientists' and clinicians' work. BPH and USs are generally considered separately, without regard for their potential combination. This approach leads to an underestimation of the functional and anatomical condition of the lower urinary tract. The treatment of such patients should be based on broader

research, taking into account the individual characteristics of the diseases. This highlights the need for further study of the issue. Furthermore, the understanding of the patient profile with IVO has significantly changed over the past few decades, becoming much more complex than previously assumed [1, 35]. This is facilitated by several factors:

- 1. Diversity of etiology. Although BPH remains the predominant etiology of lower urinary tract obstruction, conditions such as USs, bladder neck dysfunction, and neurogenic lower urinary tract disorders, as well as environmental influences, may play a significant role in the development of obstructive uropathy and be reflected in the clinical presentation [1]. A more comprehensive understanding of the pathology requires a holistic approach to diagnosis and treatment. This approach considers a variety of potential etiologies instead of focusing solely on prostate size.
- 2. Expanding diagnostic approaches. The use of diagnostic techniques such as comprehensive urodynamic testing, imaging technologies, and biomarker analysis have changed the assessment of lower urinary tract obstruction. These tools enable physicians to assess bladder function and its contribution to LUTS more accurately, allowing for a personalized approach to patient care. However, improving diagnostic capabilities increases the likelihood of overdiagnosis and biased interpretation of results, complicating clinical decision-making.
- 3. Impact of concomitant diseases. The influence of comorbidities such as diabetes mellitus, obesity, and neurological disorders on IVO-associated LUTS is increasingly recognized as significant. The impact of comorbidity on LUTS and bladder function is shifting from a secondary factor to a leading one. Comorbidities significantly modify the course of the primary pathology, necessitating interdisciplinary decision-making when choosing treatment approaches for patients with IVO. Understanding these relationships is critical to developing patient-centered treatment strategies that address both urinary symptoms and overall health.
- 4. Changing patient expectations. Currently, patients are more informed and engaged in healthcare decision-making processes. They seek effective, minimally invasive treatments that align with their lifestyle and preferences. This shift has prompted ongoing research into new approaches, such as pharmacotherapy and surgical interventions. The challenge is to balance patient expectations and the existing evidence base to achieve optimal outcomes. Understanding the potential complexity of concomitant pathologies in IVO is crucial, as the simultaneous presence of several obstructive factors may worsen symptoms, complicate treatment strategies, and ultimately affect patients' quality of life [1–3, 11].

#### CONCLUSION

The review highlights the need for an individualized approach to patients with IVO, which is caused by the possible combination of BPH and USs. Management principles for such patients may include active surveillance alongside long-term conservative therapy, as well as sequential or combined surgical treatment strategies. The lack of large-scale studies limits the availability of the statistically significant data necessary for developing treatment guidelines for the concurrent management of both conditions.

#### ADDITIONAL INFO

Author contributions: S.A. Shablakov: investigation, writing—original draft; V.P. Glukhov: conceptualization, supervision, formal analysis, writing—review & editing; A.V. Ilyash: formal analysis, writing—review & editing; V.V. Glukhova: investigation, writing—original draft; M.I. Kogan: conceptualization, formal analysis, writing—review & editing. All the authors approved the version of the draft to be published and agreed to be accountable for all aspects of the work, ensuring that issues related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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process involved a single reviewer (an editorial board member, editorial council member, or an external reviewer); double-blind review was conducted.

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#### ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. С.А. Шаблаков — поиск и анализ литературных данных, написание текста рукописи; В.П. Глухов — концепция исследования, научное руководство, анализ литературных данных, редактирование текста рукописи; А.В. Ильяш — анализ литературных данных, редактирование текста рукописи; В.В. Глухова — поиск и анализ литературных данных, написание текста рукописи; М.И. Коган — концепция исследования, анализ литературных данных, редактирование текста рукописи. Авторы одобрили версию для публикации, а также согласились нести ответственность за все аспекты работы, гарантируя надлежащее рассмотрение и решение вопросов, связанных с точностью и добросовестностью любой ее части.

Источники финансирования. Отсутствуют.

Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

**Оригинальность.** При создании настоящей работы авторы не использовали ранее опубликованные сведения (текст, иллюстрации, данные).

**Генеративный искусственный интеллект.** При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

Рассмотрение и рецензирование. Настоящая работа подана в журнал в инициативном порядке и рассмотрена по обычной процедуре. В рецензировании участвовали один рецензент (член редакционной коллегии, член редакционного совета или внешний рецензент), рецензирование двойное слепое.

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