RETROSPECTIVE STUDY OF RISK FACTORS FOR URETHRAL STRICTURE AFTER TRANSURETHRAL RESECTION OF PROSTATE AMONG THE ELDERLY IN CHENGDU, CHINA

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Page

LIST OF SYMBOLS

β	beta
SE	standard error
Wald	Wald statistic
OR	odds ratio
CI	confidence interval
†p	†p values are from the chi-square test for categorical variables

LIST OF ABBREVIATIONS

AUC	area under the curve
BPH	benign prostatic hyperplasia
BUN	blood urea nitrogen
Cr	creatinine
DCA	decision curve analysis
HGB	hemoglobin
LUTS	lower urinary tract symptoms
ROC	receiver operating characteristic curve
SD	standard deviation
TURP	transurethral resection of the prostate
US	urethral stricture
WBC	white blood cell

LIST OF APPENDICES

KAJIAN RETROSPEKTIF FAKTOR RISIKO UNTUK STRIKTUR URETRA SELEPAS RESEKSI TRANSURETRA PROSTAT DI KALANGAN WARGA EMAS DI CHENGDU, CHINA

ABSTRAK

Hiperplasia prostat benigna (BPH) semakin berleluasa dalam kalangan penduduk. Walaupun reseksi transuretra prostat (TURP) masih merupakan rawatan pembedahan standard, striktur uretra pascaoperasi lewat tetap menjadi komplikasi yang berpotensi. Kajian keratan rentas ini bertujuan untuk mengenal pasti faktor risiko untuk penyempitan uretra berikutan TURP. Data klinikal daripada 400 pesakit BPH (min umur, 74.31 ± 6.70 tahun) yang menjalani TURP di Hospital Gabungan Universiti Chengdu antara Jun 2020 dan Jun 2023 dianalisis secara retrospektif. Kajian ini membahagikan data kepada dua kumpulan: kumpulan striktur uretra dan kumpulan striktur bukan uretra. Semua data dianalisis menggunakan analisis regresi logistik univariat dan multivariate ($P < 0.05$ ditetapkan sebagai kriteria keertian). Sejumlah 35 pesakit (8.75%) mengalami striktur uretra. Analisis multivariate mengenal pasti umur (OR = 1.121, 95% CI: 1.044–1.204, P = 0.002), saiz prostat (OR = 1.038, 95% CI: 1.014–1.062, P = 0.002), kateter tinggal sebelum operasi (OR = 5.413, 95% CI: 1.872 – 15.655, P = 0.002) dan masa kateter tinggal selepas pembedahan (OR = 2.147, 95% CI: 1.405–3.280, $P < 0.001$) sebagai faktor risiko bebas untuk penyempitan uretra. manakala pelebaran uretra pra operasi (OR = 0.049, 95% CI: 0.011-0.220, $P < 0.001$) adalah faktor perlindungan bebas. Model ramalan nomogram yang ditubuhkan berdasarkan faktor pengaruh bebas di atas (AUC = 0.916) mempunyai prospek aplikasi yang baik dalam diagnosis klinikal dan penilaian risiko.

RETROSPECTIVE STUDY OF RISK FACTORS FOR URETHRAL STRICTURE AFTER TRANSURETHRAL RESECTION OF PROSTATE AMONG THE ELDERLY IN CHENGDU, CHINA

ABSTRACT

Benign prostatic hyperplasia (BPH) is becoming increasingly prevalent, and although transurethral resection of the prostate (TURP) remains the standard surgical treatment, late postoperative urethral stricture remains a potential complication. This cross-sectional study aimed to identify risk factors for urethral stricture following TURP. Clinical data from 400 BPH patients (mean age, 74.31 ± 6.70 years) who underwent TURP at Chengdu University Affiliated Hospital between June 2020 and June 2023 were retrospectively analyzed. This study divided the data into two groups: the urethral stricture group and the non-urethral stricture group. All data were analyzed using univariate and multivariate logistic regression analysis ($P < 0.05$ was set as the significance criterion). A total of 35 patients (8.75%) developed urethral stricture. Multivariate analysis identified age (OR = 1.121, 95% CI: 1.044–1.204, P = 0.002), prostate size (OR = 1.038, 95% CI: 1.014–1.062, P = 0.002), preoperative indwelling catheter (OR = 5.413, 95% CI: 1.872 – 15.655, P = 0.002), and postoperative indwelling catheter time (OR = 2.147, 95% CI: 1.405–3.280, $P < 0.001$) as independent risk factors for urethral stricture, whereas preoperative urethral dilation (OR = 0.049, 95% CI: 0.011–0.220, $P < 0.001$) was an independent protective factor. The nomogram prediction model established based on the above independent influencing factors (AUC = 0.916) has good application prospects in clinical diagnosis and risk assessment.

CHAPTER 1

INTRODUCTION

1.1 Background of the study

Benign prostatic hyperplasia (BPH) is one of the most common chronic urologic diseases in middle-aged and older men (Tian et al., 2021). Its early symptoms are usually insidious and therefore easily overlooked or misdiagnosed. As the disease progresses, patients gradually show obvious lower urinary tract symptoms (LUTS). Early symptoms are mainly characterized by progressive dysuria and waiting to urinate. However, with the worsening of lower urinary tract obstruction, the symptoms will gradually worsen (Gravas et al., 2024). These symptoms can be categorized into storage phase symptoms, voiding phase symptoms and post-voiding symptoms. Storage phase symptoms include urinary frequency, urgency, incontinence and nocturia, often caused by overactivity or instability of bladder function; voiding phase symptoms are characterized by straining to urinate, difficulty in urinating, intermittent voiding and a fine urine stream; and post-voiding symptoms include a feeling of incomplete voiding and postvoiding dribbling, which are usually associated with incomplete bladder emptying (Bausch et al., 2023, Sessa et al., 2023). BPH not only affects the patient's quality of life, but may also lead to a series of serious complications. Prolonged urinary tract obstruction can increase the risk of urinary tract infection and acute urinary retention, which in turn can lead to dilatation of the upper urinary tract and bladder dysfunction. This condition, if left untreated, may lead to progressive renal impairment and ultimately to irreversible renal failure (Murad et al., 2023, Speakman et al., 2015, Zeng et al., 2022). In addition, patients with BPH often incur high medical costs due to repeated visits to the doctor, diagnostic tests, and medications, resulting in significant financial burden and inconvenience. Understanding the natural course and risk factors of BPH and developing individualized management plans are important for improving patient prognosis and reducing the consumption of medical resources.

As the global population ages, the number of patients suffering from BPH is gradually increasing (Ojewola et al., 2017). The prevalence of BPH increases significantly with age. Global surveys show that BPH is present in about 8% of men in their 40s, and by the age of 90, the percentage is as high as 90% (McVary, 2006). Up to 50% of these men over the age of 50 and 80% of men in their 80s suffer from LUTS caused by BPH (Vos et al., 2012). Approximately half of BPH patients have symptoms related to their LUTS. Compared to other locations and ethnic groups, Asians are more likely to experience moderate to severe lower urinary tract symptoms, although having a reduced risk of getting BPH (Lee et al., 2021). In addition to age, other factors such as race and geographic region influence the prevalence and presentation of BPH. Although Asian men have a relatively low prevalence of BPH, they are more likely to experience moderate to severe LUTS than men of other regions and ethnicities. This difference may be related to differences in genetics, lifestyle, dietary habits, and health care patterns. In addition, the prevalence of BPH and severity of symptoms may be influenced by individual hormone levels, metabolic syndrome, and co-morbidities such as cardiovascular disease. Therefore, it is necessary to consider these multidimensional influences in future epidemiologic studies and health policy development. In conclusion, BPH will become a major health problem for middle-aged and older men worldwide, and its high prevalence and associated reduced quality of life need to be of great concern to the medical community.

The pathogenesis of BPH is complex and has not been fully elucidated. Possible triggers include bacterial infection, urinary reflux, dietary environmental factors and estrogenic effects (Nakai et al., 2013). In the American Urological Association (AUA) guidelines for BPH, treatments for BPH are mentioned to include medication, minimally invasive treatment and surgery (Dornbier et al., 2020). Treatment options for BPH depend on the severity of symptoms, the size of the prostate, and the patient's general health. Mild to moderate prostate enlargement can usually be managed with medications, lifestyle changes and watchful waiting (Rosenberg et al., 2014). Surgery is the treatment of choice for patients with severe symptoms or complications such as urinary retention, bladder stones or kidney damage (Chughtai et al., 2022). Open surgery is the traditional surgical method, which is the most thorough for removing prostate hyperplasia tissue, especially for patients with large prostate size or with stones or tumors. However, open prostatectomy has the disadvantages of high trauma, long bladder drainage time, long postoperative recovery time and high surgical risk (Yeong Uk Kim et al., 2021). As medical science has advanced, a number of new procedures have been progressively used to treat BPH. For larger prostates, minimally invasive alternatives to open surgery, such as robot-assisted simple prostatectomy (RASP) and holmium laser enucleation of the prostate (HoLEP), have been used more frequently (H. S. Kim et al., 2023). In addition, minimally invasive treatments for BPH include transurethral microwave therapy (TUMT), transurethral needle ablation therapy (TUNA), transurethral electrification therapy (TUVP), transurethral resection of the prostate (TURP), and intraurethral stenting, among others (Yu et al., 2007). However, Thangasamy's 2012 Meta-analysis has confirmed that TURP is the "gold standard" for the treatment of BPH (Thangasamy et al., 2012). Because TURP surgery passes through the natural cavity without passing through the pelvis, it has the advantages of less risk of bleeding, lower probability of blood transfusion, quicker postoperative recovery, and shorter hospitalization than open surgery, but it also has a higher reoperation rate (Djavan et al., 2018, Yeong Uk Kim et al., 2021).

However, TURP surgery is also associated with significant surgical risks and postoperative complications, such as higher intraoperative bleeding, clot retention, postoperative urinary incontinence, retrograde ejaculation, erectile dysfunction, and urethral stricture in the presence of a large prostate volume (Gilling et al., 2018, Schwartz et al., 2011). Intraoperative bleeding is one of the most common complications, and the risk of bleeding increases significantly, especially if the prostate is large or highly vascularized (Gan et al., 2021, Kavanagh et al., 2011). In addition, retrograde ejaculation is caused by injury to the internal urethral sphincter during surgical resection and may affect the patient's sexual function and fertility. Erectile dysfunction, on the other hand, may be associated with surgery-related neurovascular bundle damage, further affecting patients' quality of life (Bearelly et al., 2021, Egui Rojo et al., 2020). Urethral stricture can occur in various parts of the urethra such as external urethra, urethral bulb, membrane, prostate, and internal urethra, and it is usually seen in the weeks to months after surgery. Its clinical manifestation is difficulty in urination, and patients experience urinary frequency, urgency, and incontinence, causing urinary retention. If the condition is serious and lasts for a long time, it may develop into pyelonephrosis, renal atrophy, and eventually lead to kidney failure and other serious consequences (Abdeen et al., 2023, Blandy, 1980).

1.2 Problem statement & Study rationale

Urethral stricture is a narrowing of the urethra, usually due to scar tissue formation caused by a number of factors, including urethral trauma, infection, or instrumental manipulation. The pathophysiological mechanism involves injury to the urethral epithelium, leading to inflammation and spongy fibrous tissue changes. Accumulation of fibrous tissue leads to compression and constriction of the urethral lumen. The transformation of the urethral epithelium into a complex squamous epithelium makes it more susceptible to pressure changes and stretching trauma, which may further aggravate the condition (Mangir et al., 2020, Mundy et al., 2011, M. Singh et al., 1976). The main manifestations of urethral stricture after TURP include postoperative dyspareunia, painful intercourse, thinning of the urine line, divergence of the urine stream, hesitation to urinate, and subsequent urinary retention (Latini et al., 2014). Studies have shown that trauma caused by catheterization and transurethral endoscopic interventions also contribute to urethral strictures. These procedures can directly damage the lining of the urethra, leading to scar formation (Akyuz et al., 2023). In addition, urethral inflammation, catheter irritation, surgical trauma scarring, cystoscopy, and repeated movement of the electrosurgical scope in the urethra during TURP are potential risk factors for the development of postoperative urethral stricture. Inflammation of the urethra, especially chronic inflammation, can further contribute to scar tissue formation and complicate the stricture situation. Prolonged retention of the catheter may also lead to persistent damage and maladaptive healing of the local mucosa, increasing the chances of stricture development (Mangera et al., 2016, Stein et al., 2013). However, the exact etiology and mechanism of development of urethral stricture after TURP is not yet clear.

A review of the literature revealed that the exact etiology of urethral stricture after TURP is still controversial, despite the fact that there are several hypotheses that can explain the cause of urethral stricture after TURP (Wessells et al., 2023). After TURP, there are a number of potential causes of urethral stricture formation, including infection, mechanical damage, long-term indwelling catheter use, local anesthetic use, and electrical harm from stray currents. Certain forms of urethral strictures are not appropriate for a single treatment plan (Wang et al., 2020). The main factors reported to be associated with an increased incidence of urethral stricture after TURP are the use of monopolar energy, instrument calibre, and postoperative catheterization time (Pirola et al., 2022). Justin's report showed that smoking, age, infection and anterior urethroplasty were risk factors for recurrence of urethral stricture (Han et al., 2015). Ankur's study concluded that catheterization was a risk factor for the development of urethral stricture after surgery(Bansal et al., 2016). In Mang L's article, it was noted that the amount of intraoperative bleeding during TURP, residual blood clots, the duration of the procedure, the use of large-bore scope sheaths, the frequent movement of instruments during the procedure, and the adequacy of lubrication are all potential risk factors for triggering the development of urethral strictures after TURP (M. L. Chen et al., 2016). Recent reports have shown that duration of tube placement, length of hospital stay, and bladder irrigation time are risk factors for urethral stricture after TURP (F. Chen et al., 2023). However, due to the differences in geography, race, surgical procedure, sample size and other factors, there are quite a few differences in the results between different studies, and even opposite results may occur. The exact etiology and pathogenesis of urethral stricture after TURP are still not fully understood, although several possible factors have been identified. Postoperative strictures may also be significantly influenced by individual patient variations, including urethral architecture, tissue repair ability, and prior history of urethral disease. Therefore, in order to better understand the risk factors for urethral stricture following TURP surgery, this study was also carried out.

1.3 Research question(s)

This study aims to address two key research questions. First, what are the independent risk factors associated with the development of urethral stricture following transurethral resection of the prostate (TURP) in patients with benign prostatic hyperplasia (BPH)? Second, based on these identified risk factors, is it feasible to construct a predictive nomogram model that can estimate the individual risk of postoperative urethral stricture? By answering these questions, the study seeks not only to improve the understanding of potential etiological factors but also to provide clinicians with a practical tool for risk stratification and individualized patient management.

1.4 Objective

1.4.1 To identify the independent risk factors associated with the occurrence of urethral stricture following TURP in patients with BPH.

1.4.2 To construct and internally validate a nomogram model that can predict the risk of urethral stricture after TURP, thereby providing a practical tool for individualized risk assessment and clinical decision-making.

In clinical practice, early assessment of urethral stricture after TURP by urologists plays a key role in prevention and management. Therefore, it is crucial to be familiar with the risk factors associated with post-TURP urethral stricture. Despite the remarkable efficacy of TURP surgery in the treatment of BPH, the occurrence of postoperative urethral stricture remains one of the major clinical problems. Individual differences in different patients, technical operation during surgery, and postoperative management strategies may all have an impact on the incidence of urethral stricture. Therefore, the development of effective prediction models for the risk assessment of postoperative urethral stricture is of great clinical significance.

The aim of this study was to analyze in depth the causes of urethral stricture after TURP by reviewing patients' clinical data and to develop a prediction model based on these risk factors for predicting the probability of postoperative urethral stricture in patients with BPH requiring TURP surgery. To this end, detailed clinical and follow-up data of patients who underwent TURP surgery and were pathologically diagnosed with BPH between June 2020 and June 2023 at the Department of Urology, Affiliated Hospital of Chengdu University were collected in this study. These data include basic patient information (e.g., age, prostate volume, disease duration, etc.), preoperative comorbidities (e.g., hypertension, diabetes mellitus, etc.), surgery-related parameters (e.g., operative time, intraoperative bleeding, postoperative catheterization time, etc.), and laboratory indices (e.g., white blood cell counts, hemoglobin levels, etc.).

Through statistical analysis, this study delved into the specific risk factors affecting the occurrence of urethral stricture after TURP, and based on these factors, a multifactorial prediction model was established to calculate the probability of urethral stricture after TURP for each patient. The results of the study provide a scientific basis for clinical practice and help physicians conduct more accurate risk assessment and management before surgery. Based on the results, appropriate interventions, such as preoperative urethral dilatation, optimization of intraoperative techniques, rational choice of catheterization, and enhanced postoperative follow-up, can be implemented to reduce the incidence of US after TURP and improve the overall prognosis and quality of life of patients.

CHAPTER 2

LITERATURE REVIEW

2.1 Advantages of TURP

Since its introduction, TURP has rapidly replaced open prostatectomy as the treatment of choice for BPH. TURP is a minimally invasive procedure that does not require an external incision as the scope is inserted through the urethra into the prostate gland and the tissue within the prostate gland is trimmed through the natural lumen. TURP surgery is performed through the natural lumen without the need to traverse the pelvis and has the advantage of low risk of bleeding, less chance of blood transfusion, quicker postoperative recovery and shorter hospital stay compared to open surgery (Baten et al., 2017, Pirola et al., 2021). TURP is often more cost-effective than newer, more technologically advanced procedures such as robotic-assisted surgery (M. Kim et al., 2019). Studies have shown that some of the newer procedures, such as streaming radiofrequency water vapor thermotherapy (WVTT), transurethral microwave thermotherapy (TUMT), and temporary implantable nickel-titanium devices (TINDs), may result in more severe urinary symptoms compared to TURP for BPH (Franco et al., 2022). Results of an efficacy study of TUMT versus TURP for the treatment of symptomatic BPH in men showed that TURP provided greater symptomatic and urologic improvement and fewer subsequent BPH treatments (Hoffman et al., 2004). Holmium laser enucleation of the prostate (HoLEP) versus TURP for the treatment of BPH has also been shown to result in a lower incidence of postoperative dyspareunia and a shorter operative time after TURP (Yin et al., 2013). Studies comparing the cost-effectiveness and efficiency of

TUVP over TURP have shown that TUVP is less costly but less effective (Lourenco et al., 2008). In a study comparing the long-term outcomes of open prostatectomy (OP), TURP, and transurethral microwave therapy for the treatment of BPH with a follow-up of more than 10 years, the TURP had the best long-term results and was more sustainable (Reich et al., 2006). Bipolar TURP has been shown in urodynamic studies to be effective in relieving bladder outlet obstruction, and this effect appears to be durable with a low incidence of long-term complications. In vitro studies have confirmed the superior hemostatic ability of bipolar currents. Postoperative bleeding and transfusion rates were similar between bipolar and unipolar TURP, but the incidence of clot retention and TUR syndrome was significantly lower in patients receiving bipolar TURP (Mamoulakis et al., 2009, Michielsen et al., 2010, Wei et al., 2016).

In summary, taking into account the cost-effectiveness, surgical success, intraoperative bleeding risk, operative time, postoperative complications, recovery, and overall hospitalization time and cost of novel surgery versus TURP in the treatment of BPH, TURP remains the current treatment of choice for BPH.

2.2 Diagnosis of urethral stricture

The most common symptoms of urethral stricture include decreased urine flow and incomplete emptying of the bladder, which may also manifest as urinary tract infections, epididymitis, increased residual urine volume, decreased ejaculatory capacity, or difficulty urinating. Less common symptoms include hydronephrosis, urethral fistula, or periurethral abscess. Recurrent urethral strictures may cause similar symptoms. Some male patients may have associated sexual dysfunction, with erectile dysfunction being more common than ejaculatory dysfunction. In recent years, diagnostic strategies for urethral strictures have become well known to clinicians. When evaluating a patient with urethral stricture, one should begin with a detailed history taking. The possibility of urethral stricture should be highly suspected if the patient has a history of urethral hypospadias, post hypospadias repair, post urethral dilatation, or post endourethral incision with symptoms of obstruction (Gelman et al., 2020). Therefore, the diagnosis of urethral stricture is usually based on the patient's clinical symptoms, history, and signs, supplemented by a variety of imaging tests. In recent decades, many new examination techniques have been developed to more accurately determine the location and severity of urethral stricture and its surrounding scar tissue.

Urethroscopy is an easy and rapid diagnostic method to clarify the site and extent of urethral stricture (with or without cystoscopy). However, when the stricture segment is too narrow to pass through a cystoscope, no additional information about the proximal urethra can be obtained. In such cases, the use of a smaller caliber ureteroscope (e.g., 4.5 Fr or 6 Fr) may be helpful because it is able to pass through the narrowed segment, thus providing a view of the proximal urethra (Shahrour et al., 2018). It is important to note that urethroscopy is unable to visualize the peri-spongiosa, and therefore it is often considered insufficient to fully diagnose urethral strictures on the basis of urethroscopy alone. In most cases, it is necessary to combine it with additional imaging to obtain comprehensive information. Retrograde urography (RUG) is a test in which a contrast agent is injected through the urethra to visualize the entire urethra. However, RUG may result in inadequate urethral dilatation of the proximal stenotic segment, making it difficult to accurately assess the extent of the proximal stenotic segment and the condition of the urethra. To compensate for this deficiency, voiding cystourethrography (VCUG) can be an effective complement to RUG, and the combination of RUG and VCUG provides a comprehensive view of the entire urethra, providing important information about the number, length, location, and extent of strictures (Childs et al., 2019). However, when the stricture segment is located in the bulb of the urethra, dilatation of the anterior end of the stricture segment may mask the actual extent of the stricture, resulting in an underestimation of the observed stricture length. In addition, similar to cystourethroscopy, RUG is unable to visualize the peri-spongiosa. Urethral MRI and computed tomography (CT) play an important role in the diagnosis of urethral strictures. In urethral strictures caused by trauma, MRI is a very useful tool to show the extent of bleeding in the tissues surrounding the urethral stricture (e.g., corpus spongiosum). However, the routine clinical use of MRI remains controversial. Recently, Horiguchi et al. have proposed that urethral MRI can be used to measure the length and extent of urethral stricture in cases of complex trauma resulting in complete occlusion of the posterior urethra and to predict the type of urethral reconstruction surgery required based on preoperative MRI findings. This new urethral MRI shows promise in guiding urethral reconstruction in complex cases (Horiguchi et al., 2018). Meanwhile, urethral CT provides valuable information for fistula-related urethral strictures and helps to further evaluate urethral injuries(Lv et al., 2016).

First, based on the patient's readmission history, physical examination and the patient's clinical presentation, urinary tract stricture may be present in patients with symptoms such as dysuria, hesitancy to urinate, poor stream, urinary stream divergence, and dribbling of urine (Campos-Juanatey et al., 2021). The patient's maximal urinary flow rate is then further measured, and its reduction further increases the likelihood of a stricture occurring (Lambert et al., 2018). Ultimately, retrograde urethrography can confirm the occurrence of urethral strictures.

Retrograde urethrography assesses the presence, location, length, and any associated abnormalities of the stricture (Mahmud et al., 2008). In some patients, the diagnosis of urethral stricture is confirmed by an outpatient urethral ultrasonography examination (Morey, 2017).

In this study, a series of examinations were performed following the steps described above in patients with BPH who had significant voiding difficulties after undergoing TURP. The diagnosis was confirmed by further measurement of maximal urinary flow rate from the clinical manifestation of dysuria and finally by urography. A maximum flow rate of <10 mL/s measured by urine flowmetry in this study was considered to indicate the occurrence of urethral stricture (Virasoro et al., 2022). Urethroscopy and urethrography were performed to differentiate urethral stricture from bladder neck contracture. Urethral endoscopy was able to further define the stricture ring lesion (Ayoob et al., 2020). Figure 2.1 shows the test report of urethrogram in a patient with urethral stricture.

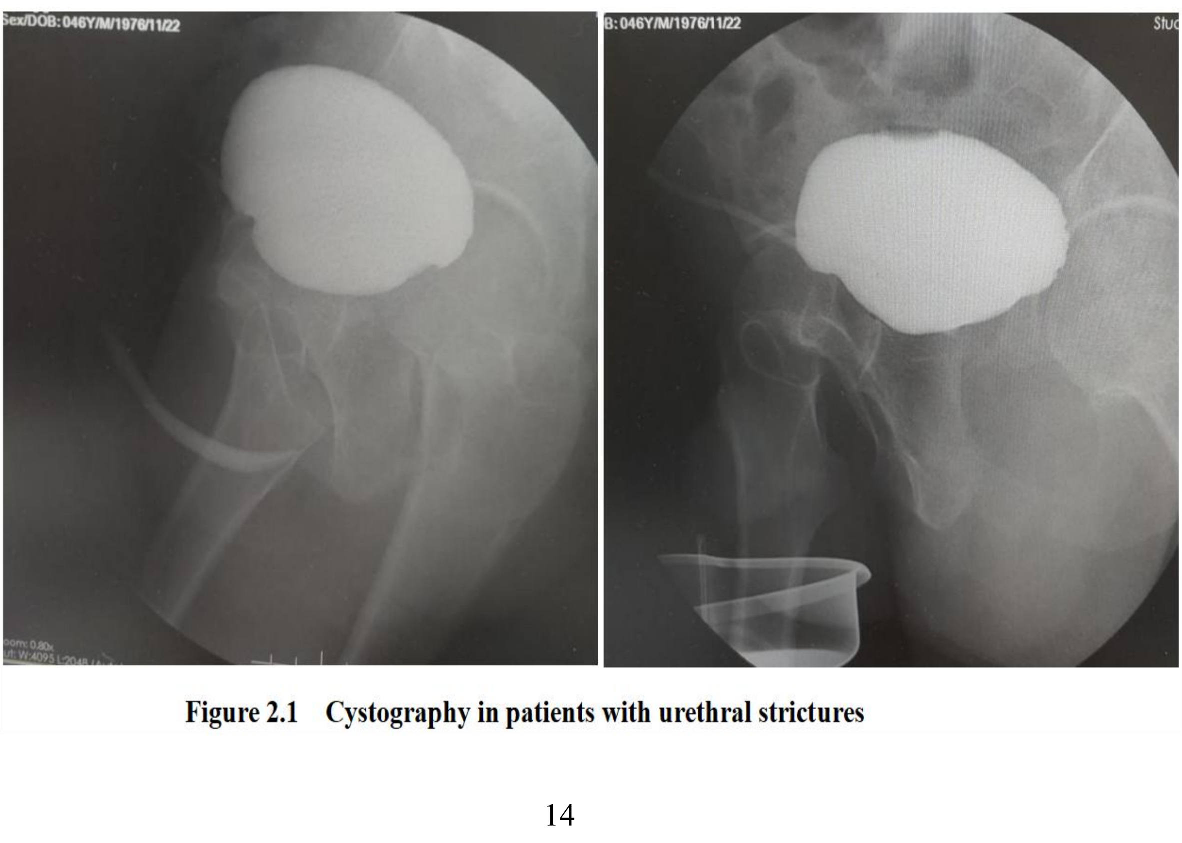

Figure 2.1 Cystography in patients with urethral strictures

2.3 Treatment of urethral stricture

Currently, the most thorough way to treat urethral stricture is surgical intervention, but the specific treatment plan needs to be determined based on the individual situation of the patient. The causes of urethral stricture include infection, trauma, congenital factors and other factors. Therefore, the most appropriate treatment method is different for different situations, including anti-inflammatory treatment, urethral dilation, internal urethrotomy and stent placement. Enter and wait. In complex cases of urethral stricture, urethroplasty surgery may need to be considered. The surgical treatments can be categorized into intraluminal and extraluminal (Reynard et al., 2003, Wessells et al., 2023). Endoluminal techniques are becoming one of the most important treatments for urethral strictures due to their ease of use, less invasiveness, rapid recovery, safety and fewer complications. With the popularization of plasma knives and lasers, as well as the use of new urethral stents and grafts, endoscopic procedures have become more convenient and less invasive. However, due to the complex anatomy and diverse etiology of urethral strictures, the results of endoluminal treatment are still not ideal, and a significant number of patients still have poor long-term outcomes (J. M. Zhu et al., 2021).

Following TURP, treatment options for urethral strictures include open surgery utilizing various urethroplasty techniques or minimally invasive endoscopic procedures such urethral dilatation and direct visualization of the incision. Despite the paucity and scarcity of scientific research on urethral strictures following TURP, we can assess each case individually using the management guidelines for urethral strictures before determining on a treatment plan (Wang and Man, 2020). Endovascular surgery, including urethral dilation and DVIU, is currently the most common and important treatment method (Xu et al., 2015). Although endoluminal techniques are still widely used to treat urethral strictures, there is a possibility of recurrence because this type of surgery only restores the continuity of the urethra without completely removing the scar tissue that forms the urethral stricture (Xu et al., 2015). Urethral dilation uses urethral probes, balloon dilators and other equipment to forcibly stretch the narrow urethra, prompting the urethral mucosa to heal again, thereby improving the symptoms of urethral stricture. However, this method is only effective in cases with short stenosis segments. Studies have shown that the stricture-free rate after high-pressure balloon dilatation (BD) for urethral stricture is 84% (Beeder et al., 2022).

2.4 Bleeding during TURP and secondary bleeding after surgery

The prostate is one of the organs with the richest blood supply in the male genitourinary system, and therefore any type of prostatectomy is accompanied by the risk of bleeding. Intraoperative and postoperative bleeding is one of the most common complications of TURP. The incidence of intraoperative blood transfusion in TURP was reported to be 2.6% by Berger et al (Berger et al., 2004). The extent of intraoperative bleeding is closely related to the size and texture of the prostate and the experience of the operator. Difficulty in positioning the prostate during prostatectomy by the operator is the main cause of bleeding (Weng et al., 2023). Arterial hemorrhage often occurs at the 5 and 7 o'clock positions at the junction of the bladder neck and the prostate envelope. Beginners often experience irregular tissue cuts, uneven surfaces and attached debris during electrodessication, making it difficult to detect bleeding points. Therefore, it is necessary to remove the uneven tissues and identify the bleeding point before effective hemostasis; if the field of view is clear, the electrodes can reach the peritoneum before hemostasis, thus speeding up the speed of electrodes.

Chow et al. reported a postoperative bleeding rate of 12% for TURP (Chow et al., 1998). Therefore, improving the operating technique of TURP surgery and adequate intraoperative hemostasis, especially strengthening hemostasis at points 5, 7, and 12 of the bladder neck, are essential to prevent postoperative bleeding. In addition, postoperative maintenance of smooth bladder irrigation as well as prevention of constipation are also key measures to prevent postoperative bleeding after TURP. In patients with recurrent recalcitrant bleeding after TURP, Frederic et al. used internal iliac artery embolization with good results (Michel et al., 2002).Discontinuation of anticoagulants and antiplatelet agents is recommended preoperatively, along with a thorough assessment of the risk of thrombosis. To minimize bleeding, pharmacological interventions such as 5α-reductase inhibitors may be considered in the perioperative period. Technically, the use of hemostatic means such as laser and bipolar electrodes should be considered (Kavanagh et al., 2011, Y. P. Zhu et al., 2015). It has been shown that short-term pretreatment of patients with finasteride and dutasteride. Both have been shown to significantly reduce perioperative bleeding during TURP with minimal negative effects on sexual function (Bansal et al., 2017, Kloping et al., 2022). However, the risk of bleeding is always present regardless of the surgical technique used. Urologists must be familiar with how to best prevent and manage bleeding complications associated with TURP

2.5 Urinary incontinence after TURP

Urinary incontinence is one of the common complications after TURP, which significantly affects the quality of life of patients (Hunter et al., 2007, Johnson et al., 2023). Once it occurs, it will seriously affect the patient's daily life. Early incontinence usually presents as urgency and is usually caused by irritants such as healing prostate fossa, associated urinary tract infection (UTI), or forcing muscle instability (Eastham et al., 1996). Symptomatic treatment should include a short-term regimen of selective anticholinergic agents and anti-inflammatory therapy. For urinary incontinence that has persisted for more than 6 months, a thorough evaluation including upper urethrogram, cystourethroscopy, and urodynamic evaluation is indicated (Castellani et al., 2022, Kollmeier et al., 2005, Zwergel, 2001). The study by Varkarakis et al. reported that the incidence of urinary incontinence after TURP was 3.5% (Varkarakis et al., 2004). The incidence of urinary incontinence has been reported to be 6.3%, with the majority of patients recovering within 12 weeks of surgery, and only a minority of patients becoming permanently incontinent (Wei Dong, 2004). The occurrence of urinary incontinence is mainly attributed to the following factors: failure of the closing mechanism of the external sphincter due to localized inflammatory edema, overactivity of the bladder's urethral muscles or decreased bladder compliance, prolonged compression by hyperplastic glands that keep the external sphincter in a state of hyperextension, mild injury to the external sphincter caused by high-frequency electrical currents, and compression of the external sphincter by misplacement of a catheter balloon in the prostate fossa (Anderson et al., 2015, Hunter et al., 2007).

In a study by Singh et al, the implantation of an artificial urethral sphincter was shown to be one of the best treatments for permanent urinary incontinence, with an efficiency rate of 96%, effectively preventing leakage by compressing the urethra (G. Singh et al., 1996). However, this method has some complications and is expensive. Other reports have shown favorable results using bulbocavernosus suspension for the treatment of severe post-prostatectomy urinary incontinence (Petrou, 2002). Specific treatment should be chosen based on the cause of the disease. If symptoms are caused by incomplete tissue removal, patients may be treated with alpha receptor blockers or undergo reoperation. Surgery may also be considered for severe urethral strictures or bladder neck contractures. If symptoms are not caused by obstruction, they can be managed with medications such as anticholinergics or β-3 adrenergic receptor agonists (Chughtai et al., 2016, Dahm et al., 2017, Yuan et al., 2015). Several studies have shown that pelvic floor muscle exercise (PME) can more quickly improve urinary symptoms and quality of life in patients after TURP. Early practice of PME can reduce symptoms of incontinence and postvoiding dribbling in the first few weeks after surgery (M. Ali et al., 2022, Porru et al., 2001, Xin et al., 2023). In addition, in a study by Hou et al, 66 patients treated with TURP were randomized into a group that received PFME (pelvic floor muscle exercise) after surgery and a control group. At the 12-week postoperative follow-up, the patients who received PFME showed significant symptomatic improvement. Therefore, it is important to instruct patients to perform bladder function training after surgery for the treatment of transient urinary incontinence (Hou et al., 2013).

2.6 Sexual dysfunction after TURP

The main effects of TURP on sexual function are penile erectile dysfunction and retrograde ejaculation. One study reported an 11% incidence of erectile dysfunction and 82% incidence of retrograde ejaculation 6 months after TURP (Liang et al., 2003). The innervation for erection comes from the pelvic plexus, and the cavernous nerves, accompanied by blood vessels, are distributed lateral to the prostatic envelope and pass posteriorly and laterally through the apical part of the prostate (at 5 and 7 o'clock), the membranous urethra at 3 and 9 o'clock, and the bulbar urethra at 1 and 11 o'clock, ultimately entering the corpus cavernosum of the penis and the cavernous body of the urethra. The deep penile artery emanates from the internal pubic artery and crosses the urogenital compartment into the corpus cavernosum. Intraoperative thermal damage to the bundle of erectile neurovascularity conducted to the extraperitoneal peritoneum may be a major cause of erectile dysfunction if the power of electrodesiccation or electrocoagulation is used inappropriately. This is usually due to the removal of the circumferential fibrous tissue in the bladder neck during electrosurgical excision of the prostate tissue in that area; if too much is removed, the normal closure of the bladder neck during ejaculation is disrupted, leading to retrograde ejaculation (Li et al., 2016, Liang et al., 2003, Zong et al., 2012). Most of the literature reports a high incidence of sexual dysfunction after TURP. The preventive measures are to avoid excessive electrocoagulation to cauterize the lateral wall of the prostate peritoneum, to ensure that the prostate peritoneum is not cut through, and to maximize. More dangerously, thrombus fragments may follow the blood flow into the blood vessels of the lungs and brain, leading to pulmonary embolism and cerebral embolism, which can significantly increase a patient's postoperative mortality. Studies have shown that urologic surgery patients are at a higher risk of bleeding within the first 4 days after surgery, and the risk of thrombosis is even more prolonged, with the possibility of VTE persisting up to 28 days after surgery.

Therefore, prevention of postoperative VTE is critical (Allaway et al., 2021, Rodrigues et al., 2002, Tikkinen et al., 2018). Studies have shown that retrograde ejaculation occurred in 136 (51.5%) of 264 post-TURP patients who were followed up. Special attention must be paid to psychological aspects before and after surgery, which may become an important factor in the decline of sexual activity (Pavone et al., 2015). In addition, data suggest that preserving some of the residual prostate tissue during TURP surgery significantly reduces the incidence of retrograde ejaculation. It is important to note that the preservation of ejaculatory function is not entirely dependent on the integrity of the internal sphincter. Most of the literature reports a high incidence of sexual dysfunction after TURP. To minimize the occurrence of this complication, it is currently recommended to avoid excessive electrocautery of the lateral prostate wall envelope during the procedure, to ensure that the prostate envelope is not cut through, and to preserve the bladder neck as much as possible (Tscholl et al., 1995).

2.7 VTE after TURP

Venous thromboembolism (VTE) is a common vascular disease that is usually categorized into deep vein thrombosis (DVT) and pulmonary thromboembolism (PE). It is a fatal complication of postoperative (Rodrigues et al., 2002, Schulman et al., 2017). Without intervention with thromboprophylaxis, patients undergoing non-oncologic surgical treatments have a higher risk of VTE within 2 months after surgery, and approximately 4% of patients die from related complications within 90 days (Expósito-Ruiz et al., 2021). VTE is a common and potentially fatal postoperative complication, the third leading cause of cardiovascular disease-related death, and has attracted increasing attention from clinicians in recent years (Allaway et al., 2021, Gerhold et al., 2024). According to Virchow, the pathogenesis of VTE can be organized into three broad categories: blood stasis, vascular endothelial damage, and hypercoagulability (Esmon, 2009). Zheng's study found that the incidence of VTE after TURP was 10.9%, with DVT at 3.0%, (PE at 0.69%, and superficial vein thrombosis at 7.9% (Zhihuan et al., 2022).

Venous thrombosis is a complication that has long-term implications for patients and may lead to an increased incidence of venous insufficiency, chronic leg swelling and ulcers. In addition, the presence of postoperative venous thrombosis can prolong the average length of a patient's hospital stay, complicate diagnostic procedures and treatment plans, and significantly increase hospitalization costs (Golash et al., 2002). Currently, thromboprophylaxis after TURP mainly relies on mechanical prophylaxis. Compared with anticoagulants, mechanical prophylaxis has a lower risk of postoperative bleeding and is relatively simple to perform, making it feasible in clinical practice. However, contraindications and limitations should be noted: mechanical prophylaxis is not suitable for patients with congestive heart failure or pulmonary edema; it is not suitable for patients with localized abnormalities of the lower limbs, such as localized skin infections or defects, severe lower limb edema, lower limb deformities, ischemic vascular disease, or gangrene, etc.; mechanical prophylaxis is not recommended in patients with diagnosed new-onset venous thrombosis or thrombophlebitis. Prophylaxis (J. Kim et al., 2023, Tikkinen et al., 2018).

2.8 Other complications after TURP

A variety of complications may occur after TURP, including acute epididymitis, seminal vesiculitis, pneumonia, and pyelonephritis, and these usually need to be managed with anti-inflammatory medications and other symptomatic treatments (Koşar et al., 1999). In addition, rare cases of penile head necrosis due to prolonged or improperly placed postoperative catheterization have been reported in the literature (Akyuz et al., 2023).

With the widespread use of TURP in clinical practice, prevention of these complications has become particularly important. To this end, urologists should be proficient in the technique of electrodesiccation, reasonably controlling the depth and range of electrodesiccation to reduce the risk of surgical trauma and bleeding;

thoroughly stopping bleeding to avoid postoperative hematoma formation; and avoiding damage to the peritoneum of the prostate to prevent the occurrence of perforation. In addition, the appropriate catheter type and specification should be selected according to the patient's individual condition, and the catheter should be left in place for as short a time as possible to reduce the risk of infection and other complications. Postoperatively, patient monitoring should also be strengthened, including regular checking of vital signs and urine status, in order to detect and manage potential infections or other complications in a timely manner. With these comprehensive measures, the complication rate after TURP can be significantly reduced, thus improving the prognosis and quality of life of patients.

2.9 Conceptual Framework

This conceptual framework provides a systematic explanation of the mechanisms underlying urethral stricture after transurethral resection of the prostate (TURP) and outlines potential strategies for prevention. It emphasizes that preoperative factors (e.g., advanced age, enlarged prostate volume, indwelling catheterization), intraoperative factors (e.g., mechanical trauma, ischemia), and postoperative factors act synergistically along a pathophysiological cascade of "urethral mucosal injury → inflammatory response → fibrosis/scar formation," ultimately leading to stricture. Based on this mechanism, a three-level prevention strategy is proposed: preoperative urethral dilation as a protective measure, minimizing intraoperative trauma, and reducing postoperative catheterization duration. Furthermore, a nomogram model with excellent predictive performance (AUC = 0.916) is incorporated for individualized risk stratification, enabling early and precise prevention. This framework integrates etiology, mechanisms, interventions, and prediction into a comprehensive and clinically applicable model (Figure 2.2).

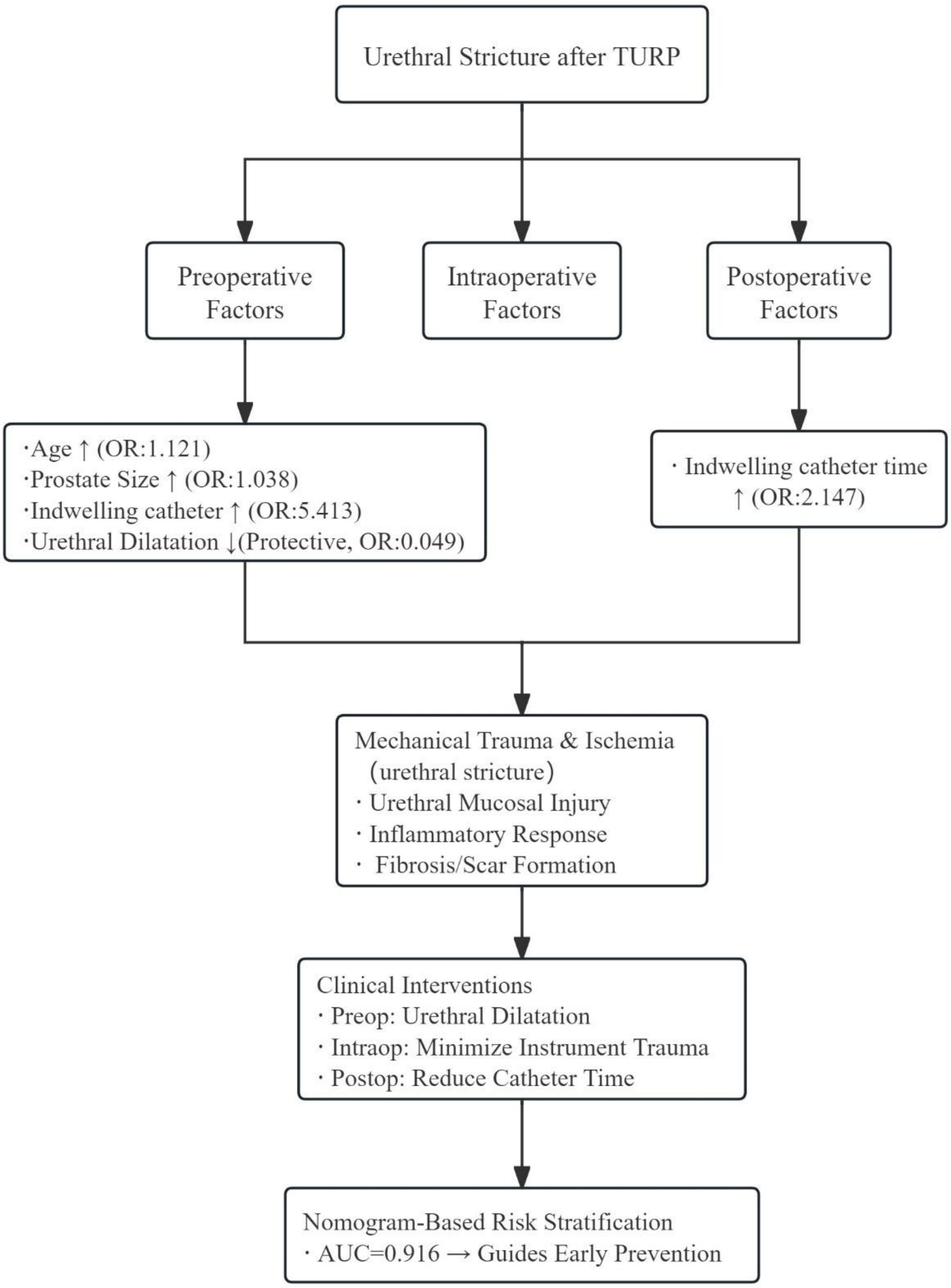

Figure 2.2 Conceptual framework diagram