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ABSTRACT

Benign prostatic hyperplasia (BPH) is a prevalent age-related condition among men and is a common cause of quality of life-impairing lower urinary tract symptoms (LUTS). Although transurethral procedures to relieve LUTS are generally considered low risk, a subset of patients experience significant short- and long-term morbidity, and, in some cases, mortality.

In this thesis, trends in surgical utilisation in Finland were assessed. Short- and long-term risks between photoselective vaporisation of the prostate (PVP) and transurethral resection of the prostate (TURP) were compared, and postoperative mortality and its risk factors after surgery for LUTS were evaluated.

The incidence of surgical interventions for LUTS remained stable (263 per 100,000) despite demographic changes. Hospital stays were shortened, while treated patients grew older. The observed trends between 2004 and 2018 reflected a shift toward outpatient care and delayed intervention, likely influenced by pharmacotherapy and the adoption of PVP. PVP showed a lower risk of reoperation due to bleeding (0.9%), which was even more pronounced in patients with atrial fibrillation. However, in the long-term 12-year follow-up, the reoperation rate after PVP was higher (23.5% vs 17.8% with TURP). These results underscored the short-term safety of PVP, particularly for patients with heightened bleeding risk. They also highlighted its limitations with respect to long-term durability compared to TURP. The real-world overall 90-day postoperative mortality rate was 1.10%, with excess mortality remaining below 0.5% across all age groups. PVP was associated with a lower mortality rate (0.59%) than TURP (1.16%). Age, Charlson Comorbidity Index, atrial fibrillation, and earlier study era were identified as independent risk factors for mortality.

These studies emphasise the importance of tailoring treatment strategies to individual patient profiles. They also highlight the need to enhance preoperative risk assessment and to pursue further research into durable surgical options to optimise the management of LUTS in an aging demographic.

KEYWORDS: Benign prostatic hyperplasia, lower urinary tract symptoms, mortality, complications

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Eturauhasen hyvänlaatuinen liikakasvu on yleinen ikääntyvien miesten sairaus, ja yksi elämänlaatua heikentävien virtsaamisoireiden aiheuttajista. Jos elintapamuutokset ja lääkkeellinen hoito osoittautuvat riittämättömiksi, eturauhasen aiheuttama obstruktio voidaan laukaista kirurgisesti. Vaikka eturauhasen hyvänlaatuisen liikakasvun kirurgista hoitoa on pidetty vähäriskisenä, toimenpiteiden jälkeen voi esiintyä komplikaatiota ja kuolleisuutta.

Tässä väitöskirjassa havainnoitiin eturauhasen kirurgisten toimenpiteiden käytön kehityssuuntia Suomessa, vertailtiin lyhyen ja pitkän aikavälin riskejä eturauhasen höyläystoimenpiteen (TURP) ja eturauhasen viherlaser höyrystyksen (PVP) välillä, sekä arvioitiin eturauhasen hyvänlaatuisen liikakasvun kirurgiseen hoitoon liittyvää kuolleisuutta ja sen riskitekijöitä.

Vuosien 2004 ja 2018 välillä virtsaamisoireiden kirurgisen hoidon esiintyvyys pysyi vakaana (263 per 100,000) väestödemografian muutoksista huolimatta. Tarkastelujakson aikana toimenpiteiden jälkeisen sairaalahoidon kesto lyheni, vaikka potilaiden keski-ikä kasvoi. PVP:en liittyi merkittävästi alhaisempi verenvuotoon liittyvien uusintatoimenpiteiden riski (0.9 %), mikä korostui eteisvärinää sairastavilla potilailla. 12 vuoden pitkäaikaisseurannassa uusintatoimenpiteiden määrä oli kuitenkin merkittävästi korkeampi PVP:n (23.5 % vs 17.8 % TURP:n) jälkeen. Nämä tulokset korostivat PVP:n välitöntä turvallisuutta erityisesti vuotoriskissä olevilla potilailla, mutta paljastivat pitkäaikaisseurannassa sen rajoitukset kestävästä oireiden lievityksestä TURP:iin verrattuna. Virtsaamisoireiden kirurgisen hoidon jälkeinen kuolleisuus oli 1.10 % 90-päivän sisällä toimenpiteestä. Ero väestön normaaliin kuolleisuusriskiin oli alle 0.5 % kaikissa ikäryhmissä. PVP:n jälkeinen kuolleisuusriski (0.59 %) oli alhaisempi kuin TURP:n (1.16 %). Potilaan ikä, perussairauksien taakka, diagnosoitu eteisvärinä sekä toimenpide tutkimusjakson aikaisemmalla puolikkaalla olivat riskitekijöitä korkeammalle kuolleisuusriskille.

Väitöskirjan tulokset korostavat yksilöllisen hoitosuunnitelman ja potilasvalinnan tärkeyttä, ja kannustavat kehittämään perioperatiivista riskinarviota, sekä tutkimaan toimenpidevaihtoehtoja miesten virtsaamisoireiden hoidon optimoimiseksi ikääntyvässä väestössä.

AVAINSANAT: Eturauhasen hyvänlaatuinen liikakasvu, virtsaamisoireet, kuolleisuus, komplikaatiot

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Abbreviations

5-ARI	5α-reductase inhibitor
AE	Adverse event
AF	Atrial fibrillation
BNS	Bladder neck stenosis
BOO	Bladder outlet obstruction
BPE	Benign prostatic enlargement
BPH	Benign prostatic hyperplasia
BPO	Benign prostatic obstruction
B-TURP	Bipolar transurethral resection of the prostate
CCI	Charlson Comorbidity Index
CI	Confidence interval
CRHF	Care Register for Healthcare in Finland
DAN-PSS	Danish prostate symptom score
EAU	European Association of Urology
EEP	Endoscopic enucleation of the prostate
HoLEP	Holmium laser enucleation of the prostate
HR	Hazard ratio
ICIQ	International Consultation on Incontinence Questionnaire
IFA	Irrigation fluid absorption
IPSS	International prostate symptom score
IPTW	Inverse probability of treatment weighting
IQR	Interquartile range
LUTS	Lower urinary tract symptoms
MACE	Major adverse cardiovascular event
MISP	Minimally invasive simple prostatectomy
MRI	Magnetic resonance imaging
M-TURP	Monopolar transurethral resection of the prostate
NCSP	NOMESCO Classification of Surgical Procedures
NNT	Number needed to treat
NOMESCO	Nordic Medico-Statistical Committee
OAC	Oral anticoagulation

OP	Open prostatectomy
PAE	Prostatic artery embolisation
PCA	Prostate cancer
PSA	Prostate-specific antigen
PUL	Prostatic urethral lift
PVP	Photoselective vaporisation of the prostate
PVR	Post-void residual urine
Q_{max}	Peak flow rate
Qol	Quality of life
RASP	Robotic-assisted simple prostatectomy
RCT	Randomised controlled trial
RR	Relative risk
SD	Standard deviation
SMD	Standardised mean difference
TUIP	Transurethral incision of the prostate
TULSA	Transurethral ultrasound ablation
TUMT	Transurethral microwave thermotherapy
TUNA	Transurethral needle ablation
TUR	Transurethral resection
TURP	Transurethral resection of the prostate
TUVP	Transurethral vaporisation of the prostate
UTI	Urinary tract infection

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Salmivalli, A., Boström, P., Nurminen, P., Kinnala, P., Kytö, V., & Ettala, O. (2024). National trends of surgery for benign prostatic hyperplasia in Finland. Scandinavian Journal of Urology, 59, 70–75. https://doi.org/10.2340/sju.v59.32425

II Salmivalli, A., Ettala, O., Nurminen, P., Kinnala, P., Boström, P. J., & Kytö, V. (2023). Short- and long-term risks of photoselective laser vaporization of the prostate: a population-based comparison with transurethral resection of the prostate. Annals of Medicine, 55(1), 1287–1294. https://doi.org/10.1080/07853890.2023.2192046

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III Salmivalli, A., Ettala, O., Boström, P.J. et al. Mortality after surgery for benign prostatic hyperplasia: a nationwide cohort study. World J Urol 40, 1785–1791 (2022). https://doi.org/10.1007/s00345-022-03999-0

1 Introduction

Lower urinary tract symptoms (LUTS) have typically been associated with bladder outlet obstruction (BOO). This most commonly occurs when histological benign prostatic hyperplasia (BPH) advances to benign prostatic enlargement (BPE) and subsequently to benign prostatic obstruction (BPO) (Abrams et al., 2002; Kupelian, 2006).

Current evidence reveals a greater complexity in this relationship. An increasing number of studies have shown that LUTS are a group of symptoms that are not specific to gender or organ. They are often associated with aging and are usually progressive in nature. (Chapple et al., 2008) Inability to empty the bladder may be due to BOO, detrusor underactivity of the bladder, or a combination of the two. Historically, storage symptoms in older men have been associated with prostatic pathology, whereas in women identical symptoms have been thought to originate from the bladder. (Chapple et al., 2008) However, BPH is a common condition in the aging male population, characterised by the non-malignant proliferation of prostatic tissue (Berry et al., 1984), which may cause LUTS.

The overall prevalence of BPH is increasing at a concerning pace globally. There seems to be a particularly pronounced impact in low- and middle-income countries experiencing swift demographic and epidemiological shifts. As global life expectancy continues to extend, the overall burden of BPH is anticipated to escalate further in the forthcoming years. This underscores the critical need for ongoing surveillance and strategic planning to address potential pressures on healthcare systems. (Awedew et al., 2022) As the prevalence of BPH grows, LUTS are becoming an increasingly common burden on quality of life in the aging male population. They also impose a significant economic burden (Hashim et al., 2025). Reducing urinary symptoms improves quality of life and may also reduce the risk of mortality (Welk & McClure, 2023).

Although pharmacological treatment, behavioural and dietary modifications constitute the first line of treatment, surgical intervention is necessary when pharmacological treatment is not suitable or sufficient. This is also required if the patient develops urinary retention, overflow incontinence, recurrent urinary tract infections, bladder stones, recurrent haematuria, renal insufficiency due to poor

bladder emptying, or a large bladder diverticulum (Lower urinary tract symptoms: Current Care Guidelines, 2025). Although transurethral resection of the prostate (TURP) continues to serve as the most utilised surgical treatment for BOO (LaBossiere et al., 2019; Malaeb et al., 2012; Morton et al., 2020; Patel & Bariol, 2019; Peyronnet et al., 2015; Schroeck et al., 2012), and remains the most extensively studied procedure (Cornu et al., 2025), a range of other transurethral ablative methods have been introduced. Among these, laser vaporisation of the prostate, mainly with a 532 nm "GreenLight" laser, has been widely adopted (Kaplan et al., 2024; Malaeb et al., 2012; Schroeck et al., 2012). The advent of newer techniques has sustained the use of traditional open prostatectomy (OP), particularly for larger prostates. However, its application is progressively declining (Bhojani et al., 2014; Cornu et al., 2015; Gilfrich et al., 2016).

Given the safety considerations for elderly and comorbid individuals, it is pertinent to explore the durability and mortality rates of the already adopted and widely accepted treatment modalities. The majority of ongoing clinical trials concentrate on medical interventions (Thomas et al., 2019) or newer minimally invasive treatments (Cornu et al., 2022). Estimates of mortality risk following endourologic surgery exhibit variation, and large-scale investigations are scarce (Eredics et al., 2018; Gilfrich et al., 2016; Patel et al., 2015). Moreover, definitive evidence remains lacking to conclusively determine whether the postoperative mortality rates differ among the more traditional procedure types (Bhojani et al., 2014).

Despite the growing popularity of endoscopic enucleation techniques (EEP), holmium laser enucleation of the prostate (HoLEP) appears to be underutilised. In contrast, photoselective vaporisation of the prostate (PVP) continues to be the most widely adopted laser-based method. (Kaplan et al., 2024; Shin et al., 2025) However, the evidence supporting the safety and long-term effectiveness of PVP relative to TURP remains insufficient, particularly for patients at elevated risk due to the use of oral anticoagulation therapy (OAC) (Cornu et al., 2025). Long-term follow-up data concerning PVP are predominantly available for up to 3 or 5 years postoperatively, with reoperation rates showing considerable variability (Al-Ansari et al., 2010; Elshal et al., 2012, 2013; Mordasini et al., 2018; Rassweiler et al., 2006; Ruszat et al., 2008).

As a multitude of newer minimally invasive treatment modalities for BOO are being introduced (Cornu et al., 2023; Cornu et al., 2025.), it is enlightening to look back at how the last major shift, the introduction of PVP, has changed the utilisation of other surgical modalities. The trends of surgical utilisation differ between countries; in the US (Florida), laser prostatectomies increased by 400%, replacing about half of the TURP procedures (Schroeck et al., 2012). In contrast, in Canada

(Ontario), the proportion of TURP decreased by 15.2% (LaBossiere et al., 2019), and in France the number of TURP and OP procedures decreased by 34.4% (Peyronnet et al., 2015), concurrent with the increase in PVP use. The past temporal trends may help to reflect future adaptations and navigate through the changing field of treatment for LUTS.

The aim of this thesis was to investigate changing utilisation trends of surgical treatment for BPH/LUTS, to evaluate and compare short- and long-term risks of photoselective vaporisation of the prostate and transurethral resection of the prostate, and to assess postoperative mortality rates and risk factors for mortality regarding transurethral resection of the prostate, laser vaporisation of the prostate, and open prostatectomy.

2 Review of the Literature

2.1 Epidemiology and risk factors of benign prostatic hyperplasia

The prevalence of BPH increases significantly with age (Berry et al., 1984; Kupelian, 2006; Martin et al., 2011), making it a major urological health issue globally (Awedew et al., 2022; Launer et al., 2021; Lee et al., 2017; Speakman et al., 2015). The global number of clinical diagnoses of BPH increased by 70.5% between 2000 and 2019. The age-standardised prevalence of the diagnosis was 2,480 (range 1,940–3,090) per 100,000 men (Awedew et al., 2022). The prevalence of histologically confirmed BPH is 50% in men aged 51–60 and increases up to 90% in men aged 81–90 years (Berry et al., 1984). The overall prevalence of LUTS in the population is estimated to be 18.7% (Kupelian, 2006) and increases up to 34% and 46% in age groups of men aged 60–69 and 70–80 years, respectively (Martin et al., 2011). The prevalence of BPH diagnosis varies geographically. The highest age-standardised prevalence rates are observed in Eastern Europe, Central Latin America, and Andean Latin America. The lowest rates occur in North Africa, the Middle East, and sub-Saharan Africa. (Awedew et al., 2022)

2.1.1 Age, genetic, and familial contributions

One of the strongest risk factors for BPH is age. BPH development likely begins before a male reaches 30 years of age. (Berry et al., 1984) As men age, the prostate continues to grow by an average of 2.5% per year (Sharkey et al., 2022). During the early phase of BPH growth (men aged 31–50), the weight of hyperplastic tissue doubles approximately every 4.5 years. In the mid phase (men aged 51–70), the doubling time extends to around 10 years and increases to more than 100 years in men aged over 70 (Berry et al., 1984). Growth of the peripheral zone volume of the prostate increases with age and peaks at 60–70 years of age. In contrast, the growth of the transition zone remains continuous without a peak across all ages (Sharkey et al., 2022).

There appears to be a genetic contribution to the aetiology of BPH. Family history is one of the risk factors for clinical BPH, and studies have suggested

Mendelian dominant inheritance of a gene associated with early-onset BPH (Pearson et al., 2003; Sanda et al., 1994). However, symptomatic or clinical BPH appears to have a weaker genetic component than early-onset BPH (Pearson et al., 2003). Male relatives of men with early-onset BPH face a 66% cumulative lifetime risk of surgical treatment for BPH, compared to a 17% risk among relatives in the control group (Sanda et al., 1994).

2.1.2 Geographic and ethnic influences

Geography and ethnicity are also among the risk factors for BPH. There is a substantial geographical variation in the prevalence of BPH diagnosis globally. In 2019, the highest prevalence was in Eastern Europe (6,480 per 100,000), followed by Central Latin America (4,140 per 100,000) and Andean Latin America (3,610 per 100,000). The lowest prevalence was in North Africa and the Middle East (987 per 100,000). However, access to care, applied statistics, varying case definitions, and research methodologies cloud the assessment of prevalence. (Awedew et al., 2022) These factors leave open the question of whether there is a true biological difference or rather differences in the health care system. In the United States, Hispanic men seem to have the highest prevalence of LUTS, followed by African American, White, and Asian men (Van Den Eeden et al., 2012). In another study, there were statistically significant differences in American Urological Association Symptom Index score between ethnicities. However, the actual difference in symptom score was deemed clinically insignificant. (Kupelian, 2006)

2.1.3 Modifiable risk factors

Several modifiable risk factors are implicated in LUTS attributed to BPH. Studies show that there is a strong positive association between obesity and BPH/LUTS (Parsons et al., 2013). Increased adiposity is consistently associated with greater prostate volume and enlargement, suggesting that obesity contributes to prostate growth (Freedland et al., 2006; Lee et al., 2006; Parsons et al., 2006, 2013). For instance, a 1 kg/m^2 increase in BMI corresponds to a 0.41 cc increase in prostate volume (Parsons et al., 2006). Obesity also elevates the risk of clinical BPH across multiple indicators, such as the need for BPH medical treatment, non-cancer prostate surgery, physician-diagnosed BPH, histological confirmation, and reduced urinary flow rate (Parsons et al., 2013). Additionally, obesity increases the risk of LUTS, as assessed by validated questionnaires (Parsons et al., 2013; Rohrmann et al., 2018). Obese men also have a higher risk of persistent storage LUTS after surgical treatment of BOO. This is due to increased waist circumference being associated with persistent postoperative LUTS. (Gacci et al., 2015)

2.1.4 Hormonal influences

It is widely recognised that androgens play a permissive role in BPH pathogenesis. There is also increasing evidence for the role of oestrogens. (Ho & Habib, 2011) Therefore, it is plausible that hormonal imbalances contribute as one of the risk factors for BPH and LUTS. Still, there is conflicting evidence regarding the effects of testosterone replacement therapy. In a meta-analysis by Kohn et al., there was no statistically significant difference in changes in the International Prostate Symptom Score (IPSS) between men receiving testosterone replacement therapy and placebo (Kohn et al., 2016). In prostate biopsies of aging men with late-onset hypogonadism, 6 months of testosterone replacement therapy had little effect on cellular functions or androgen levels in prostate tissue (Marks et al., 2006). In contrast to the aforementioned studies, Kathrins et al. stated in their systematic review that current literature demonstrates a causative relationship between testosterone replacement therapy, prostate volume, and de novo or worsening LUTS (Kathrins et al., 2016). In hypogonadal males undergoing more than 2.5 years of testosterone replacement therapy, there is a 32% higher risk of receiving a BPH diagnosis. However, testosterone replacement therapy did not alter the risk of BPH interventions. (Fendereski et al., 2024)

2.1.5 Role of chronic inflammation

Chronic inflammation in the prostate, observed in 77.6% of men in the REDUCE trial with a mean prostate volume of 46 mL, seems to be a risk factor for BPH (Nickel et al., 2008). More severe inflammation of the prostate tissue is associated with higher IPSS scores. Still, these correlations were small, indicating weak, even though statistically significant, associations. (Nickel et al., 2008) In a prospective study of inflammatory cell markers in transition zone biopsies, moderate to severe inflammation was strongly associated with an increased risk of clinical progression or acute urinary retention compared to participants without inflammation at prostate biopsy (Gandaglia et al., 2017). Preclinical studies indicate that pathological mechanisms triggering a chronic inflammatory response in the prostate significantly contribute to the development and progression of BPH. Men with BPH-related LUTS and chronic inflammation of the prostate appear to be at higher risk of symptom progression and acute urinary retention. (Gandaglia et al., 2017)

2.1.6 Lifestyle factors and associated conditions

There is inconsistent evidence regarding the effect of lifestyle factors on the progression of BPH/LUTS. Physical activity has been associated with a reduced risk of BPH progression and LUTS in some studies (Martin et al., 2014; Maserejian

et al., 2012; Parsons et al., 2013; Parsons & Kashefi, 2008; Rohrmann et al., 2005). However, other cohorts found no protective effect (Penson et al., 2011; Rohrmann et al., 2018). Similarly, alcohol consumption has been linked to LUTS progression in certain analyses (Maserejian et al., 2012), while other studies report no association (Rohrmann et al., 2018). The relationship of smoking with LUTS shows mixed results. Some evidence suggests a positive association among former heavy smokers (Rohrmann et al., 2005). This is contrasted by studies finding no such effect in men (Maserejian et al., 2012; Rohrmann et al., 2018). BPH/LUTS frequently coexist with erectile dysfunction (Ponholzer et al., 2004). This comorbidity shares similar risk factors with cardiovascular disease (Thompson et al., 2005). A shared cardiovascular aetiology of BPH/LUTS and erectile dysfunction could explain the association with the same modifiable lifestyle factors, including obesity, diabetes, and hyperlipidaemia (Martin et al., 2014; Parsons & Kashefi, 2008).

The pathophysiology of BPH/LUTS and erectile dysfunction is hypothesised to share a common origin. These mechanisms include reduced nitric oxide–cyclic guanosine monophosphate pathway, increased RhoA–Rho-kinase signalling, autonomic hyperactivity, and pelvic atherosclerosis. These pathogenic mechanisms lead to reduced function of nerves and endothelium, altered smooth muscle relaxation or contractility, and arterial insufficiency. Ultimately, they cause reduced blood flow and subsequently hypoxia-related tissue damage. (Gacci et al., 2011)

2.2 Pathophysiology of benign prostatic hyperplasia

The pathogenesis and progression of BPH are most likely multifactorial and complex, and are not yet fully understood (De Nunzio et al., 2020). Due to the intimate anatomical relationship between the prostate, bladder neck, and urethra, histological BPH advancing to BPE might cause varying degrees of BOO. This progression can lead to BPO and might cause LUTS. (Abrams et al., 2002; Cornu et al., 2025; Kupelian, 2006; Lee et al., 1995) Other causes of male LUTS, besides BPO, include overactive bladder/detrusor overactivity, nocturnal polyuria, underactive bladder/detrusor underactivity, chronic pelvic pain syndrome, neurogenic bladder dysfunction, urinary tract infection/inflammation, foreign body, urethral stricture, bladder tumour, and distal ureteric stone (Cornu et al., 2025).

2.2.1 Pathogenesis of benign prostatic hyperplasia

2.2.1.1 Aging, hormonal dysregulation, and androgen signalling

BPH is a histological diagnosis, characterised by the non-malignant proliferation of glandular epithelial cells, smooth muscle, and connective tissue in the prostatic transition zone due to a multifactorial process (Lerner et al., 2021a). The exact aetiology of BPH is still unknown. However, the development of BPH requires aging and the presence of functional testes or testosterone. (Lee et al., 1995; Lerner et al., 2021a) Testosterone is converted to its active metabolite, dihydrotestosterone, by 5α-reductase. After this, it forms a complex with the androgen receptor, which is then transported to the nucleus. Within the nucleus, this receptor complex initiates normal development, growth, and hyperplasia of the prostate. (Andriole et al., 2004) BPH develops when there is an imbalance between growth and apoptosis in the prostate tissue (Andriole et al., 2004; Lerner et al., 2021a). This process likely begins early before a male reaches 30 years of age (Berry et al., 1984). Despite age-related declines in circulating testosterone, intraprostatic dihydrotestosterone levels remain elevated, sustaining prostate growth (Ho & Habib, 2011). Studies have shown that 5α-reductase inhibitors reduce prostate volume by inhibiting dihydrotestosterone production. This confirms the critical role of androgens in the process of BPH growth. (Stoner & Sharp, 1990) Additionally, the prostate is a target tissue for oestrogen. Aging men have an increased oestrogen-to-androgen ratio, and this seems to enhance androgen receptor signalling and stimulate hyperplastic growth. (Nicholson & Ricke, 2011)

2.2.1.2 Chronic inflammation, immune activation, and cellular proliferation

Chronic inflammation in the prostate contributes to both the initiation and progression of BPH. Intraprostatic inflammation might be triggered by a number of stimuli, such as bacterial infections, viruses, sexually transmitted diseases, autoimmune responses, urine reflux, or metabolic syndrome. During a prostatic inflammatory response, large infiltrates of lymphocytes migrate to glandular, periglandular, and stromal areas of the prostate. These cells promote the release of cytokines and growth factors. In response to chronic inflammatory stimuli, T lymphocytes release cytokines and growth factors. This results in tissue injury, a chronic immune response, and abnormal tissue remodelling processes leading to fibromuscular growth. (Gandaglia et al., 2017) A recent study investigating the effect of tumour necrosis factor-alpha (TNF-α) inhibitor therapy on prostate gland growth demonstrated a negative correlation between the use of TNF-α inhibitors and the

prostate growth rate. This suggests that inflammatory mediators may play a regulatory role in prostate growth. (Al-Faouri et al., 2023)

The hyperplastic process of BPH is a result of imbalance between cell proliferation and apoptosis, driven by growth factors and hormonal signalling (Berry et al., 1984; Gandaglia et al., 2017; Lee et al., 1995). Stromal-epithelial interactions have a homeostatic role and reciprocally maintain tissue differentiation and growth-quiescence. When this homeostasis is interrupted, stromal cells produce growth factors that stimulate epithelial hyperplasia. Meanwhile, epithelial cells influence stromal remodelling. (Cunha et al., 2004)

2.2.2 Physiology of benign prostatic obstruction and lower urinary tract symptoms

Parallel to the development of BPH, the prevalence of LUTS and the severity of symptoms increase with age (Lerner et al., 2021a). LUTS are divided into urine storage, voiding/emptying, and post-micturition symptoms (Abrams et al., 2002; Lerner et al., 2021a). Storage symptoms are experienced during the storage phase of the bladder. They include pollakiuria (increased daytime frequency), nocturia, urgency, and urinary incontinence. Voiding symptoms, experienced during the voiding phase, include slow stream, splitting or spraying of the urine stream, hesitancy, straining, and terminal dribble. Post-micturition symptoms, appearing immediately after voiding, include the feeling of incomplete emptying and post-micturition dribble. (Abrams et al., 2002)

An increasing number of studies have shown that LUTS are a group of symptoms that are not specific to gender or organ. However, they are often associated with aging and are usually progressive in nature (Chapple et al., 2008). Inability to empty the bladder may be due to BOO, detrusor underactivity of the bladder, or a combination of the two. Historically, storage symptoms in older men have been associated with prostatic pathology. In women, identical symptoms have been thought to originate from the bladder. (Chapple et al., 2008) Effective voiding demands a balance between bladder contractility and a reasonable bladder outlet (Drake, 2018). BOO leads to increased bladder contractility via detrusor muscle adaptation and enhanced neurological input. This compensates for the obstruction, enabling normal lower urinary tract function. (Drake, 2018) This plasticity in the human body might be one of the reasons that BPE leading to BOO does not always result in LUTS.

The most common underlying conditions relating to male LUTS, with BPO excluded, are detrusor overactivity and detrusor underactivity. Detrusor overactivity is a urodynamic observation characterised by involuntary detrusor contractions that may be spontaneous or provoked during bladder filling (Abrams et al., 2002). It is

usually associated with an overactive bladder, which is characterised by urinary urgency, with or without urgency incontinence, and often pollakiuria and nocturia, if there is no proven infection or other obvious pathology (Drake, 2014). Detrusor underactivity is also a urodynamic definition, characterised by decreased detrusor pressure while voiding, leading to a reduced urinary flow rate (Chapple et al., 2018). Detrusor underactivity is one of the causes of underactive bladder syndrome, which has similar voiding symptoms to those caused by BPO (Chapple et al., 2018). It is a common underlying mechanism of LUTS in men, with an estimated prevalence of up to 39% (Thomas et al., 2005). Detrusor contractility appears resistant to worsening due to long-term BOO. Nor does surgical relief of BOO improve it. (Thomas et al., 2005)

2.2.2.1 Mechanisms of benign prostatic obstruction

BPO is a form of BOO and may be diagnosed when the cause of outlet obstruction is known to be benign prostatic enlargement (Abrams et al., 2002). It arises from the growth of the prostate's transition zone, where hyperplasia of epithelial and stromal cells compresses the urethra, creating a static obstruction (Berry et al., 1984). There appears to be a significant link between autonomic nervous system overactivity and LUTS. However, it remains unclear whether the autonomic nervous system contributes directly to the physiological obstruction by sympathetic activation of the stromal smooth muscle, increasing urethral resistance through heightened muscle tone. (McVary et al., 2005) Nevertheless, increased smooth muscle tone and resistance within the enlarged prostate form the dynamic component of the obstruction (Lerner et al., 2021a). The static and dynamic components of obstruction increase bladder outlet resistance, leading to obstructive LUTS when the body's natural plasticity responses are impaired or insufficient.

Although the relationship between prostate size and the severity of LUTS is debated (Corica et al., 1999; Kok et al., 2009), some research indicates that larger prostate size significantly predicts a greater risk of LUTS progression in men with pre-existing symptoms (Aktas et al., 2014; Crawford et al., 2006). In the REDUCE trial, prostate size was associated with a higher risk of developing incident LUTS presumed to be due to BPH (Simon et al., 2016). One of the arguments explaining the inconsistency between prostate volume and severity of LUTS is that the volume of the prostate's transition zone may be more closely related to LUTS. This is due to its anatomical relation to the prostatic urethra and the fact that BPH growth occurs in the transition zone. However, central or transition zone volume does not appear to correlate more closely with LUTS than total prostate volume (Corica et al., 1999; Witjes et al., 1997). Another argument is that changes in the urethra within the prostate resulting from BPE might be the underlying aetiology of male LUTS.

Prostatic urethral length-to-prostate volume ratio seems to significantly correlate with the severity of voiding symptoms (Ko et al., 2017). An increase in the total volume of the prostate might also affect LUTS via degeneration of the posterior bladder neck muscles (Hinata et al., 2016). Bladder neck muscles seem to be progressively affected by fibrosis, with the circular muscle fibres becoming thin and fragmented, as prostatic hyperplasia advances (Hinata et al., 2016).

2.2.2.2 Bladder's response to obstruction

Chronic BPO may induce physiological changes in the bladder, contributing to both obstructive and irritative LUTS. Hypertrophy and hyperplasia of the smooth muscle in the urinary bladder, as well as hypertrophic growth of the detrusor muscle, can occur in response to BOO (Andersson & Arner, 2004). Morphologically, these changes in obstructed bladders are similar to those of aging (Thomas & Abrams, 2000). An increase in strain on the bladder is also associated with cellular and molecular alterations. Growth of the bladder wall involves alterations in its extracellular matrix and non-smooth muscle components. These structural changes in the bladder can be associated with detrusor overactivity. (Andersson, 2003) However, detrusor overactivity may also result from exaggerated symptomatic expression of peripheral autonomic activity (Drake et al., 2001). Detrusor overactivity is often present in an overactive bladder and is frequently the cause of these symptoms (Abrams et al., 2002). BOO may lead to detrusor overactivity through cholinergic denervation of the detrusor muscle, resulting in heightened sensitivity of muscarinic receptors to acetylcholine (Chapple & Roehrborn, 2006). Elevated resistance at the bladder outlet may also lead to ischaemia, an increase in detrusor collagen content, as well as alterations in the electrical characteristics of the detrusor smooth muscle cells and reorganisation of the spinal micturition reflex. All of these changes have been linked to the emergence of detrusor overactivity in animal models. Nevertheless, the coexistence of BOO and detrusor overactivity does not invariably indicate a direct causal relationship between the two conditions. (Chapple & Roehrborn, 2006)

2.3 Diagnostic evaluation

The diagnostic evaluation of patients with LUTS serves two primary objectives: to identify the differential diagnosis, since the aetiology of LUTS is often multifactorial, and to define the clinical profile. The evaluation should include an assessment of the risk of disease progression to provide appropriate care. The diagnostics and treatment chart based on the Finnish Current Care Guidelines is illustrated in Figure 1 at the end of the chapter.

2.3.1 Questionnaires and surveys

Validated symptom score questionnaires are recommended for assessing male LUTS by all published guidelines (Cornu et al., 2025; Lerner et al., 2021a). Symptom scores are useful in quantifying LUTS and identifying predominant symptoms. However, they are not disease-, gender-, or age-specific (Cornu et al., 2025). Symptom scores are not adequate on their own to diagnose BOO, since individual symptoms and questionnaires are not significantly associated with one another (D'Silva et al., 2014). Nevertheless, symptom questionnaires are especially useful in monitoring treatment outcomes. In Finland, the IPSS and the Danish Prostate Symptom Score (DAN-PSS) are commonly used (Lower urinary tract symptoms: Current Care Guidelines, 2025). The IPSS questionnaire is comprised of eight items, which include seven questions on symptoms and one on quality of life (Barry et al., 1992). The DAN-PSS questionnaire is divided into Part A (severity of the symptom) and Part B (subjective bother caused by the symptom). Questions 1–5 enquire about voiding symptoms, whereas questions 6–12 enquire about storage symptoms. (Barry et al., 1992; Lower urinary tract symptoms: Current Care Guidelines, 2025)

The symptom questionnaires are interpreted as follows:

Table 1. Symptom score questionnaires, adopted from Lower urinary tract symptoms: Current Care Guidelines, 2025

Symptom score questionnaire	Mildly symptomatic	Moderately symptomatic	Severely symptomatic
IPSS-SCORE	0–7	8–19	20–35
DAN-PSS-SCORE	0–7	8–18	> 18

The European Association of Urology (EAU) guidelines also mention the International Consultation on Incontinence Questionnaire (ICIQ) for Male LUTS. It is a widely used and validated questionnaire, which consists of 13 items. (Cornu et al., 2025) The ICIQ-MLUTS measures all LUTS that affect a male's quality of life, and it includes individual symptom bother scores (Ito et al., 2020). The Symptoms of Lower Urinary Tract Dysfunction Research Network Symptom Index 10 is another symptom questionnaire. It correlates strongly with the IPSS but extends symptomatology to include incontinence and bladder pain. (Glaser et al., 2023)

2.3.1.1 Frequency volume charts and bladder diaries

Frequency volume charts record voided volumes and the time of each micturition, whereas bladder diaries record voided volumes, the time of micturition, incontinence

episodes, pad usage, fluid intake, and the degree of urgency, as well as the degree of incontinence (Abrams et al., 2002). Both are recommended to be recorded for at least 3 days (Yap et al., 2007). Currently, the ICIQ bladder diary is the only fully validated bladder diary (Bright et al., 2014). The frequency volume charts and bladder diaries are pivotal tools for clinical assessment in nocturia and help target the underlying mechanism(s) (Cornu et al., 2012; Weiss et al., 2012).

2.3.2 Physical examination, imaging, and laboratory tests

2.3.2.1 Physical examination

The patient needs to be examined thoroughly. It is recommended to palpate the abdomen, inspect the suprapubic area and the external genitalia, the perineum, and the lower limbs (Cornu et al., 2025). During physical examination, urethral discharge, meatal stenosis, phimosis, and penile cancer should be excluded (Cornu et al., 2025). Digital-rectal examination is one of the elementary components of the physical examination of a male with LUTS (Cornu et al., 2025; Lower urinary tract symptoms: Current Care Guidelines, 2025). The objective of digital rectal examination is to assess the size of the prostate, its symmetry, tenderness, and possible nodules (Lower urinary tract symptoms: Current Care Guidelines, 2025). Unfortunately, the correlation between volume assessment with digital rectal examination and actual prostate volume is poor, since there is a distinct underestimation of prostate size with digital rectal examination (Roehrborn, 1998).

2.3.2.2 Imaging

Imaging of the prostate can be performed by various methods, such as transabdominal ultrasound, transrectal ultrasound, computed tomography, and magnetic resonance imaging (MRI). However, in daily practice, mainly transrectal ultrasound performed by a urologist is used. Transrectal ultrasound is more accurate in assessing the volume of the prostate than digital rectal examination (Cornu et al., 2025). It can also be used to reliably detect intravesical prostatic protrusion of the median lobe (Lower urinary tract symptoms: Current Care Guidelines, 2025). BPH nodules can usually be visualized on transrectal ultrasound as low-echo areas. However, many adenomas are isoechoic to the rest of the gland. (Loch et al., 2007) The size and shape of the prostate, visualised by transrectal ultrasound, guide the selection of interventional treatment and medical therapy (Cornu et al., 2025). MRI is mainly used in the differential diagnosis when there is a suspicion of clinically significant prostate cancer (PCA). Upper urinary tract imaging with ultrasonography is recommended if hydronephrosis caused by poor drainage of the bladder is

suspected. In case of macrohaematuria, the urinary tract should be imaged with ultrasonography or computed tomography. If the differential diagnosis is urolithiasis, computed tomography of the urinary tract should be performed. (Lower urinary tract symptoms: Current Care Guidelines, 2025)

2.3.2.3 Urinalysis, prostate-specific antigen, and renal function measurement

Dipstick or microscopy urinalysis is one of the primary evaluations of any patient with LUTS. It is able to identify urinary infections, microhaematuria, and diabetes, in which case further evaluation is needed (Cornu et al., 2025). Prostate-specific antigen (PSA) correlates strongly with prostate volume in men with BPH and no evidence of PCA, and this relationship depends on age (Roehrborn et al., 1999). A PSA threshold value of 1.5 ng/mL can best predict a prostate volume of >30 mL. If PSA is <1.5 ng/mL, the probability of an enlarged (>30 mL) prostate is low. (Bohnen et al., 2007) According to the Finnish Current Care Guidelines, PSA should be routinely tested as a part of the primary evaluation of a LUTS patient, if the diagnosis of PCA affects the intended treatment (Lower urinary tract symptoms: Current Care Guidelines, 2025). Serum PSA is also a strong predictor of future prostate growth. Baseline PSA can also predict the risk of acute urinary retention and BPO-related surgery. In summary, serum PSA testing is recommended when a diagnosis of PCA would influence treatment choice and when baseline PSA levels are relevant for clinical management. (Cornu et al., 2025) In case of repeatedly increased PSA values, abnormal digital rectal examination, or MRI findings, prostate biopsies are indicated (Lower urinary tract symptoms: Current Care Guidelines, 2025).

Serum creatinine or estimated glomerular filtration rate should be used to assess renal function if renal impairment is suspected based on history and clinical examination (Cornu et al., 2025). Hydronephrosis, renal impairment, and urinary retention are more common in patients with BPO. However, diabetes and hypertension are the most likely causes of elevated serum creatinine levels. (Gerber et al., 1997)

2.3.3 Urethrocystoscopy and urodynamics

2.3.3.1 Urethrocystoscopy

Urethrocystoscopy is recommended during diagnostic evaluation if the differential diagnosis of the aetiology of the patient's LUTS includes urethral stricture or bladder neck stenosis (BNS). It is also indicated if the patient presents with macrohaematuria or if the presence of bladder tumour is suspected. (Cornu et al., 2025; Lower urinary tract symptoms: Current Care Guidelines, 2025) When considering interventional

treatments for which the presence of a prostate median lobe may influence the treatment offered (for example, Urolift or transurethral incision of the prostate (TUIP)), the possible median lobe should likewise be assessed with urethrocystoscopy (Cornu et al., 2025).

2.3.3.2 Non-invasive urodynamics

2.3.3.2.1 Uroflowmetry

Uroflowmetry is one of the widely used basic non-invasive urodynamic tests in diagnostic evaluation and monitoring treatment outcomes in LUTS (Lower urinary tract symptoms: Current Care Guidelines, 2025). The key parameters of uroflowmetry are peak flow rate (Qmax), voided volume, post-void residual (PVR) urine, and flow pattern. Parameters are reliable when voided volume is >150 mL (Cornu et al., 2025). Due to within-subject variation (Kranse & Van Mastrigt, 2003), repeated uroflowmetry is useful, especially when voided volume is <150 mL, or when Qmax or flow pattern is abnormal (Cornu et al., 2025). A threshold Qmax of 10 mL/s indicates BOO with a specificity of 70% and a sensitivity of 47% (Reynard et al., 1998). However, a low Qmax may be caused by detrusor underactivity or an under-filled bladder (Lower urinary tract symptoms: Current Care Guidelines, 2025). As a diagnostic test, it is therefore unable to discriminate between underlying mechanisms (Cornu et al., 2025).

2.3.3.2.2 Post-void residual urine

Post-void residual urine (PVR) can be measured via transabdominal ultrasound, bladder scan, or catheterisation (Cornu et al., 2025; Lower urinary tract symptoms: Current Care Guidelines, 2025). A large PVR can be associated with BOO or detrusor overactivity (Rule et al., 2005), and it is not a contraindication to watchful waiting or medical therapy (Cornu et al., 2025). However, a large PVR may indicate a poor response to conservative treatment, and a high baseline PVR (>350 mL) may predict symptom deterioration (Roehrborn & ALTESS Study Group, 2006). Monitoring changes in PVR over time may help identify patients at risk of acute urinary retention (Emberton, 2006). This is particularly relevant for the treatment of patients using bladder function-degrading medications, such as antimuscarinics (Cornu et al., 2025). There is no PVR threshold for treatment. However, in Finland, PVR >300 mL is generally considered to be significant (Lower urinary tract symptoms: Current Care Guidelines, 2025).

2.3.3.3 Invasive urodynamics

The main goal of invasive urodynamics in men presenting with LUTS is to elucidate the underlying pathophysiological mechanisms, pinpoint risk factors for unfavourable clinical outcomes, and provide essential information to support shared decision-making. Current literature does not support the routine use of urodynamics in men undergoing investigation for LUTS. It should be used selectively (Drake et al., 2020), particularly when there is a disparity between patients' symptoms and clinical findings. Urodynamic studies should also be performed if the patient has a comorbidity affecting voiding or storage functions such as multiple sclerosis, Parkinsonism, spinal cord injury, other neurological disease, or patient a history of brain infarction. (Lower urinary tract symptoms: Current Care Guidelines, 2025)

Cystometry is the foundation for assessing urinary storage symptoms (Winters et al., 2012). In the case of an overactive bladder, when first-line conservative and medical treatment has failed, cystometry may provide useful information that might affect the ultimate treatment decision (Winters et al., 2012). Detrusor overactivity can be identified during the filling phase of cystometry by involuntary detrusor contractions, which may be spontaneous or provoked (Abrams et al., 2002).

Pressure flow studies are used to diagnose the severity of BOO. BOO can be differentiated from detrusor underactivity, which is characterised by decreased detrusor pressure during voiding in combination with a decreased urinary flow rate (Abrams et al., 2002). There is no urodynamic standard for obstruction, but the classic "high pressure–low flow" pattern is characteristic of male BOO (Winters et al., 2012).

2.4 Conservative and medical management

A majority of men with LUTS are not bothered enough by their symptoms to require medical or surgical treatment. In cases of low bother and uncomplicated LUTS, watchful waiting is a viable treatment option. However, all men with LUTS should undergo primary evaluation prior to any allocation of treatment in order to recognise patients with complicated LUTS. (Cornu et al., 2025; Lower urinary tract symptoms: Current Care Guidelines, 2025) The diagnostics and treatment chart based on the Finnish Current Care Guidelines is illustrated in Figure 1 at the end of the chapter.

The medical treatment of LUTS has improved dramatically over the past three decades. Table 2 below lists some of the pivotal, landmark randomised controlled trials (RCTs) that have influenced the clinical treatment of LUTS.

Table 2. Landmark double-blind randomised controlled trials of benign prostatic hyperplasia medical treatment.

Study name	N	Design	Key findings	Citation
PLESS	3,040	4-year RCT of finasteride or placebo	Finasteride reduced the risk of acute urinary retention by 57% and the risk of surgery by 55% compared with placebo. Prostate volume decreased by 18% with finasteride treatment, while it increased by 14% in the placebo group.	Mcconnell et al., 1998
MTOPS	3,047	4.5-year RCT of finasteride (5 mg), doxazosin (4-8 mg), combination therapy or placebo	Doxazosin and finasteride both significantly improve symptom scores and reduce the risk of overall clinical progression, but combination therapy is superior to either monotherapy. The risks of acute urinary retention and the need for surgery were reduced significantly by combination therapy and finasteride, but not by doxazosin.	McConnell et al., 2003
ARIA	4,325	2-year RCT of dutasteride (0,5 mg) or placebo	Dutasteride reduced prostate volume by 25% and improved symptom scores significantly from 6 months onward. It reduced the risk of acute urinary retention by 57% and the risk of surgery by 48%.	Roehrborn et al., 2002
CombAT	4,844	4-year RCTof dutasteride (0.5 mg), tamsulosin (0.4 mg) or combination therapy	Combination therapy was significantly superior to tamsulosin, but not to dutasteride monotherapy, in reducing the risk of acute urinary retention or BPH-related surgery. At 4 years, combination therapy provided superior symptom relief compared with monotherapies.	Roehrborn et al., 2010
Veterans Affairs Cooperative study	1,229	1-year RCT of terazosin (10 mg), finasteride (5 mg), combination or placebo	Terazosin significantly improved symptom scores compared with placebo, with no significant additive effect from combination therapy with finasteride.	Lepor et al., 1996
ALTESS	1,522	2-year RCT of alfuzosin (10 mg) or placebo	Alfuzosin significantly reduced the risk of symptom deterioration (11.7%), but it did not significantly reduce the risk of acute urinary retention or the risk of surgery.	Roehrborn & ALTESS Study Group, 2006
ARTS	1,228	1-year RCT of silodosin (8 mg), tamsulosin (0.4 mg) or placebo	The improvement of IPSS total score was superior with tamsulosin and silodosin compared with placebo, and silodosin also significantly reduced nocturia. Silodosin's overall efficacy was not inferior to tamsulosin.	Chapple et al., 2011

2.4.1 Conservative management

Regardless of treatment allocation, all patients should be educated about their condition, including the causes as well as the prognosis of LUTS. It is customary to include lifestyle advice and self-management. These include the reduction of fluid intake at specific times, moderation of caffeine and alcohol intake, urethral milking to prevent post-micturition dribble, bladder retraining, reviewing and optimising the patient's medication, and treating constipation (Brown et al., 2007; Yap et al., 2009). Patients managed with watchful waiting should be re-evaluated within 6–12 months and thereafter on an individual basis. This is necessary to recognise symptom deterioration and the possible need for medical or surgical intervention. (Lower urinary tract symptoms: Current Care Guidelines, 2025)

2.4.2 α1-adrenoceptor antagonists

α1-adrenoceptor antagonists (α1-blockers) reduce BOO and the tone of the prostate by inhibiting prostate smooth muscle contraction. α1-adrenoceptors also affect smooth muscle contraction in the bladder and urethra. They may also be involved in micturition control in parts of the spinal cord. (Michel & Vrydag, 2006) The exact mechanism of symptom relief in patients with LUTS remains unclear. α1-adrenoceptors located outside the prostate, in blood vessels, other non-prostatic smooth muscle, and the central nervous system may cause adverse events (AEs). Currently available α1-blockers include alfuzosin hydrochloride, doxazosin mesylate, silodosin, tamsulosin hydrochloride, terazosin hydrochloride, and naftopidil. (Cornu et al., 2025) In Finland, alfuzosin hydrochloride, silodosin, and tamsulosin hydrochloride are available (Lower urinary tract symptoms: Current Care Guidelines, 2025).

All α1-blockers have comparable efficacy in improving symptoms when administered at full therapeutic dose (Djavan et al., 2004). They reduce both storage and voiding LUTS (Cornu et al., 2025). They can generate significant urodynamic outcomes in terms of the BOO index and detrusor pressure at maximum urinary flow rate (Fusco et al., 2016). α1-blockers improve the total symptom score by 40–45% (additional benefit of 10–20% over placebo) and Qmax by 15–30% (additional benefit of 10–15% over placebo) (Djavan et al., 2004). α1-blockers seem to be more efficacious in patients with prostates smaller than 40 mL (Roehrborn et al., 2002, 2008). Overall, α1-blockers prevent clinical progression of BPH, but they do not reduce the primary occurrence of acute urinary retention (Roehrborn & ALTESS Study Group, 2006).

α1-adrenoceptor antagonists are primarily associated with vasodilatory side effects, including asthenia, dizziness, and orthostatic hypotension (Cornu et al., 2025). These effects might be more pronounced in patients with cardiovascular

comorbidities or those taking vasoactive medications (Barendrecht et al., 2005). Vasodilatory AEs may lead to falls, fractures, and institutionalisation in elderly patients (Djavan et al., 2004). The use of α1-blockers has been associated with a modestly elevated risk of cardiac failure, with nonselective agents posing a greater hazard (Lusty et al., 2021). There has been concern regarding a possible association with dementia. However, this association was not substantiated in Finnish cohorts. (Latvala et al., 2022) Initiation of α1-blockers should be avoided prior to scheduled cataract surgery due to the risk of intraoperative floppy iris syndrome (Chatziralli & Sergentanis, 2011). Ejaculatory dysfunction is notably higher with tamsulosin and silodosin compared to placebo, whereas doxazosin and terazosin show a comparable risk (Djavan et al., 2004; Gacci et al., 2014). Paradoxically, this side effect correlates with improved urinary symptoms and flow rate, indicating greater α1-blockade efficacy (Gacci et al., 2014). However, discontinuation rates are more driven by vasodilatory AEs than ejaculatory dysfunction, since overall sexual function tends to improve with α1-blocker treatment (Djavan et al., 2004).

2.4.3 5α-reductase inhibitors

Dihydrotestosterone is an active metabolite of testosterone mediating androgen effects on the prostate. Dihydrotestosterone has been suggested to have a particular role in the aetiology of BPH, since intraprostatic dihydrotestosterone levels remain high in aging men despite decreasing circulating testosterone levels. The conversion of testosterone to dihydrotestosterone is catalysed by the enzyme 5α-reductase, which has two isoforms. (Andriole et al., 2004) Type 1 5α-reductase has predominant expression and activity in the skin and liver, whereas type 2 5α-reductase is active predominantly in the prostate (Cornu et al., 2025).

Currently, there are two 5α-reductase inhibitors (5-ARIs) available: finasteride and dutasteride. Finasteride is a selective inhibitor of type 2 5α-reductase, whereas dutasteride inhibits both 5α-reductase enzyme isoforms (Andriole et al., 2004). The 5-ARIs relieve BOO via reduction of prostate size through a combination of atrophy and apoptosis of epithelial cells in the prostate (Rittmaster et al., 1996). The 5-ARIs reduce the size of the prostate by 18–27%, improve Qmax by 1.4–2.7 mL/sec, and decrease circulating PSA levels by about 50% after 6–12 months of treatment (Naslund & Miner, 2007). The effect of 5-ARIs starts slowly, and clinical effects comparable to placebo are seen after treatment of at least 6 months (Cornu et al., 2025).

In a double-blind study comparing finasteride and dutasteride, there was no significant difference in symptom relief at 12 months (Nickel et al., 2011). The obtained symptom relief of 5-ARIs depends on initial prostate size, and finasteride may not be efficacious in men with prostates <40 mL (Boyle et al., 1996). In contrast,

dutasteride seems to decrease prostate volume, peak urinary flow, and symptom score measurements even in patients with slightly enlarged prostates (30–40 mL) (Gittelman et al., 2006). In the long term, 5-ARIs significantly reduce the risk of clinical progression of BPH and the risk of acute urinary retention and the need for invasive therapy (Gittelman et al., 2006; McConnell et al., 2003; Roehrborn et al., 2010). 5-ARIs may also improve nocturia but may not lead to improved sleep (Kuhlmann et al., 2021).

The most common AEs of 5-ARIs are erectile dysfunction (7%), decreased libido (3%), abnormal ejaculation (2.7%), and gynecomastia (2%) (Gacci et al., 2014; McConnell et al., 2003; Roehrborn et al., 2010). 5-ARIs are associated with a statistically higher risk of cardiac failure (hazard ratio (HR) 1.09; 95% CI 1.02–1.17). However, the risk of cardiac failure is lower with sole 5-ARI use compared with α1-blockers (HR 1.22; 95% CI 1.18–1.26) or combination therapy (HR 1.16; 95% CI 1.12–1.21). (Lusty et al., 2021) There has been concern regarding psychiatric problems potentially associated with 5-ARIs. There may be an increased risk of self-harm and a new diagnosis of depression among men using 5-ARI medications, but there is no evidence of an increased suicide rate (Welk et al., 2017).

2.4.4 Other medical therapies

2.4.4.1 α1-blocker + 5α-reductase inhibitor combination therapy

Combination therapy of an α1-blocker and a 5α-reductase inhibitor appears to be superior to monotherapy in terms of symptom benefit, reducing the risk of acute urinary retention and the need for surgery (McConnell et al., 2003; Roehrborn et al., 2010). The effects of α1-blockers manifest within hours or days, whereas 5α-reductase inhibitors require several months to produce a clinically significant effect. A fixed-dose combination of dutasteride and tamsulosin resulted in rapid and sustained improvement in LUTS and reduced the relative risk of clinical progression by 43.1% ($p < 0.001$, 95% CI 22.5–58.2) when compared with watchful waiting (with the potential to initiate tamsulosin), with a number needed to treat (NNT) of 9 (Roehrborn et al., 2015). The AEs of combination therapy are those typical of both α1-blocker and 5α-reductase inhibitor monotherapies. The prevalence of drug-related AEs is higher with combination therapy compared with monotherapies (McConnell et al., 2003; Roehrborn et al., 2010). The cardiac failure risk of combination therapy was lower than that associated with the sole use of an α1-blocker (Lusty et al., 2021).

2.4.4.2 Muscarinic receptor antagonists

Muscarinic receptors, especially the M3 receptor, appear to be the physiologically most important mediators of urinary bladder contraction (Fetscher et al., 2002). In animal studies, the detrusor muscle is innervated by parasympathetic nerves via acetylcholine, which stimulates muscarinic receptors on smooth muscle cells (Cornu et al., 2025). Muscarinic receptor antagonists, such as darifenacin hydrobromide, fesoterodine fumarate, oxybutynin hydrochloride, solifenacin succinate, tolterodine tartrate, and trospium chloride, are used in Finland to treat overactive bladder and storage symptoms (Lower urinary tract symptoms: Current Care Guidelines, 2025). Tolterodine has been investigated most thoroughly for the treatment of male LUTS. However, large placebo-controlled studies in men with overactive bladder symptoms are needed to establish the efficacy and safety of antimuscarinic treatment in men. (Chapple & Roehrborn, 2006) Antimuscarinics are used in combination with α1-blockers and/or 5α-reductase inhibitors (Vouri et al., 2018). However, long-term studies remain scarce for combinations of antimuscarinics and α1-blockers, and are lacking for antimuscarinics in combination with 5α-reductase inhibitors (Cornu et al., 2025). In a Cochrane database systematic review, combination therapy was found to result in little or no difference in symptom scores but likely increased AEs. (Pang et al., 2021)

The most common antimuscarinic-related AEs are those of anticholinergic inhibition: dry mouth, constipation, micturition difficulties, nasopharyngitis, and dizziness (Cornu et al., 2025). One of the concerns regarding antimuscarinic treatment of storage or overactive bladder symptoms in men with BOO is the inhibitory effect on detrusor contraction, which might lead to voiding difficulties and cause urinary retention (Chapple & Roehrborn, 2006). However, in a meta-analysis of the effects of antimuscarinic treatment in overactive bladder, only oxybutynin was associated with an increased rate of urinary retention (Chapple et al., 2005). In urodynamic studies, when comparing tolterodine with placebo in men with BOO, there were no clinically meaningful changes in Qmax, PVR, or urinary retention (Abrams et al., 2006).

2.4.4.3 β-3 agonists

β-adrenoceptors mediate relaxation of smooth muscle in the bladder, urethra, and prostate. Therefore, β-3-adrenoceptor agonists serve as promising drug candidates in the treatment of overactive bladder (Michel & Vrydag, 2006). Mirabegron is the first clinically available β-3-adrenoceptor agonist for treatment of overactive bladder. Mirabegron monotherapy in male patients with overactive bladder and BOO is safe. However, storage symptom improvement was less pronounced in patients with BOO than in those without. (Liao & Kuo, 2018) Mirabegron is safe to use as an add-on

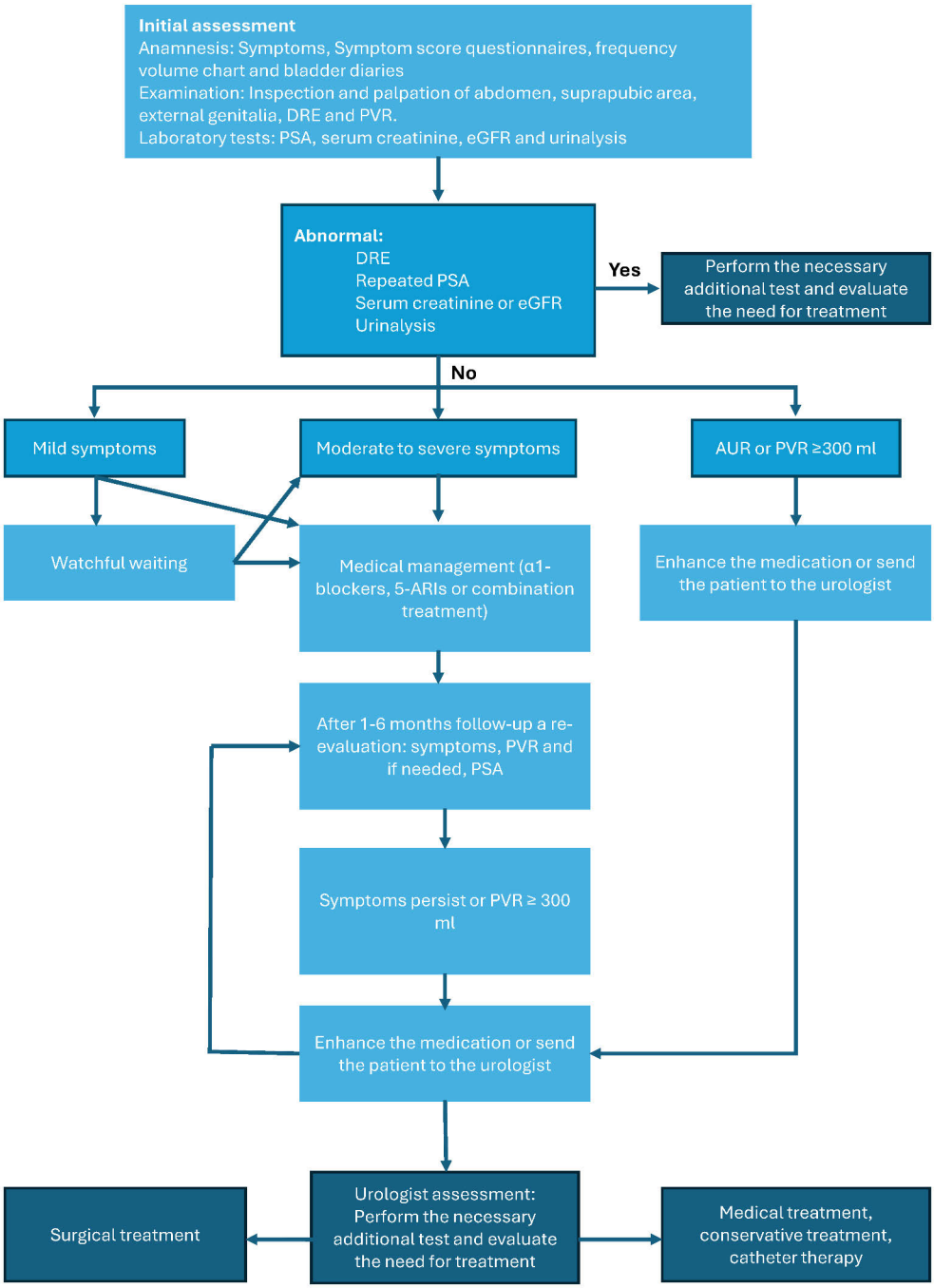
therapy in men with overactive bladder receiving tamsulosin for BPH (Herschorn et al., 2021; Kaplan et al., 2020). Mirabegron might be advantageous compared with antimuscarinic therapy in terms of persistence and adherence due to its different AE profile (Chapple et al., 2013). The most common AEs after mirabegron treatment are hypertension, urinary tract infection, dry mouth, nasopharyngitis, and headache (Chapple et al., 2013; Liao & Kuo, 2018). Mirabegron is contraindicated in patients with severe uncontrolled hypertension. Blood pressure should be measured prior to treatment initiation and monitored regularly during treatment. (Cornu et al., 2025)

2.4.4.4 Phosphodiesterase 5 inhibitors

Phosphodiesterase 5 isoenzymes are highly expressed in the lower urinary tract. Inhibition of phosphodiesterase 5 leads to smooth muscle relaxation in the bladder neck, prostate, and urethra, resulting in increased blood perfusion and oxygenation in the lower urinary tract. (Giuliano et al., 2013) Tadalafil has been licensed for treatment of male LUTS (Cornu et al., 2025). In a Cochrane database systematic review, phosphodiesterase 5 inhibitors provided a similar improvement in IPSS total score to α1-blockers and appeared to provide small additional benefit when used in combination with α1-blocker or a 5-ARI compared with monotherapy of the latter (Pattanaik et al., 2018). The most common AEs after phosphodiesterase 5 inhibitor administration are flushing, gastroesophageal reflux, headache, and dyspepsia (Gacci et al., 2012). The use of tadalafil is contraindicated in patients with major adverse cardiovascular events (Cornu et al., 2025).

2.4.5 Follow-up of medical treatment

The patient’s response to treatment should be evaluated after 3 months of initiating medical therapy. In the case of 5-ARIs, the evaluation should be performed after 6 months of treatment. Re-evaluation should involve monitoring possible adverse effects, IPSS or DAN-PSS symptom scores, and, if needed, PSA, digital rectal examination, and PVR. The PSA value after 6 months of 5-ARI use should be the patient’s new reference PSA value if the medication is continued. If the treatment response is insufficient, the adverse effects are intolerable, or if the patient prefers, the possibility of surgical treatment should be evaluated. (Lower urinary tract symptoms: Current Care Guidelines, 2025).



DRE = Digital rectal examination, PVR = Post-void residual, PSA = Prostate-specific antigen, eGFR = Estimated glomerular filtration rate, AUR = Acute urinary retention, 5-ARI = 5α-reductase inhibitor

Figure 1. Diagnostic and treatment chart modified from the Finnish Current Care Guidelines for lower urinary tract symptoms (2025).

2.5 Surgical treatment

2.5.1 Indications for surgical treatment

The indications for surgical treatment are divided into absolute and relative. Absolute indications include recurrent or refractory urinary retention, overflow incontinence, recurrent urinary tract infections, bladder stones or bladder diverticula, treatment-resistant macroscopic haematuria due to BPE, or dilation of the upper urinary tract due to BPO (with or without renal insufficiency). Relative indications include cases in which surgical treatment is offered when the patient's symptoms have not adequately improved with conservative treatment. (Cornu et al., 2025; Lower urinary tract symptoms: Current Care Guidelines, 2025; Lerner et al., 2021b)

2.5.2 Risk assessment and patient selection

The prevalence of LUTS increases with age. As the population ages, the need for surgical treatment in older and more comorbid patients increases. The indication for de-obstructive surgery needs to be balanced against functional outcome, life expectancy, and the risk of complications and mortality after surgery. Increased age and comorbidities are associated with an increased risk of experiencing complications after surgical treatment (Patel et al., 2015). Frailty is associated with worse postoperative outcomes, complications, and mortality, and should be considered a more relevant risk factor than chronological age. (Seib et al., 2018; Suskind et al., 2016) The Charlson Comorbidity Index (CCI) (Charlson et al., 1987) may predict return visits to the emergency department or readmission after surgery for LUTS (Shamout et al., 2021). In addition to the American Society of Anaesthesiologists (ASA) class, it appears to correlate with the risk of serious complications (Guo et al., 2016; Mandal et al., 2013; Patel et al., 2015). Nik-Ahd et al. deconstructed the CCI and the Claims-Based Frailty Index to develop the UroARC Surgical Calculator to support risk assessment in men undergoing surgery for BOO (Nik-Ahd et al., 2024). The most prognostically significant risk factors for surgical complications identified in their study are presented in Table 3 below.

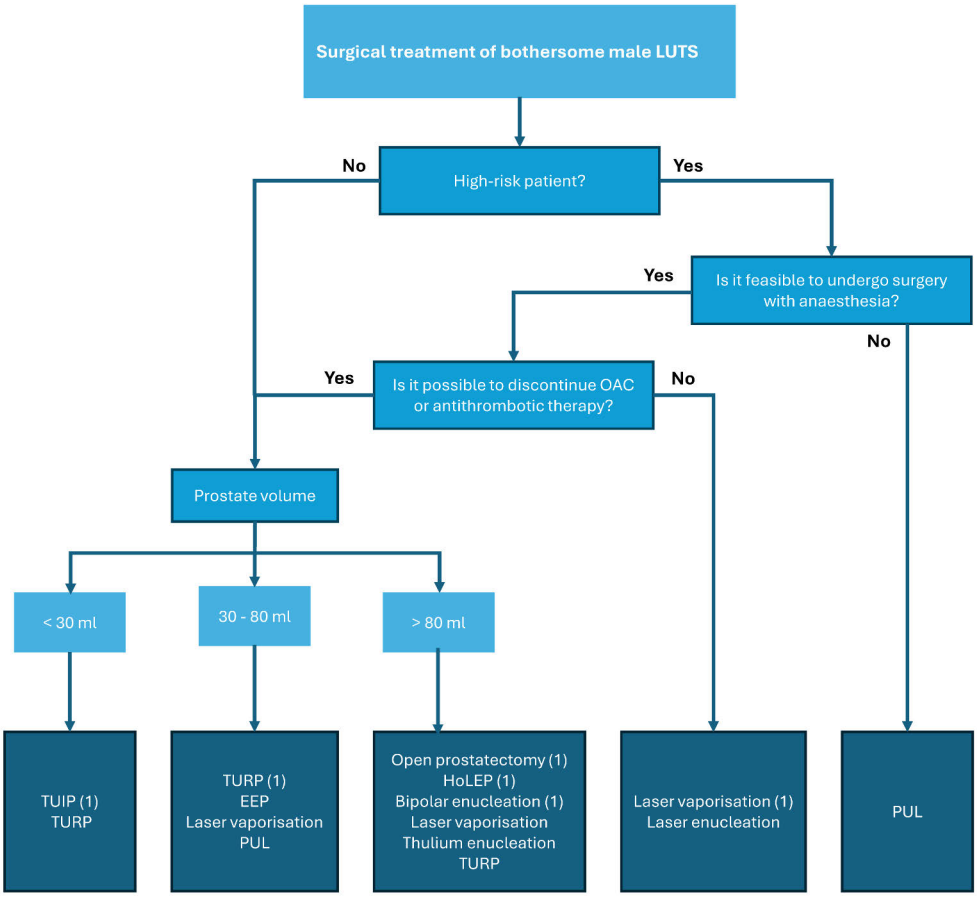
Table 3. Prognostic variables of the UroARC Surgical Calculator, modified from Nik-Ahd et al., Journal of Urology, 2024.

Age
Setting of residence
Primary malignancy
Anaemia or platelet disorder
Coronary artery disease
Chronic lung disease
Renal disease
Venous/lymphatic/thrombotic disorders
Cerebrovascular accidents/stroke and sequalae
Congestive heart failure
Dementia, psychiatric conditions or substance abuse
Neurodegenerative or neurological disease
Chronic liver disease
Secondary or metastatic malignancy
Pneumonia or influenza in the past year

According to the EAU 2025 guidelines, the surgical treatment algorithm is stratified by the patient's ability to undergo anaesthesia, the possibility of discontinuing oral anticoagulation (OAC) or antiplatelet therapy, and prostate volume, as shown in Figure 2. When anaesthesia is not possible, prostatic urethral lift (PUL) might be considered. If discontinuation of OAC is not possible, laser vaporisation should be the first treatment choice. Regarding prostate volume, in small prostates (<30 mL), TUIP should be the first choice; in medium-sized prostates (30–80 mL), the gold standard is TURP. In large prostates (>80 mL), the surgical options include open prostatectomy, HoLEP, or bipolar enucleation. (Cornu et al., 2025)

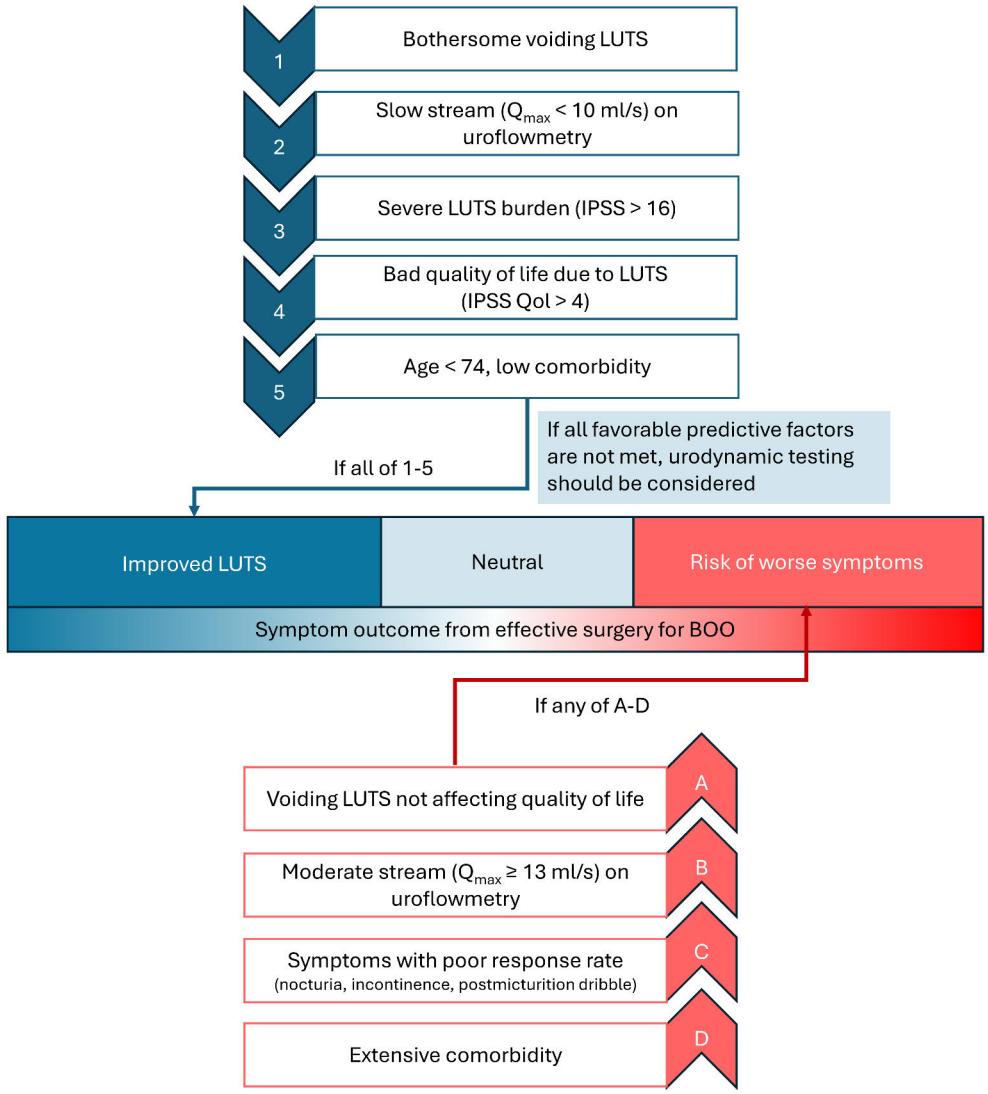
Ito et al. developed three statistical models to predict symptom outcomes after prostate surgery. They concluded that surgical outcomes may be unsatisfactory if baseline Qmax is >13 mL/s, LUTS do not affect the patient's quality of life, the patient has symptoms with a poor response to surgical therapy (such as nocturia, incontinence, or postmicturition dribble), or the patient has extensive comorbidity. They also reported that LUTS surgery is more likely to result in symptom improvement when symptoms are bothersome (ICIQ-MLUTS voiding subscore >8), baseline Qmax is <10 mL/s, the overall burden of LUTS is severe (ICIQ-MLUTS >18 or IPSS >16), quality of life is impaired due to LUTS (IPSS quality-of-life score >4), and the patient is <74 years old with a low comorbidity burden. If the patient's

Qmax is >13 mL/s, urodynamic studies are recommended to reduce the risk of symptom worsening after surgery (Ito et al., 2024). A simplified version of Ito et al.'s surgery outcome prediction model is presented in Figure 3.



LUTS = Lower urinary tract symptoms, OAC = Oral anticoagulation, TUIP = Transurethral incision of the prostate, TURP = Transurethral resection of the prostate, EEP = Endoscopic enucleation of the prostate, PUL = Prostatic urethral lift, HoLEP = Holmium laser enucleation of the prostate.

Figure 2. Treatment algorithm for bothersome male LUTS refractory to conservative and medical treatment, modified from the EAU Guidelines (2025).



LUTS = Lower urinary tract symptoms, Qmax = Peak flow rate, IPSS = International prostate symptom score, IPSS QoI = IPSS quality of life, BOO = Bladder outlet obstruction

Figure 3. Prediction of surgical outcomes for male LUTS, modified from Ito et al., European Urology Focus, 2024.

2.5.3 Transurethral resection of the prostate

Transurethral resection of the prostate is currently performed either as traditional monopolar transurethral resection of the prostate (M-TURP) or bipolar transurethral resection of the prostate (B-TURP) (Cornu et al., 2025). The difference between the two systems is that in the monopolar system the return electrode is usually placed on

the patient's skin (buttock or thigh), whereas the active electrode is located in the surgical instrument. This necessitates the use of hypo-osmolar irrigation, as the current travels through the body to complete the circuit. In the bipolar circuit, both electrodes are within close proximity to each other in the resection instrument. As the bipolar circuit is completed locally, the use of normal saline as an irrigation fluid is permitted. (Issa, 2008)

TURP removes tissue from the transition zone of the prostate, resulting in a prostate volume and PSA reduction of 25–58% (Cornu et al., 2025). TURP can be performed using various approaches. Nesbit described starting the procedure with the ventral parts (between 11 and 1 o'clock), followed by resection of both lateral lobes and the median lobe and finishing with the apex. Flocks and Gulp, on the other hand, recommended starting with the median lobe and then segmenting the lateral lobes at 9 and 3 o'clock. Mauermayer, Hartung, and May divided TURP into four phases: median (mid-) lobe resection, paracollicular resection, resection of the lateral and ventral parts of the gland, and, lastly, apical resection. (Rassweiler et al., 2006)

In a recent meta-analysis and systematic review, TURP decreased IPSS scores by a mean of 16 points, Qmax improved by a mean of 13 mL/s, and PVR decreased by a mean of 73 mL at 1 year after surgery (Porto et al., 2024). B-TURP has been shown to be as effective as M-TURP, but with a lower rate of complications (Alexander et al., 2019; Cornu et al., 2015). TURP delivers durable results with follow-up ranging from 8 to 22 years (Reich et al., 2006). In a long-term study of urodynamic results after TURP with a mean follow-up of 13 years, symptomatic failure and decreased flow rate were more strongly associated with detrusor underactivity than with adenoma regrowth (Thomas et al., 2005). According to the EAU 2025 guidelines, TURP is recommended as the first-line procedure for men with prostate sizes of 30–80 mL and bothersome moderate-to-severe LUTS secondary to BPO (Figure 2). Complication rates increase with prostate size (Reich et al., 2008), and the suggested upper limit for TURP, based on guideline panel consensus, is 80 mL. (Cornu et al., 2025)

2.5.3.1 Alternative resection techniques

Thulium:yttrium–aluminium garnet laser resection of the prostate using front-firing fibres has been described. However, due to the high proportion of vaporisation during the procedure, the term vaporesection has been introduced. (Bach et al., 2012) Thulium vaporesection has a longer operating time (Lan et al., 2018), and it is not more cost-effective than TURP (Noble et al., 2020). Thulium vaporesection appears to have similar efficacy to TURP (Lan et al., 2018; Tang et al., 2014), but evidence of mid- to long-term outcomes remains limited (Cornu et al., 2025).

2.5.4 Photoselective laser vaporisation of the prostate

Photoselective laser vaporisation of the prostate (PVP) using an 80-W, 532 nm potassium–titanyl–phosphate laser was introduced as an alternative to TURP in a pilot study in 2003 (Hai & Malek, 2003). The laser is strongly absorbed by haemoglobin; therefore, its thermal energy penetrates prostate tissue superficially to a depth of around 1–2 mm. The laser vaporises cellular water rapidly, causing tissue lysis and leaving behind a 2 mm rim of coagulated tissue (Kuntzman et al., 1996).

PVP has since evolved from the original 80-W system to high-performance 120-W lasers and subsequently to the 180-W GreenLight XPS Laser System. These higher power systems were developed to enable faster vaporisation and improved tissue penetration. During PVP, it is recommended to work with the fibre positioned slightly further from the cystoscope, except at the bladder neck. This improves visual perspective and orientation and reduces the risk of cystoscope damage. At the bladder neck, the fibre should be kept closer to both the cystoscope and the tissue to avoid damage to the ureteric orifices. Especially when using higher-power lasers, the fibre should be moved continuously but slowly to prevent accidental excessive tissue penetration and to distribute energy evenly, thereby creating a smooth surface.

The rotation angle of the fibre should be maintained between 5 and 7 o'clock, and the working distance of the laser (with a 120-W system) should be kept below 4 mm, as vaporisation efficiency increases at shorter distances. In contrast, with the 80-W laser, direct contact with tissue should be avoided to prevent fibre damage due to overheating. The recommended stepwise PVP technique involves creating a working channel, possibly using a lower power setting of 80 W, followed by higher power settings for vaporisation of the lateral lobes, apex, median lobe, and bladder neck. In contrast to some other laser techniques, PVP aims to create a TURP-like cavity configuration rather than a narrow cylindrical channel. (Muir et al., 2008)

In the GOLIATH study, GreenLight XPS laser was deemed non-inferior to TURP. At 1 year after surgery, PVP decreased mean IPSS score by 14 points (difference 1.2, 95% CI –0.2 to 2.6), Qmax improved by 13 mL/s (difference –1.7, 95% CI –4.5 to 1.0), prostate volume (measured by transrectal ultrasound) decreased by 27 mL (SD 11.0 mL), and PVR decreased by 67 mL (SD 57 mL). Efficacy outcomes remained stable and comparable to TURP at 24 months' follow-up. (Thomas et al., 2016)

In a meta-analysis comparing PVP using 80-W and 120-W lasers with TURP, there were no significant differences in Qmax or IPSS between the procedures; however, blood transfusions were significantly less frequent in the PVP group. (Thangasamy et al., 2012) In another systematic review and meta-analysis comparing 120-W GreenLight PVP with TURP, immediate outcomes, including a lower risk of perioperative transfusion, reduced catheterisation time, and shorter length of hospital stay, favoured PVP, while functional outcomes were similar

between groups at 12 months. (Cornu et al., 2015) As a comparatively newer treatment modality, long-term follow-up data for PVP remain less extensive as those available for TURP.

One of the factors making PVP appealing is its apparent safety in high-risk patients receiving OAC. This perception is based largely on case series (Chung et al., 2011; Reich et al., 2005; Ruszat et al., 2007; Sandhu et al., 2005). A meta-analysis of 11 studies, varying in methodological quality and choice of OAC, concluded that PVP is a safe and effective option for high-risk patients. It also reported that discontinuation of OAC is not necessary during PVP. (Zheng et al., 2019) In a recent propensity score-matched study, OAC use was not identified as a statistically significant risk factor for overall complications in multivariate analysis; however, it was associated with an increased risk of postoperative haematuria. (Jacquey et al., 2024)

2.5.4.1 Alternative vaporisation techniques

Bipolar transurethral vaporization of the prostate (B-TUVP) utilises a bipolar electrode and a high-frequency generator to create a vapour pocket at the tip of the surgical device, characterised by low thermal mass and very high temperature. Prostate tissue in contact with this vapour pocket is vaporised, and the postoperative zone of coagulation necrosis is approximately 1 mm. The size of the vapour pocket depends on applied voltage; in coagulation mode, the vapour pocket is not formed. (Botto et al., 2001)

Due to its thinner coagulation zone, B-TUVP may cause fewer irritative side effects and less stress urinary incontinence than M-TURP. Over the last decade, the focus of TUVP has shifted towards “plasma” TUVP systems with “mushroom- or button-like” electrodes. (Cornu et al., 2025)

RCTs evaluating TUVP have mainly been short-term studies with follow-up of less than 1 year, and B-TUVP has mainly been compared with M-TURP. Functional outcomes reported in RCTs have been contradictory, and due to trial heterogeneity, non-standardised techniques, and methodological limitations, a meta-analysis and systematic review by Cornu et al. was unable to draw firm conclusions. (Cornu et al., 2015) Another meta-analysis of six RCTs concluded that B-TUVP appears to be a safe and effective procedure in the short term (Wroclawski et al., 2016). Overall, B-TUVP seems to offer similar short-term efficacy to TURP, with a favourable short-term safety profile (Cornu et al., 2025). However, high-quality RCTs with substantially longer follow-up are still required to establish long-term outcomes (Cornu et al., 2015).

Diode lasers (a group of lasers using a semiconductor bar to generate laser radiation) are also marketed for prostate vaporisation but have been evaluated in only

in a limited number of RCTs. Diode laser systems demonstrate comparable or superior tissue ablation rates and lower bleeding rates when compared with GreenLight lithium triborate lasers; however, they are associated with significantly greater tissue necrosis and penetration depth. (Bach et al., 2012) The EAU 2025 guidelines state that laser vaporisation of the prostate using a 120-W, 980 nm diode laser demonstrates favourable intra- and perioperative parameters compared with TURP. However, post-operative complications, including severe storage symptoms and persistent incontinence, have been associated with diode laser vaporisation. (Cornu et al., 2025)

2.5.5 Open prostatectomy

Open prostatectomy (OP) is the oldest surgical treatment modality for LUTS due to BPO. The procedure can be performed either via transvesical approach (Freyer) or through the anterior prostatic capsule (Millin). In both techniques, adenomas are enucleated using the index finger. OP is an effective and durable procedure but represents the most invasive surgical option for the treatment of LUTS. According to the current guidelines, it is recommended only for large prostates (>80 mL) in the absence of endoscopic enucleation techniques. (Cornu et al., 2025) At 12 months postoperatively, OP reduces mean IPSS by 13 (SD ± 6) to 23 (SD ± 2) points, improves Qmax by 16 (SD ± 7) to 25 (SD ± 7.5) mL/s, and reduces PVR by 104 (SD ± 12) to 286 (SD ± 12) mL (Kuntz et al., 2008; Naspro et al., 2006; Varkarakis et al., 2004).

2.5.5.1 Minimally invasive simple prostatectomy

Traditional OP is associated with a relatively high mortality and complication rate (Gratzke et al., 2007). Consequently, the need for an alternative choice has emerged (Meyer et al., 2018). Minimally invasive simple prostatectomy (MISP) techniques, including laparoscopic and robotic approaches, have become increasingly common (Pariser et al., 2015). Laparoscopic simple prostatectomy for BPH was first introduced by Mariano in 2002. After 6 years of experience involving 60 patients, they reported minor complications, significant improvements in IPSS and Qmax, shorter hospital stays, and early return to normal activity. (Mariano et al., 2006) However, the laparoscopic approach did not gain popularity (Meyer et al., 2018), and robotic-assisted simple prostatectomy (RASP) was later introduced (Sotelo et al., 2008). Compared with laparoscopy, RASP offers advantages such as improved ergonomics and more dexterous instrumentation (Sotelo et al., 2008).

Several technical variations have been described for this operation (Meyer et al., 2018). Broadly, these procedures can be categorised into transcapsular (Millin) and

transvesical (Freyer) approaches (Cornu et al., 2025). Transperitoneal and extraperitoneal approaches can be used in both laparoscopic and robotic prostatectomies. In RASP, various additional technical refinements, such as Retzius-sparing and urethra-sparing pure adenomectomy approaches, have been described. (Meyer et al., 2018) Another novel technique is single-port transvesical robot-assisted simple prostatectomy, which has demonstrated fast recovery and improvement in LUTS at 1-year follow-up of 117 patients (Ramos et al., 2024). In a meta-analysis comparing OP with laparoscopic, RASP, and single-port techniques, minimally invasive approaches achieved similar improvements in Qmax and IPSS, while being associated with less blood loss, shorter catheterisation times, and shorter hospital stays (Lucca et al., 2015).

2.5.6 Alternative techniques

2.5.6.1 Transurethral incision of the prostate

Transurethral incision of the prostate (TUIP) is a procedure used to treat LUTS in men with small prostates (<30 mL) without relevant tissue removal (Cornu et al., 2025). The bladder outlet is incised using electrocautery or alternative energy sources, such as the holmium laser (Bansal et al., 2016). TUIP is considered a less morbid alternative to standard TURP in the treatment of LUTS. In a meta-analysis comparing TUIP and TURP, TURP was clearly superior in terms of urodynamic improvement in Qmax; nevertheless, TUIP provided equivalent symptomatic improvement with a reduced risk of AEs. (Lourenco et al., 2010) In conclusion, TUIP is an effective treatment option for moderate-to-severe LUTS, but the choice between TURP and TUIP should be based primarily on prostate volume (<30mL) (Cornu et al., 2025; Lourenco et al., 2010).

2.5.6.2 Endoscopic enucleation of the prostate

Endoscopic enucleation of the prostate (EEP) has gained popularity as a replacement for traditional OP. HoLEP served as the pioneering technique (Gilling et al., 1998) and was subsequently followed by similar procedures using various energy sources. Different lasers offer differing wavelengths and tissue interaction properties relevant to surgical use. In enucleation procedures, lasers with shallow tissue penetration are generally preferred to minimise collateral damage. In contrast, vaporisation techniques favour either deeper tissue penetration or energy absorption by haemoglobin to improve coagulation (Bach et al., 2012). However, it has been argued that the choice of energy source is often secondary and largely determined by available resources and surgeon preference (Herrmann, 2016).

The enucleation procedure itself can be performed using three-lobe, two-lobe, or en-bloc enucleation techniques, with further variation within the en-bloc group. Specific surgical approaches, such as the omega sign, en-bloc no touch, and en-bloc early apical release techniques have been described. (Capogrosso et al., 2023; Ericson et al., 2022; Gilling et al., 1998; Rücker et al., 2021)

During the enucleation phase, a plane between the surgical capsule and the adenoma is developed using a combination of blunt dissection with the tip of the laser resectoscope and laser energy. After completion of the dissection, the enucleated prostate lobes are pushed into the bladder. When deemed necessary by the surgeon, the lateral walls of the prostatic fossa may be incised at 3 and 9 o'clock to widen the cavity. During the morcellation phase, two concomitant irrigation fluid lines are used to keep the bladder full, and, when required, monopolar resection may be used to complete morcellation. In patients with prostate volumes >200 mL, or in the presence of a large bladder diverticulum, open cystotomy may be performed to remove the enucleated lobes and address the diverticulum. (Capogrosso et al., 2023) There appears to be no significant difference in postoperative symptom outcomes between en-bloc, two-lobe, and three-lobe techniques. However, en-bloc and two-lobe techniques may be advantageous in terms of operative time and efficiency. (Cantiello et al., 2024; Rücker et al., 2021; Tamalunas et al., 2023)

2.5.6.2.1 Holmium laser enucleation of the prostate

Holmium laser enucleation of the prostate (HoLEP) is currently the only endoscopic enucleation technique with a strong recommendation in the EAU 2025 guidelines. It is the most widely used and extensively studied EEP technique. HoLEP is also recommended as an alternative for TURP or OP (Cornu et al., 2025). It uses a holmium:yttrium-–aluminium garnet laser of 2,140-nm wavelength, which is a pulsed solid-state laser with a short absorption length in tissue (Gilling et al., 1995). Due to its wavelength and short, high-peak laser power pulses, it creates vigorously expanding and collapsing steam bubbles that can be used like a chisel in enucleation (Bach et al., 2012).

At 1 year after surgery, HoLEP improved the mean IPSS score by 14 points (range 0–21), improved Qmax by 13 (SD ± 2 mL/s) to 24 (SD ± 9.7 mL/s; range 11–49 mL/s), and reduced PVR by 270 (SD ± 16.7 mL; range 0–90 mL) to 280 (range 0–380 mL) mL, with symptom relief persisting during 5–7 years of follow-up (Elzayat et al., 2005; Gilling et al., 2012; Kuntz et al., 2008). In a systematic review and meta-analysis comparing HoLEP with TURP in prostates <100 g, HoLEP demonstrated favourable perioperative outcomes, as well as higher Qmax, lower PVR, and greater improvement in IPSS at 6 and 12 months postoperatively (Zhong et al., 2019). In another meta-analysis, HoLEP was associated with less perioperative

bleeding compared with TURP or OP, showed outcomes favourable to TURP and similar to OP in terms of IPSS, Qmax, and PVR during follow-up, and had similar complication rates (Cornu et al., 2015).

One limitation of HoLEP is its steep learning curve and the relatively small number of surgeons with expertise in the field (Reich et al., 2006). Moreover, HoLEP is considered a challenging procedure even for surgeons who have completed the learning curve and is not devoid of complications, even in the hands of highly skilled operators (Capogrosso et al., 2023).

2.5.6.2.2 Enucleation with other energy sources

EEP can also be performed using the thulium:yttrium–aluminium garnet laser, which has a wavelength of 1,940–2,013 nm and emits continuous-wave energy. It penetrates tissue shallowly, to approximately 0.2 mm, resulting in rapid tissue lysis. It is used mainly with front-firing fibres, although side-firing techniques are also available. (Bach et al., 2012)

The thulium:yttrium–aluminium garnet laser can be applied in enucleation as thulium vapoenucleation of the prostate or as thulium laser enucleation of the prostate, the latter relying predominantly on blunt enucleation. Thulium laser enucleation appears to offer similar efficacy and safety results to TURP, bipolar enucleation, and HoLEP, whereas thulium vapoenucleation is not supported by RCTs. Bipolar transurethral enucleation of the prostate can be performed using two technologies: plasmakinetic enucleation of the prostate or bipolar plasma enucleation of the prostate. (Cornu et al., 2025) Plasmakinetic enucleation has demonstrated favourable perioperative and long-term symptomatic outcomes in 5-year follow-up compared with TURP (Zhu et al., 2013).

Diode lasers with various wavelengths are marketed for vaporisation and enucleation in prostate surgery (Cornu et al., 2025). Compared with the GreenLight laser, different diode systems demonstrate comparable or superior tissue ablation and lower bleeding rates; however, their tissue penetration depth and the extent of tissue necrosis are significantly greater. (Bach et al., 2012) Diode laser enucleation appears to offer efficacy and safety comparable to TURP or plasmakinetic enucleation, although this impression is based on a limited number of low-quality RCTs.

The 532 nm GreenLight laser can also be used for EEP, as well as for vapoenucleation of the prostate (Cornu et al., 2025). GreenLight vapoenucleation has demonstrated perioperative outcomes similar to those of HoLEP and superior to those of B-TURP. While functional outcomes were comparable between the techniques, the retreatment rate after GreenLight vapoenucleation was higher than that observed after HoLEP. (Elshal et al., 2020)

2.5.6.3 Aquablation: image-guided robotic waterjet ablation

Aquablation is an ablative therapy that uses hydrodissection to resect adenomatous tissue while preserving the verumontanum and ejaculatory ducts. Prostatic tissue is ablated under real-time visualisation with transrectal ultrasound, without the generation of thermal energy. After completion of ablation, haemostasis is achieved using focal non-resective electrocautery or a Foley balloon catheter with light traction.

In the double-blind randomised controlled WATER trial, aquablation was deemed non-inferior to TURP with respect to symptom relief and was associated with a lower risk of sexual dysfunction. At 6 months, the mean IPSS decreased by 17 points (SD ± 5), Qmax improved by 10.9 mL/s (SD ± 11 mL/s), and PVR decreased by 55 mL (SD ± 50 mL). (Gilling et al., 2018) Symptom relief persisted over time; at 5-year follow-up, IPSS reduction was 15 points (SD ± 7), mean Qmax improvement was 8.7 mL/s (SD ± 9.1 mL/s), and PVR was reduced by 62 mL (SD ± 86 mL) (Gilling et al., 2022).

In the WATER II trial, 41% of the 101 patients experienced a Clavien-Dindo grade ≥2 AE at 6 months, with bleeding-related AEs observed in 14% of patients (Desai et al., 2019). During longer-term follow-up, aquablation provided functional outcomes non-inferior to TURP. However, concerns remain regarding bleeding management, and high-quality RCTs with longer follow-up are needed to better define the clinical value of aquablation. (Cornu et al., 2025) Nevertheless, aquablation may represent a valid alternative, as it appears to facilitate preservation of ejaculation and sexual function (Nedbal et al., 2024).

2.5.6.4 Prostatic artery embolisation

Prostatic artery embolisation (PAE) can be performed by an interventional radiologist as a day-case procedure under local anaesthesia. A unilateral femoral sheath is placed in the common femoral artery, and the prostatic arterial supply is identified using selective internal iliac arteriography. The prostatic arteries are then selectively catheterised and embolised. The procedure is considered successful when complete statis of flow in the prostatic arteries is demonstrated on angiography. (Abt et al., 2018)

In a randomised non-inferiority trial comparing PAE with TURP, non-inferiority of PAE could not be demonstrated (Abt et al., 2018). In the same trial, 21% of patients initially treated with PAE underwent TURP within 2 years of follow-up due to unsatisfactory clinical outcomes (Abt et al., 2021). At 5-year follow-up, the mean reduction in IPSS was 7.8 points (difference 3.8, 95% CI –0.7 to 8.2; $p = 0.092$ compared with TURP), Qmax improved by 3.6 mL/s (difference –5.7 mL/s, 95% CI –10.7 to –0.7; $p = 0.027$), and PVR decreased by 27.8 mL (difference 192.15, 95%

CI 83.8–300.5; $p = 0.001$). Overall, PAE was inferior to TURP across all objective parameters and patient-reported secondary outcomes, except for erectile function (Müllhaupt et al., 2024).

In a Cochrane systematic review, PAE may provide symptom score improvements comparable to TURP; however, it is likely to increase retreatment rates, and the certainty of evidence was low or very low for most outcomes, with the exception of retreatment rates. (Jung et al., 2022)

2.5.6.5 Prostatic urethral lift

Prostatic urethral lift (PUL) is a minimally invasive procedure in which encroaching lateral lobes are compressed by small permanent implants delivered under cystoscopic guidance. It is performed under local or general anaesthesia, and the procedure does not involve removing, cutting, or coagulating prostate tissue (Cornu et al., 2025). The implants are sized in situ according to the size of the lateral lobe. Typically, 4–6 implants are deployed to create a continuous anterior channel through the prostatic fossa. (Rukstalis et al., 2016)

At 1-year follow-up, PUL decreased IPSS by 11.4 points (SD ± 8.4), improved Qmax by 4.0 mL/s (SD ± 4.8 mL/s), and did not reduce PVR (Sønksen et al., 2015). According to the BPH6 study results, compared with TURP, the improvement in IPSS after PUL was inferior at 1 and 2 years, and Qmax was inferior at all time points; however, PUL was superior in the preservation of ejaculatory function (Gratzke et al., 2017). The surgical reintervention rate with PUL is estimated at 6% per year (95% CI 3.0–8.9), and appears to be higher in studies with longer follow-up (Miller et al., 2020). PUL has not yet been adequately studied in men with an obstructing or protruding median lobe. Its effectiveness in large prostates has also yet to be demonstrated, and long-term studies are lacking. (Cornu et al., 2025) Overall, compared with TURP, PUL may result in little to no difference in urological symptoms; however, the certainty of evidence is low owing to major concerns regarding study bias, imprecision, and inconsistency. (Franco et al., 2022)

2.5.6.6 Convective water vapour energy ablation: the Rezūm system

Convective water vapour energy ablation is a minimally invasive surgical treatment for LUTS/BPH. In the Rezūm system, radiofrequency is used to create thermal energy in the form of water vapour, which is then injected into targeted prostatic tissue, usually one to three injections per lateral lobe and one to two injections into the median lobe. The water vapour condenses from steam to liquid upon contact with cells and transfers thermal energy to the prostatic tissue, causing cell necrosis.

(Cornu et al., 2025; Janakiraman et al., 2023) The procedure can be performed without general anaesthesia in an office-based setting, and a further advantage is the preservation of sexual function (Janakiraman et al., 2023).

At 1 year after treatment in a cohort of 50 patients, Rezūm decreased IPSS by 9.8 points (SD ± 3 points; –57.1% from baseline), improved Qmax by 6.1 mL/s (SD ± 1.4 mL/s, +75% from baseline), and decreased PVR by 33.6 mL (SD ± 24.6 mL, −55% from baseline). Compared with TURP, the Rezūm group demonstrated inferior outcomes in IPSS, quality of life (QoL), Qmax, PVR, PSA, and residual prostate size at 24 months of follow-up. (Samir et al., 2024)

One concern regarding this treatment is the persistence of LUTS in some men following the procedure. Up to 50% of men treated with Rezūm experienced persistent LUTS 1–3 months postoperatively, and 18% continued to have persistent symptoms at 12 months. In the study in question, each additional month after Rezūm treatment increased the odds of clinically significant LUTS improvement by 9% (adjusted OR 0.91, $p = 0.003$). (Janakiraman et al., 2023) An earlier Cochrane review of MISTs reported that Rezūm may result in worse urological symptom scores compared with TURP at short-term follow-up; however, the certainty of evidence was low due to major concerns regarding within-study bias, imprecision, and inconsistency. (Franco et al., 2022)

2.5.6.7 Treatment modalities considered experimental and not currently recommended by the European Association of Urology guidelines

Transurethral microwave thermotherapy (TUMT) is a minimally invasive treatment in which microwave radiation delivers heat to the prostate via an intraurethral antenna. This results in tissue destruction, apoptosis, and denervation of α-receptors. TUMT was previously considered a true outpatient procedure for men with prostate volumes of 30–80 mL. (Oelke et al., 2013) However, it was removed from the EAU guidelines in 2019 and from the American Urological Association guidelines in 2023 (Sandhu et al., 2024). In a systematic review and meta-analysis of minimally invasive surgical therapies, TUMT was found to be less efficacious than TURP; however, it provided comparable improvement in QoL. (Cornu et al., 2023)

Transurethral needle ablation (TUNA) is likewise a legacy technology that was removed from the EAU guidelines at the same time as TUMT. Its use was not recommended in the 2018 American Urological Association guidelines or thereafter. (Foster et al., 2018; Gravas et al., 2024) In the TUNA procedure, low-level radiofrequency energy is delivered to the prostate via needles inserted transurethrally into the prostatic tissue. This approach was intended to induce coagulation necrosis

within the prostatic transition zone, resulting in volume reduction. (Oelke et al., 2013) However, prostatic volume reduction was less than anticipated, likely due to scar formation (Foster et al., 2018).

MRI-guided transurethral ultrasound ablation (TULSA) is a novel treatment method for LUTS. It integrates real-time MRI guidance, high-intensity directional ultrasound delivered via the urethra, and closed-loop temperature feedback control to enable tailored prostate ablation. This technique incorporates active cooling of the prostatic urethra and rectum to protect these structures from thermal injury. TULSA remains an experimental approach, with findings from two recent prospective studies shedding light on its outcomes. (Viitala et al., 2022) Following encouraging results from a non-randomised, single-arm, single-centre phase I study involving 10 patients (Viitala et al., 2022), the study was extended to include 30 patients as an early phase II trial (Viitala et al., 2025). At 1 year after TULSA, Qmax improved by 7.2 mL/s (median Qmax 21.8 mL/s, interquartile range 17.6–26.5 mL/s), and IPSS decreased by 13.5 points (median score 4.0, interquartile range 2.3–6.3). In the phase II study, all patients were continent without leakage at 1 year. In addition, among patients with adequate erectile function at baseline, 94% (17/18) maintained erectile function (Viitala et al., 2025). Future RCTs with larger cohorts and long-term follow-up are required to validate these findings and to assess the long-term durability of TULSA.

2.6 Complications of surgical treatment

> *"We want perfection without practise. Yet everyone is harmed if no one is trained for the future."*
>
> Atul Gawande, *Complications: A Surgeon's Notes on an Imperfect Science*

Every treatment has its complications, and invasive surgical interventions carry a higher risk of complications than watchful waiting or medical treatment. Arguably, the most important strategy for preventing surgical complications is not the choice of surgical procedure itself, but appropriate patient selection. The balance between risks and benefits of surgical treatment is particularly important when the primary treatment goal is improvement in QoL, as is the case with LUTS. Premature surgical intervention in patients with mild-to-moderate symptoms may result in harm that outweighs the potential benefit (Drake, 2018). In this chapter, the typical complications of surgical treatment for LUTS are discussed in further detail.

2.6.1 The Clavien-Dindo Classification

The Clavien-Dindo Classification is a standardised and validated tool for recording surgical complications. It focuses mainly on the therapeutic consequences of a complication, emphasising the intervention required to treat it. The Clavien-Dindo classification was originally described for hepatobiliary surgery but has since been validated for use in the general surgery population. (Dindo et al., 2004) It has also been adopted as a new standard for reporting urological complications (Morgan et al., 2009). However, it is rarely used in the current literature when reporting complications.

In a recent analysis of the ACS-NSQIP database, 30-day complications of 38,399 TURP, 19,121 PVP, and 3,797 EEP procedures were reported by Clavien-Dindo grade. The majority of complications were grade I-II (5.4% for TURP [2,060 patients], 5% for PVP [956 patients], and 4% for EEP [153 patients]). However, surgical, endoscopic, or radiological intervention (Clavien-Dindo III) was required in 1.7% [639 patients], 1.1% [205 patients], and 1.4% [53 patients] of cases for TURP, PVP, and EEP, respectively.

Life-threatening complications (Clavien-Dindo IV) were reported in 1.3% [519 patients] of TURP, 1.7% [317 patients] of PVP, and 0.9% [34 patients] of EEP procedures. Clavien-Dindo V complications, corresponding to 30-day mortality, were reported in 0.3% [104 patients)] after TURP, 0.2% [45 patients] after PVP, and 0.1% [4 patients] after EEP. (Labban et al., 2022)

The modified Clavien-Dindo Classification, including examples of potential complications of LUTS surgery and their management, is presented in Table 4. Complication rates by Clavien-Dindo classification reported in the literature are provided in Table 5.

Table 4. Modified Clavien-Dindo Classification with examples of complications of LUTS surgery and their management (adapted from Dindo et al., Annals of Surgery, 2004).

Grade	Definition	Complication	Management
Grade I	Any deviation from the normal postoperative course not requiring pharmacological treatment, or surgical, endoscopic, or radiological interventions. Allowed therapeutic regimens include: antiemetics, antipyretics, analgesics, diuretics, electrolytes, physiotherapy.	Haematuria	Bedside bladder irrigation, catheter traction
		Catheter malfunction due to clot or tissue	Bedside catheter change
		AUR or failed voiding trial after catheter removal	Bedside recatheterisation
		Transient evaluation of serum creatinine	Watchful regulation of fluid balance
		Lower urinary tract infection	Antibiotics
		Fever	Antipyretics
Grade II	Requiring pharmacological treatment with drugs other than those permitted for Grade I complications	Intraoperative haemorrhage / haematuria	Transfusion
	Requiring pharmacological treatment with drugs other than permitted for Grade I complications	Urinary tract infection with signs of bacteraemia	Intravenous antibiotics
		Supraventricular tachycardia	Antiarrhythmic agents
		Pulmonary embolism or deep vein thrombosis	Anticoagulants
Grade III	Requiring surgical, endoscopic, or radiological intervention		
III a	Intervention not under general anaesthesia		
III b	Intervention under general anaesthesia	Haematuria	Return to theatre to control bleeding
Grade IV	Life-threatening complications requiring intensive care management		
IV a	Single-organ dysfunction (including dialysis)	Major Adverse Cardiovascular Event	Admission to intensive care unit
IV b	Multi-organ dysfunction	TUR syndrome	Admission to intensive care unit
		Urosepsis	Admission to intensive care unit
Grade V	Death of a patient		

Table 5. Complication rates by Clavien-Dindo classification identified in the review of the literature.

Operation type	Time frame	Grade I (%)	Grade II (%)	Grade III (%)	Grade IV (%)	Grade V (%)	Source
TURP	30 d	5.4		1.7	1.3	0.3	Labban et al., 2022
	12 m	29.3	16.5	21.8			Bachmann et al., 2015
PVP	30d	89.8	6.1	1.6	2.2	0.7 (90d)	Cindolo et al., 2018
	30 d	5.0		1.1	1.7	0.2	Labban et al., 2022
	12 m	36	23.5	15.4			Bachmann et al., 2015
HoLEP/EEP	30 d	6.5	6.9	0.4			Capogrosso et al., 2023
	30 d	4.0		1.4	0.9	0.1	Labban et al., 2022
	12 m	0.4	1.2	2.4			Capogrosso et al., 2023
RASP/MISP	30 d	15	6	9	0	0	Pokorny et al., 2015
	90 d	5.5	3.3	1.1	0.1	0.1	Autorino et al., 2015
PUL		68	7	9			Sønksen et al., 2015
Aquablation	90 d	33.6	16.4	6	0.9		Gilling et al., 2018
		18.0	7.9	11.2			Bach et al., 2020
PAE				2.5			Zumstein et al., 2019

2.6.2 Short-term complications

Postoperative complications may occur early or late after surgery. One of the primary focuses of this thesis is the mortality associated with surgery for BPH/LUTS. Thirty-day mortality may underestimate outcomes, whereas 90-day mortality may represent a more reliable metric (Hirji et al., 2020). The 90-day definition captures mortality and possible AEs related to other comorbidities. These may be of less interest to surgeons, but they are valuable when counselling patients before surgery. (Damhuis et al., 2012) It is also worth recognising that the choice of treatment may be considered unjustified if the patient dies within 90 days of surgery performed to improve QoL. In the current literature, the timeframes and definitions of

complications vary considerably, making comparisons between procedures challenging. Procedure-specific complications vary, but so do overall complication rates. In a recently published retrospective study of trends in surgical interventions for BPE, less invasive treatments were associated with significantly lower odds of in-hospital complications. The 30-day short-term overall complication rates, among a total of 155,874 patients, were 18.1% for OP (95% CI 15.9–20.4), 12.3% for TURP (95% CI 12.1–12.4), 11.2% for TUVP (95% CI 10.3–12.2), 10.2% for HoLEP (95% CI 9.7–10.6), 10.7% for TUIP (95% CI 9.9–11.4), 14.6% for PVP (95% CI 13.7–15.5), 8.4% for PUL (95% CI 7.6–9.2), 12.3% for PAE (95% CI 10.6–14.1), and 9.4% for Rezūm (95% CI 7.7–11.1). (Page et al., 2025)

2.6.2.1 Clot retention and bleeding

Intraoperative arterial bleeding can be more severe in cases of a congested gland due to preoperative urinary infection or retention. Preoperative 5-ARI treatment may reduce operative bleeding in patients with prostates ≥50 mL (Busetto et al., 2015). Venous bleeding usually occurs due to capsular perforation or opening of venous sinusoids. During transurethral surgery, larger arteries may need to be compressed to visualise the bleeding stump. Arteries should be coagulated circumferentially to seal the stump. At the end of the operation, minimal irrigation flow should be used to identify the source of small bleeders. Extra care should be taken when inspecting the bladder neck and apex for bleeders. (Rassweiler et al., 2006)

Recurrent or persistent bleeding after transurethral surgery may result in clot formation, which can cause bladder tamponade. Obstructing clots should be evacuated, and bladder tamponade or ongoing bleeding may require reintervention. An obstructed balloon catheter should be replaced under rectal palpation, clots removed with bedside bladder irrigation, and, in cases of bleeding, the balloon catheter placed under traction. Catheter traction is ineffective in the presence of active arterial bleeding, which may be suspected when the irrigation outflow intermittently changes from clear to red, especially if bleeding occurs at the bladder neck. (Rassweiler et al., 2006)

One of the most common complications of M-TURP is postoperative bleeding and clot retention (Mebust et al., 1989). However, blood transfusion rates, which historically were reported to be as high as 22%, have decreased to 0.4–7.1% due to technical improvements (Rassweiler et al., 2006). The risk of blood transfusion and clot retention appears to be similar between M-TURP and B-TURP. Historically, this may have been one of the driving factors behind the investigation of alternative endoscopic technologies to replace TURP. (Ahyai et al., 2010)

In a recent study of 629 patients evaluating perioperative bleeding risk associated with OAC during TURP, the 113 patients receiving OAC had a 1.6-fold increased

risk of acute bleeding (OAC: 16.6%, $p < 0.01$; no OAC: 10.4%, $p = 0.02$). They also had an 11-fold increased risk of prolonged haematuria (OAC: 16.8%, $p < 0.01$; no OAC: 1.5%, $p < 0.01$), despite OAC therapy being withheld for an average of 4.5 days prior to surgery. (Kuo et al., 2024)

In a meta-analysis by Ahyai et al., clot retention was most frequent after TUVP (5.3%, range 0–14) and similar between M-TURP (4.9%, range 0–39) and B-TURP (4.3%, range 0–16). In the same study, no cases of clot retention were reported after HoLEP or PVP. However, the rate of secondary coagulation revision was higher after HoLEP (1.4%, range 0–5) than after M-TURP (1.0%, range 0.0–14.3). Secondary haemorrhage was highest after PVP (0.7%, range 0–3) compared with M-TURP, B-TURP, B-TUVP, and HoLEP (0.5%, range 0–8; 0.5%, range 0–8; 0.5%, range 0–1; and 0%, respectively). (Ahyai et al., 2010) In another systematic review and meta-analysis, EEP appeared to be associated with a lower risk of bleeding compared to B-TURP, and HoLEP required fewer blood transfusions than M-TURP or OP (Cornu et al., 2015). PVP was associated with a lower risk of perioperative transfusion than TURP (Cornu et al., 2015) and fewer bleeding-related complications (Gill et al., 2024). Overall, blood transfusions and clot retention were less likely after PVP than after TURP (Cornu et al., 2015). Nevertheless, despite the lower bleeding risk with PVP, intraoperative bleeding may may still seriously impair visibility and necessitate conversion to TURP (Ahyai et al., 2010).

While PUL is commonly recognised as a less invasive intervention, it has been reported to cause severe postoperative haematuria necessitating return to theatre for endoscopic surgery, open surgery, or prostatic artery embolisation to achieve adequate haemostasis. PUL has also been reported to cause pelvic haematoma, which has mainly been managed conservatively. However, cases of active arterial bleeding following PUL have required embolisation or emergency laparotomy (Juliebø-Jones et al., 2023).

Another analysis of the Food and Drug Administration Manufacturer and User Facility Device Experience database reported that bleeding was the most frequently reported adverse event after PUL and that nearly half of the reported AEs required operative intervention (Weiss et al., 2021). In the same study, fewer severe AEs were reported after Rezūm; bleeding requiring operative intervention still occurred in four cases. In a systematic review of complication rates associated with MISTs, postoperative bleeding rates were 7% after aquablation (interquartile range 3–9), 2% after PUL, and 3% after Rezūm (Lambertini et al., 2024). Following PAE, reported haematuria rates range from 0% to 18.6% (Zumstein et al., 2019).

One of the reasons to pursue surgical treatments for LUTS with a lower bleeding risk is the increasing use of anticoagulant and antiplatelet therapy. According to the EAU guidelines, the perceived safety of PVP in high-risk patients receiving OAC is based largely on case series (Cornu et al., 2025). In these small-sample studies

(including 162, 66, and 24 patients) involving high-risk patients on varying OAC or antithrombotic regimens, few or no bleeding complications or blood transfusions were reported (Chung et al., 2011; Reich et al., 2005; Sandhu et al., 2005).

In more recent, larger-scale studies of 180-W PVP in patients receiving OAC or antithrombotic therapy (422 and 373 patients), there was no statistically significant difference in Clavien-Dindo grade ≥II bleeding AEs compared to patients not receiving OAC (Knapp et al., 2017; Meskawi et al., 2019). Nevertheless, grade I haematuria (not requiring blood transfusion) was more frequent among patients receiving OAC or antithrombotic medication (Meskawi et al., 2019). Other higher-grade Clavien-Dindo events were also more common in patients receiving OAC or antithrombotic medication (Knapp et al., 2017).

In a small sample size study of 116 men undergoing aquablation, no Clavien-Dindo grade II bleeding events were observed in either the control group or the antithrombotic users. However, 2.4% of antithrombotic users (one patient) experienced a Clavien-Dindo grade IIIa bleeding event, while 2.7% of non-users (two patients) had grade IIIb bleeding events (Sadri et al., 2023). Table 6 summarises selected clot retention, bleeding, and transfusion rates reported in the current literature, categorised by operation type.

Table 6. Clot retention, bleeding and transfusion rates identified in the review of the literature.

Clot retention, bleeding and/or transfusion						
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**	**Additional relevant details**
OP	Titus et al., 2024	Meta-analysis	487*		8.42	Transfusion
	Varkarakis et al., 2004	Contemporary patient series	232		6.8	Transfusion
	Gratzke et al., 2007	Prospective study	902	30 d	11.2	Transfusion and revision for bleeding.
	Gilfrich et al., 2016	Retrospective register study	8,376	30 d	20.46	Transfusion and revision for bleeding.
TURP	Ahyai et al., 2010	Meta-analysis	440*B 954*M		6.7 8.4	Clot retention, transfusion, coagulation revision, secondary haemorrhage.
	Gill et al., 2024	Meta-analysis	918*†		20.7	Clot retention and transfusion
	Geavlete et al., 2011	Prospective study	170B 170M	30 d	4.2 14.1	Transfusion, clot retention, rehospitalization due to bleeding
	Cornu et al., 2015	Systematic review and meta-analysis	1,198*B 1,206*M 1,419*B 1,424*M		3.1 6.4 2.1 4.4	Clot retention Transfusion
	Tascı et al., 2011	Retrospective register study	3,589	30 d	2.6	Clot retention and transfusion
	Reich et al., 2008	Prospective multicentre study	10,654	30 d	2.9	Transfusion
	Gilfrich et al., 2016	Retrospective register study	78,192	30 d	10.76	Transfusion and revision for bleeding.
	Bhojani et al., 2014	Retrospective register study	4,794	30 d	2.0	Transfusion
	Patel et al., 2015	Retrospective register study	4,968	30 d	1.8	Clot retention and transfusion
	Al-Ansari et al., 2010	Randomized controlled trial	60	30 d	30	Clot retention and transfusion

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. B = B-TURP. M = M-TURP

Clot retention, bleeding and/or transfusion						
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**	**Additional relevant details**
PVP	Ahyai et al., 2010	Meta-analysis	142*		0.7	Clot retention, transfusion, coagulation revision, secondary haemorrhage.
	Gill et al., 2024	Meta-analysis	839*†		2	Clot retention and transfusion
	Cornu et al., 2015	Systematic review and meta-analysis	347*		0.3	Transfusion
	Ruszat et al., 2008	Single center prospective study	500	30 d	0.4	Transfusion
	Cindolo et al., 2018	Retrospective register study	813	30 d	0.7	Transfusion
	Gilfrich et al., 2016	Retrospective register study	6,409	30 d	9.74	Transfusion and revision for bleeding.
	Bhojani et al., 2014	Retrospective register study	2,439	30 d	0.5	Transfusion
	Patel et al., 2015	Retrospective register study	2,853	30 d	0.46	Clot retention and transfusion
	Al-Ansari et al., 2010	Randomized controlled trial	60	30 d	0	Clot retention and transfusion
	Elshal et al., 2013	Randomized controlled trial	52	30 d	1.9	Clot retention
HoLEP/EEP	Capogrosso et al., 2023	Single center prospective study	243	30 d	5.8	Clot retention and transfusion
	Ahyai et al., 2010	Meta-analysis	363*		1.4	Clot retention, transfusion, coagulation revision, secondary haemorrhage.
	Cornu et al., 2015	Systematic review and meta-analysis	97*		2.0	Transfusion
	Romero-Otero et al., 2020	Retrospective register study	963	30 d	7.2	Clot retention and transfusion
	Elzayat & Elhilali, 2007	Retrospective analysis	118		1.7	Transfusion
	Shah et al., 2007	Retrospective register study	280		2.45	Clot retention and transfusion
	Gilfrich et al., 2016	Retrospective register study	2,600	30 d	11.83	Transfusion and revision for bleeding
	Bhojani et al., 2014	Retrospective register study	126	30 d	2.4	Transfusion

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

Clot retention, bleeding and/or transfusion						
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**	**Additional relevant details**
RASP/MISP	Pokorny et al., 2015	Retrospective study	67	30 d	6	Transfusion and revision for bleeding
	Autorino et al., 2015	Retrospective register study	1,330	90 d	0.9	Transfusion and revision for bleeding
	Mariano et al., 2006	Prospective study	60		1.7	Clot retention
	Lucca et al., 2015	Systematic review and meta-analysis	764*†		15.7	Transfusion
PUL	Sønksen et al., 2015	Prospective randomized multinational study	45		2	Transfusion
	Lambertini et al., 2024	Systematic review	291*†		2	Postoperative bleeding
Aquablation	Lambertini et al., 2024	Systematic review	3,125*†		7	Revision for bleeding
	Gilling et al., 2018	Double-blind, multicenter prospective study	117	90 d	3.4	Transfusion
	Bach et al., 2020	Prospective multicenter study	178		9.0	Transfusion and revision for bleeding
	Desai et al., 2020	Prospective multicenter study	101	90 d	19.8	Bleeding
Rezūm	Lambertini et al., 2024	Systematic review	648*†		3	Postoperative bleeding
	Minore et al., 2024	Retrospective cohort study	426	30 d	1.9	Clot retention and transfusion
	Roehrborn et al., 2017	Randomized controlled trial	135	90 d	11.3	Gross hematuria
TUIP	Lourenco et al., 2010	Systematic review	266*		1.1	Transfusion
	Madersbacher & Marberger, 1999	Review	270*		0.4	Transfusion
TUVP	Ahyai et al., 2010	Meta-analysis	186*		6.3	Clot retention, transfusion, coagulation revision, secondary haemorrhage.
	Geavlete et al., 2011	Prospective study	170	30 d	2.4	Transfusion, clot retention, rehospitalization due to bleeding
	Madersbacher & Marberger, 1999	Review	189*		0	Transfusion
TUMT	Madersbacher & Marberger, 1999	Review	98*		0	Transfusion
TUNA	Madersbacher & Marberger, 1999	Review	117*		0	Transfusion

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

2.6.2.2 Transurethral resection syndrome

Transurethral resection (TUR) syndrome is caused by irrigation fluid absorption (IFA) exceeding 1,000 mL, with acute symptoms appearing when IFA exceeds 2,500 mL (Ortner et al., 2022). Classical TUR syndrome results from the absorption of glycine or other electrolyte-free irrigation fluids, leading to dilutional hyponatraemia (serum sodium <125 mEq/L). It is characterised by mental confusion, nausea, vomiting, hypertension, bradycardia, and visual disturbances. Untreated, it may progress to cerebral or bronchial oedema. When TUR syndrome is suspected, serum sodium levels should be measured immediately. In cases of significant hyponatraemia, the procedure must be terminated and treatment initiated with 20 mg of furosemide and intravenous hypertonic sodium chloride. (Rassweiler et al., 2006) In a large prospective study of 10,654 German men, the overall incidence of TUR syndrome was 1.4%, increasing to 3.0% in patients with a resection weight of ≥60 g (resection weight >60 g vs ≤30 g: OR 2.58, 95% CI 1.5–4.42) (Reich et al., 2008).

The risk of TUR syndrome was initially thought to have been eliminated with the introduction of B-TURP and other procedures using isotonic saline as the irrigation fluid. In a systematic review and meta-analysis comparing M-TURP with B-TURP, the decline in serum sodium was less pronounced after B-TURP, and no cases of TUR syndrome were observed after B-TURP (Cornu et al., 2015). In another meta-analysis of complications after transurethral surgery, TUR syndrome occurred in 0.8% of M-TURP patients (range 0–5), but no cases were reported after B-TURP, B-TUVP, HoLEP, or PVP (Ahyai et al., 2010). A more recent meta-analysis comparing PVP and TURP reported TUR syndrome incidences of 0.2% and 1.1%, respectively (risk ratio 0.41, 95% CI 0.09–1.84, $p = 0.24$) (Gill et al., 2024).

The use of saline as an irrigation fluid eliminates the risk of haemolysis, hyponatraemia, and glycine intoxication. However, IFA of isotonic saline leads to more pronounced plasma volume expansion and may result in acute cardiac decompensation, or pulmonary oedema. This non-classical TUR syndrome is a less recognised complication and might occur after B-TURP or laser prostate surgery. (Ortner et al., 2022)

Several factors influence the amount of IFA, including the choice of surgical technique, prostate size, size and number of transected veins, capsular perforation, resection depth, and intravesical pressure during surgery (Tokas et al., 2021).

In EEP procedures, the morcellation phase requires adequate bladder distension to avoid bladder perforation; however, this is associated with increased intravesical pressure and consequently greater IFA. During B-TURP, mean IFA has been reported to range from 133 to 915 mL, with recorded maximum values from 1,146 mL to ≥2,000 mL. In HoLEP, maximum IFA ranged from 300 to 930 mL, and in PVP from 615 to 4,579 mL. (Ortner et al., 2022)

In a study assessing IFA during PVP, intraoperative irrigation was performed with isotonic saline containing 1% ethanol. A positive ethanol breath test, indicating

IFA, was observed in 44% of 50 patients, and 13% of these patients (6% of the entire cohort) developed symptoms potentially related to IFA. (Hermanns et al., 2015)

In conclusion, non-classical TUR syndrome should be considered in patients who develop cardiopulmonary or neurological symptoms after transurethral surgery using saline irrigation (Hermanns et al., 2015; Ortner et al., 2022). Intraoperative ethanol breath testing may be worthwhile considering, and prevention of excessive IFA should be an interdisciplinary goal (Ortner et al., 2022). Table 7 summarises identified TUR syndrome rates in the current literature review.

Table 7. Transurethral resection syndrome rates identified in the review of the literature.

Operation type	TUR-syndrome				
	Source	Design	N	Time frame	Rate (%)
TURP	Ahyai et al., 2010	Meta-analysis	440*B 954*M		0 0.8
	Gill et al., 2024	Meta-analysis	918*†		1.1
	Geavlete et al., 2011	Prospective study	170B 170M	30 d	0 1.8
	Cornu et al., 2015	A systematic review and meta-analysis	1,329*B 1,339*M		0 1.4
	Tascı et al., 2011	Retrospective register study	3,589	30 d	0
	Reich et al., 2008	Prospective multicentre study	10,654	30 d	1.4
	Al-Ansari et al., 2010	Randomized controlled trial	60	30 d	5
PVP	Ahyai et al., 2010	Meta-analysis	142*		0
	Gill et al., 2024	Meta-analysis	839*†		0.2
	Al-Ansari et al., 2010	Randomized controlled trial	60	30 d	0
TUIP	Lourenco et al., 2010	A systematic review	139*		0
TUVP	Ahyai et al., 2010	Meta-analysis	186*†		0
	Geavlete et al., 2011	Prospective study	170	30 d	0
HoLEP/EEP	Ahyai et al., 2010	Meta-analysis	363*		0
	Romero-Otero et al., 2020	Retrospective register study	963	30 d	0.4
	Elzayat & Elhilali, 2007	Retrospective analysis	118		0

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. B = B-TURP. M = M-TURP

2.6.2.3 Capsular perforation

Capsular perforation during transurethral surgery is a common complication that may lead to bleeding, more pronounced IFA, and extravasation of irrigation fluid into the extraperitoneal space (Rassweiler et al., 2006). In a meta-analysis of

complications, capsular perforation was reported in 0.1% of M-TURP procedures (range 0–2.7) and 0.2% of HoLEP procedures (range 0–2), but no cases were observed after B-TURP, B-TUVP, or PVP (Ahyai et al., 2010). In another systematic review, one study reported capsular perforation in 3% of aquablation patients (Lambertini et al., 2024). A more recent meta-analysis comparing TURP and PVP reported capsular perforation rates of 4.6% and 0.6%, respectively (risk ratio 0.27, 95% CI 0.04–2.12; $p = 0.22$) (Gill et al., 2024). In a long-term comparative study of TUVP, B-TURP, and M-TURP, capsular perforation occurred in 1.2% (2 patients), 7.1% (12 patients), and 9.4% (16 patients) of cases, respectively (Geavlete et al., 2011). Capsular perforation has been reported in up to 18% of HoLEP cases (18 patients) (Capogrosso et al., 2023), 21.1% after M-TURP (12 patients), and 27.5% after B-TURP (19 patients, $p = 0.527$) (Skolarikos et al., 2016). The estimated rates vary considerably depending on the source, as demonstrated in Table 8.

Table 8. Capsular perforation rates identified in the review of the literature.

Operation type	Capsular perforation				
	Source	Design	N	Time frame	Rate (%)
TURP	Ahyai et al., 2010	Meta-analysis	440*B 954*M		0 0.1
	Gill et al., 2024	Meta-analysis	918*†		4.6
	Geavlete et al., 2011	Prospective study	170B 170M	30 d	7.1 9.4
	Tascı et al., 2011	Retrospective register study	3,589	30 d	0.75
	Al-Ansari et al., 2010	Randomized controlled trial	60	30 d	16.7
PVP	Ahyai et al., 2010	Meta-analysis	142*		0
	Gill et al., 2024	Meta-analysis	839*†		0.6
	Cindolo et al., 2018	Retrospective register study	813	30 d	0.6
	Al-Ansari et al., 2010	Randomized controlled trial	60	30 d	0
TUVP	Ahyai et al., 2010	Meta-analysis	186*		0
	Geavlete et al., 2011	Prospective study	170	30 d	1.2
HoLEP/EEP	Capogrosso et al., 2023	Single center prospective study	243	30 d	18
	Ahyai et al., 2010	Meta-analysis	363*		0.2
	Romero-Otero et al., 2020	Retrospective register study	963	30 d	1.2
	Shah et al., 2007	Retrospective register study	280		9.6

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. B = B-TURP. M = M-TURP

2.6.2.4 Epididymitis, urinary tract infection, and urosepsis

Urinary infection (epididymitis, urinary tract infection, urosepsis) rates can be reduced by routine preoperative urinalysis, which is used to rule out significant untreated urinary tract infection (UTI). Risk factors for postoperative infection and septic shock include preoperative bacteriuria, procedure duration exceeding 70 minutes, preoperative hospital stay longer than 2 days, and tamponade evacuation. (Rassweiler et al., 2006)

The use of prophylactic antibiotics in transurethral surgery has been debated, with the central question being whether they effectively prevent UTIs. It also remains debated which antibiotic is most appropriate and what duration of administration is optimal. (Mebust, 1993) In a meta-analysis by Berry and Barratt, prophylactic antibiotics markedly reduced the incidence of bacteriuria and clinical septicaemia in men with sterile urine prior to TURP. A range of antibiotics, including quinolones, cephalosporins, and co-trimoxazole, significantly reduced bacteriuria. In addition, short-course antibiotic protocols appeared to be more effective than single-dose administration. (Berry & Barratt, 2002)

The 2025 EAU Guidelines on Urological Infections recommend screening for and treating asymptomatic bacteriuria before urological procedures that involve breaching the mucosa. According to the guidelines, treatment should be guided by the pathogen's susceptibility profile, and treatment should be individualised rather than empirical. (Cornu et al., 2025) Rates of infectious complications are listed in Table 9.

Table 9. Urinary infection rates identified in the review of the literature.

Urinary tract infection					
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**
OP	Titus et al., 2024	Meta-analysis	388*		10.18
	Varkarakis et al., 2004	Contemporary patient series	232		2.6
	Gratzke et al., 2007	Prospective study	902	30 d	5.1
TURP	Ahyai et al., 2010	Meta-analysis	440*B 954*M		2.6 4.1
	Gill et al., 2024	Meta-analysis	918*†		9.6
	Geavlete et al., 2011	Prospective study	170B 170M	30 d	2.9 3.5
	Cornu et al., 2015	Systematic review and meta-analysis	843B 844M		4.3 4.1
	Tascı et al., 2011	Retrospective register study	3,589	30 d	6.5
	Reich et al., 2008	Prospective multicentre study	10,654	30 d	3.6
	Bhojani et al., 2014	Retrospective register study	4,794	30 d	6.0
	Patel et al., 2015	Retrospective register study	4,968	30 d	6.0
PVP	Ahyai et al., 2010	Meta-analysis	142*		12
	Gill et al., 2024	Meta-analysis	839*†		10.6
	Cornu et al., 2015	Systematic review and meta-analysis	287*		6.3
	Ruszat et al., 2008	Single center prospective study	500	30 d	7.2
	Cindolo et al., 2018	Retrospective register study	813	30 d	1.9
	Bhojani et al., 2014	Retrospective register study	2,439	30 d	6.0
	Patel et al., 2015	Retrospective register study	2,853	30 d	6.2
	Elshal et al., 2013	Randomized controlled trial	52	30 d	5.7

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. B = B-TURP. M = M-TURP

Urinary tract infection					
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**
TUIP	Lourenco et al., 2010	Systematic review	110*		4.5
TUVP	Ahyai et al., 2010	Meta-analysis	186*		0
	Geavlete et al., 2011	Prospective study	170	30 d	2.4
HoLEP/EEP	Capogrosso et al., 2023	Single center prospective study	243	30 d	1.6
	Ahyai et al., 2010	Meta-analysis	363*		0.9
	Romero-Otero et al., 2020	Retrospective register study	963	30 d	3.5
	Elzayat & Elhilali, 2007	Retrospective analysis	118		1.7
	Shah et al., 2007	Retrospective register study	280		3.9
	Bhojani et al., 2014	Retrospective register study	126	30 d	3.2
RASP/MISP	Pokorny et al., 2015	Retrospective study	67	30 d	4.5
	Autorino et al., 2015	Retrospective register study	1,330	90 d	2.3
	Mariano et al., 2006	Prospective study	60		6.7
	Lucca et al., 2015	Systematic review and meta-analysis	764*†		3.5
PUL	Sønksen et al., 2015	Randomized controlled trial	45		7
	McNicholas et al., 2013	Retrospective register study	102		5.9
	Raizenne 2022	Retrospective register study	1,362	90 d	2.0
Aquablation	Lambertini et al., 2024	Systematic review	3,125*†		7.6
	Gilling et al., 2018	Double-blind, multicenter prospective study	117	90 d	9.5
	Bach et al., 2020	Prospective multicenter study	178		5.6
	Desai et al., 2020	Prospective multicenter study	101	90 d	7.9
Rezūm	Lambertini et al., 2024	Systematic review	648*†		11.2
	Roehrborn et al., 2017	Randomized controlled trial	135	90 d	7.5
PAE	Zumstein et al., 2019	Systematic review and meta-analysis	381*		6.0
	Raizenne 2022	Retrospective register study	335	90 d	4.9

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

2.6.3 Long-term complications

2.6.3.1 Urethral stricture

Urethral strictures may develop at any urethral location, extending from the external urethral meatus to the bladder neck. Any process that results in urethral trauma has the potential to contribute to the formation of a urethral stricture. (Lumen et al., 2009) Meatal strictures are usually caused by a mismatch between the diameter of surgical instrumentation and the urethral meatus (Rassweiler et al., 2006).

Following transurethral surgery, the urethral mucosa may become abraded and oedematous, leading to increased permeability and loss of integrity. This allows urine to extravasate into the subepithelial space, which enhances the inflammatory response and may subsequently result in scar formation. In cases of severe urethral trauma and inflammation, thrombophlebitis of the corpus spongiosum may develop, leading to focal thrombosis and scar formation. This process may become self-perpetuating, as progressive urethral narrowing increases intramural voiding pressure and further promotes urine extravasation. (Nielsen & Nordling, 1990) In M-TURP, bulbar strictures have been hypothesised to result from inadequate insulation by the lubricant, allowing the current to leak into surrounding tissues (Rassweiler et al., 2006). However, the incidence of urethral strictures appears to be similar after B-TURP and M-TURP (Cornu et al., 2015; Geavlete et al., 2011). The formation of bulbar strictures appears to be related to instrument size, supporting the hypothesis that mucosal damage is caused by friction from the resectoscope shaft (Günes et al., 2015). Other risk factors for urethral stricture include slower resection speed (longer operation time), postoperative infection (Tao et al., 2016), traumatic insertion of the resectoscope (Rassweiler et al., 2006), and improper urethral catheterisation (Lumen et al., 2009).

In a retrospective analysis of 268 patients undergoing urethroplasty, 56% of the strictures caused by prostatectomy (simple or radical) were located in the posterior urethra (five patients), while 33% (three patients) were bulbar and 11% (one patient) multifocal in the anterior urethra. Strictures caused by transurethral resection (of the bladder, prostate, or urethral valves) were located in the penile urethra in 13% (seven patients), bulbar urethra in 62% (32 patients), posterior urethra in 8% (four patients), and multifocally in the anterior urethra in 17%, (nine patients). (Lumen et al., 2009) The majority of the urethral strictures following PVP also appear to be located in the bulbar urethra (Ruszat et al., 2008).

The incidence of urethral strictures after M-TURP ranges from 2.2% to 9.8% (Rassweiler et al., 2006). After OP, rates of approximately 1.76–1.9% have been observed (Titus et al., 2024; Varkarakis et al., 2004). Following PVP, urethral stricture rates of 4.8% (risk ratio compared with TURP 0.83, 95% CI 0.52–1.33;

$p = 0.44$) and 6.3% (range 3–10) have been reported (Ahyai et al., 2010; Gill et al., 2024). Estimated incidences of urethral strictures associated with other surgical modalities are summarised in Table 10.

Table 10. Urethral stricture rates identified in the review of the literature.

Operation type	Urethral stricture				
	Source	Design	N	Time frame	Rate (%)
Open	Titus et al., 2024	Meta-analysis	320*		1.76
	Varkarakis et al., 2004	Contemporary patient series	151	3.5 y	1.9
	Kuntz et al., 2007	Randomized controlled trial	60	5 y	1.7
TURP	Ahyai et al., 2010	Meta-analysis	440*B		2.4
			954*M		4.1
	Gill et al., 2024	Meta-analysis	918*†	2 y	6.5
	Geavlete et al., 2011	Prospective study	170B	1.5 y	6.5
			170M		5.3
	Cornu et al., 2015	Systematic review and meta-analysis	268*B	2–5 y	6.3
			282*M		6.7
	Tascı et al., 2011	Retrospective register study	3,589	3.5 y	3.2
	Bachmann et al., 2015	Randomized controlled trial	142	1 y	3.8
PVP	Ahyai et al., 2010	Meta-analysis	142*		6.3
	Gill et al., 2024	Meta-analysis	839*†	2 y	4.8
	Cornu et al., 2015	Systematic review and meta-analysis	142*	1 y	5.6
	Elshal et al., 2013	Randomized controlled trial	52	5.8 y	7.7
	Elshal et al 2012	Longitudinal study	288	3.3 y	2.1
	Bachmann et al., 2015	Randomized controlled trial	139	1 y	1.5
	Ruszat et al., 2008	Single center prospective study	500	5 y	4.4

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. B = B-TURP. M = M-TURP

Urethral stricture					
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**
TUIP	Madersbacher & Marberger, 1999	Review	270*		4.1
TUVP	Ahyai et al., 2010	Meta-analysis	186*		1.9
	Geavlete et al., 2011	Prospective study	170	1.5 y	4.7
	Madersbacher & Marberger, 1999	Review	189*		3.4
HoLEP/EEP	Capogrosso et al., 2023	Single center prospective study	243	1 y	0.8
	Ahyai et al., 2010	Meta-analysis	363*		4.4
	Cornu et al., 2015	Systematic review and meta-analysis	287*	1 y	13.2
	Romero-Otero et al., 2020	Retrospective register study	963	1 y	1.6
	Elmansy et al., 2011	Retrospective analysis	949	10 y	1.6
	Kuntz et al., 2007	Randomized controlled trial	60	5 y	3.3
	Elzayat & Elhilali, 2007	Retrospective analysis	118	4 y	1.7
	Shah et al., 2007	Retrospective register study	280		4.6
PUL	Sønksen et al., 2015	Prospective randomized multinational study	45	1 y	0
Aquablation	Lambertini et al., 2024	Systematic review	3,125*†		4.81
	Gilling et al., 2020	Double-blind, multicenter prospective study	117	> 3 y	3.5
	Bach et al., 2020	Prospective multicenter study	178		1.7
	Desai et al., 2020	Prospective multicenter study	101	2 y	9.9
Rezūm	Lambertini et al., 2024)	Systematic review	648*†		1.9
PAE	Zumstein et al., 2019	Systematic review and meta-analysis	102*		0
TUMT	Madersbacher & Marberger, 1999	Review	98*		0

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

2.6.3.2 Bladder neck stenosis

Bladder neck stenosis (BNS) is thought to occur after transurethral surgery due to obliteration of the microvasculature supplying the bladder neck, leading to tissue ischemia and subsequent scar formation. (Parker & Simhan, 2015) Severe storage LUTS and smaller prostate size are associated with a higher risk of BNS (Tao et al., 2016). Diabetes, smoking, and cardiovascular disease have been identified as modifiable risk factors (Parker & Simhan, 2015). Prophylactic bladder neck incision may reduce the incidence of BNS when treating smaller prostates (<30 g) (Rassweiler et al., 2006).

Regarding PVP, earlier treatment modalities using the 80-W system appear to be associated with a higher incidence of BNS at 3 months postoperatively. However, at 12-month follow-up, incidence rates were similar between the 80-W and 180-W systems (Hu et al., 2016). In a large-scale study of 43,000 patients with 5 years of follow-up, the treatment rate for urethral stricture or BNS was 6.8% after TURP (reference group for HR), 3.2% after OP (HR 0.45, 95% CI 0.37–0.55, $p < 0.001$), 6.7% after PVP (HR 1.03, 95% CI 0.87–1.22, $p = 0.7$), and 6.1% after EEP (HR 0.88, 95% CI 0.67–1.17, $p = 0.4$) (Gilfrich et al., 2021).

In a systematic review and meta-analysis focusing on BNS, the pooled incidence was 1.3% after TURP (range 0.5–15.4%), 0.66% after enucleation (range 0.5–3.6%, including HoLEP, ThuLEP, diode, monopolar, and bipolar enucleation), and 1.2% after ablation (range 0.4–8.7% including PVP, laser vaporisation, and TUVP) (Castellani et al., 2021). Selected BNS rates reported in the literature are presented in Table 11.

Table 11. Bladder neck stenosis rates identified in the review of the literature.

		Bladder neck stenosis				
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**	**Additional relevant details**
Open	Titus et al., 2024	Meta-analysis	320*		4.25	
	Varkarakis et al., 2004	Contemporary patient series	151	3.5 y	3.3	
	Gilfrich et al., 2021	Retrospective register study	3,651	5 y	3.2	US and BNS
	Kuntz et al., 2007	Randomized controlled trial	60	5 y	5.0	
	Gilfrich et al., 2016	Retrospective register study	8,376	1 y	1.51	

* = Pooled N, US = Urethral stricture, BNS = Bladder neck stenosis

Bladder neck stenosis						
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**	**Additional relevant details**
TURP	Ahyai et al., 2010	Meta-analysis	440*		0.5	B-TURP
			954*		2	M-TURP
	Gill et al., 2024	Meta-analysis	918*†	2 y	2.9	
	Mordasini et al., 2018	Randomized controlled trial	126	5 y	7.1	US and BNS
	Geavlete et al., 2011	Prospective study	170	1.5 y	3.5	B-TURP
			170		4.1	M-TURP
	Cornu et al., 2015	Systematic review and meta-analysis	964	1 y	5.4	B-TURP
			986		4.6	M-TURP
			268	2–5 y	5.2	B-TURP
			282		4.6	M-TURP
	Tascı et al., 2011	Retrospective register study	3,589	3.5 y	1.08	
	Gilfrich et al., 2021	Retrospective register study	34,526	5 y	6.8	US and BNS
	Bachmann et al., 2015	Randomized controlled trial	142	1 y	2.3	
	Kaplan et al., 2024	Retrospective register study	22,649	1 y	0.03	
	Gilfrich et al., 2016	Retrospective register study	78,192	1 y	1.8	
	Al-Ansari et al., 2010	Randomized controlled trial	60	3 y	3.6	
HoLEP/EEP	Capogrosso et al., 2023	Single center prospective study	243	1 y	2.4	
	Ahyai et al., 2010	Meta-analysis	363*		1.2	
	Romero-Otero et al., 2020	Retrospective register study	963	1 y	2.4	
	Elmansy et al., 2011	Retrospective analysis	949	10 y	0.8	
	Gilfrich et al., 2021	Retrospective register study	1,814	5 y	6.1	US and BNS
	Elzayat & Elhilali, 2007	Retrospective analysis	118	4 y	0.8	
	Shah et al., 2007	Retrospective register study	280		0.4	
	Gilfrich et al., 2016	Retrospective register study	2,600	1 y	1.57	
	Kuntz et al., 2007	Randomized controlled trial	60	5 y	1.7	

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. US = Urethral stricture, BNS = Bladder neck stenosis

Bladder neck stenosis						
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**	**Additional relevant details**
TUIP	Lourenco et al., 2010	Systematic review	263*		8.7	US and BNS
TUVP	Ahyai et al., 2010	Meta-analysis	186*		0.5	
	Geavlete et al., 2011	Prospective study	170	1.5 y	0.6	
PVP	Ahyai et al., 2010	Meta-analysis	142*		5.0	
	Gill et al., 2024	Meta-analysis	839*†	2 y	2.9	
	Al-Ansari et al., 2010	Randomized controlled trial	60	3 y	7.4	
	Cornu et al., 2015	Systematic review and meta-analysis	196*	1 y	2.6	
	Gilfrich et al., 2021	Retrospective register study	3,050	5 y	6.7	US and BNS
	Elshal et al 2012	Longitudinal study	288	3.3 y	3.4	
	Elshal et al., 2013	Randomized controlled trial	52	5.8 y	9.6	
	Bachmann et al., 2015	Randomized controlled trial	139	1 y	4.4	
	Ruszat et al., 2008	Single center prospective study	500	5 y	3.6	
	Kaplan et al., 2024	Retrospective register study	11,392	1 y	0.05	
	Mordasini et al., 2018	Randomized controlled trial	128	5 y	4.7	US and BNS
	Gilfrich et al., 2016	Retrospective register study	6,409	1 y	2.33	
PUL	Sønksen et al., 2015	Prospective randomized multinational study	45	1 y	0	US and BNS
	Kaplan et al., 2024	Retrospective register study	7,529	1 y	0.1	
	Raizenne et al., 2022	Retrospective register study	1,362	2 y	0.3	US and BNS
Aquablation	Gilling et al., 2020	Double-blind, multicenter prospective study	117	> 3 y	2.6	
Rezūm	Kaplan et al., 2024	Retrospective register study	1,597	1 y	0.0	
	Roehrborn et al., 2017	Randomized controlled trial	135	1–2 y	1.9	
PAE	Raizenne et al., 2022	Retrospective register study	335	2 y	0	US and BNS

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. US = Urethral stricture, BNS = Bladder neck stenosis

2.6.3.3 Urinary incontinence

Urinary incontinence occurs in the early postoperative period due to detrusor instability or healing of the resection bed (Parker & Simhan, 2015; Rassweiler et al., 2006). Late postoperative urinary incontinence (persisting beyond 6 months) should be evaluated with urodynamic studies. It may be associated with sphincter incompetence, detrusor instability, mixed incontinence, residual adenoma, BNS, or urethral stricture. After TURP, early urinary incontinence may occur in up to 40% of patients, whereas late iatrogenic urinary incontinence occurs in fewer than 0.5%. (Rassweiler et al., 2006)

Similarly, following HoLEP, significant stress and/or urge incontinence occurs in 24% of patients within 0–6 months, decreasing to 6.5% at 6–12 months, 3.3% at 12 months to 5 years, and 7% beyond 5 years of follow-up (Krambeck et al., 2010). In another study of 243 HoLEP patients, of whom 85% were continent preoperatively, 30.4% required one or more pads daily at 1 month after surgery; this proportion decreased to 4.9% at 12 months. (Capogrosso et al., 2023)

In a cohort of 84 patients undergoing PVP, de novo urge urinary incontinence occurred in up to 27.4% at 1 month postoperatively and resolved to 0% at 6 months. Transient urinary incontinence after PVP might be associated with older age (OR 1.282, 95% CI 1.122–1.465, $p < 0.001$), high storage symptom scores (OR 1.239, 95% CI 1.054–1.455, $p = 0.009$), longer time to Qmax (OR 0.945, 95% CI 0.913–0.979, $p = 0.015$), lower bladder volume at first desire to void (OR 0.962, 95% CI 0.944–0.980, $p < 0.001$), and reduced maximum cystometric capacity (OR 0.991, 95% CI 0.986–0.996, $p = 0.001$). (Bae et al., 2016) In a recent meta-analysis comparing TURP with PVP, the pooled incontinence rate was estimated to be 6.6% after TURP and 11.8% after PVP. Reported incontinence rates vary considerably across studies, as demonstrated in Table 12.

Table 12. Urinary incontinence rates identified in the review of the literature.

Operation type	Source	Incontinence Design	N	Time frame	Rate (%)
Open	Titus et al., 2024	Meta-analysis	557*		3.74
	Varkarakis et al., 2004	Contemporary patient series	151	3.5 y	0
	Gilfrich et al., 2016	Retrospective register study	8,376	1 y	0.09
TURP	Ahyai et al., 2010	Meta-analysis	440*B 954*M		0 0.6
	Gill et al., 2024	Meta-analysis	918*†	2 y	6.6
	Geavlete et al., 2011	Prospective study	170B 170M	1.5 y	1.2 2.4
	Cornu et al., 2015	Systematic review and meta-analysis	527B 534M	1 y	1.5 2.2
	Tascı et al., 2011	Retrospective register study	3,589	3.5 y	0
	Bachmann et al., 2015	Randomized controlled trial	142	1 y	1.5
	Kaplan et al., 2024	Retrospective register study	22,649	1 y	0.0
	Gilfrich et al., 2016	Retrospective register study	78,192	1 y	0.14
PVP	Ahyai et al., 2010	Meta-analysis	142*		0
	Gill et al., 2024	Meta-analysis	839*†	2 y	11.8
	Elshal et al., 2013	Randomized controlled trial	52	> 1 y	3.8
	Elshal et al 2012	Longitudinal study	288	3.3 y	1.1
	Bachmann et al., 2015	Randomized controlled trial	139	1 y	2.9
	Ruszat et al., 2008	Single center prospective study	500	5 y	1.2
	Kaplan et al., 2024	Retrospective register study	11,392	1 y	0.02
	Gilfrich et al., 2016	Retrospective register study	6,409	1 y	0.29

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. B = B-TURP. M = M-TURP

Incontinence					
Operation type	**Source**	**Design**	**N**	**Time frame**	**Rate (%)**
TUIP	Lourenco et al., 2010	Systematic review	163*		1.8
TUVP	Ahyai et al., 2010	Meta-analysis	186*		0
	Geavlete et al., 2011	Prospective study	170	1.5 y	0.6
HoLEP/EEP	Ahyai et al., 2010	Meta-analysis	363*		0.9
	Capogrosso et al., 2023	Single center prospective study	243	1 y	8.2
	Romero-Otero et al., 2020	Retrospective register study	963	1 y	2.3
	Elmansy et al., 2011	Retrospective analysis	949	10 y	0.5
	Elzayat & Elhilali, 2007	Retrospective analysis	118	4 y	2.5
	Shah et al., 2007	Retrospective register study	280		0.7
	Gilfrich et al., 2016	Retrospective register study	2,6	1 y	0.20
RASP/MISP	Pokorny et al., 2015	Retrospective study	67	6 m	0
	Mariano et al., 2006	Prospective study	60	6 m	0
PUL	Sønksen et al., 2015	Prospective randomized multinational study	45	1 y	2
	Kaplan et al., 2024	Retrospective register study	7,529	1 y	0.03
Aquablation	Lambertini et al., 2024	Systematic review	3,125*†		< 2
	Bach et al., 2020	Prospective multicenter study	178		0.6
	Desai et al., 2020	Prospective multicenter study	101	2 y	1.0
Rezūm	Kaplan et al., 2024	Retrospective register study	1,597	1 y	0.0
PAE	Ray et al., 2018	Observational study	216	1 y	1.0
	Zumstein et al., 2019	Systematic review and meta-analysis	327*		0.6
TUMT	Stenmark et al., 2022	Retrospective register study	570	11 y	0

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

2.6.3.4 Retrograde ejaculation and erectile dysfunction

The evaluation of the impact of transurethral surgery for BPO on sexual function is difficult for many reasons. First, the underlying pathophysiology remains poorly understood. Second, the literature primarily focuses on erectile and ejaculatory function, assessed using a wide variety of symptom scales. Third, multiple confounding factors interact with sexual symptoms, including LUTS and the associated symptom burden. Furthermore, the pathophysiology of BPH/LUTS and erectile dysfunction is hypothesised to share a common origin, further confounding the assessment of cause-and-effect relationships. (Gacci et al., 2011) The pathophysiology of ejaculatory dysfunction following surgery for BPO is also not fully understood, but preservation of tissue around the verumontanum and the bladder neck may reduce the risk (Sokolakis et al., 2022).

In a systematic review and meta-analysis evaluating the impact of surgery for BPO on erectile and ejaculatory function, pooled analyses of TURP revealed no statistically significant changes in erectile function, as measured by the five-item International Index of Erectile Function ($p = 0.08$). In contrast, TURP was associated with a statistically significant risk of retrograde ejaculation, with reported rates in RCTs ranging from 27.7% to 100% (relative risk [RR] 13.31, 95% CI 8.37–21.17; $p < 0.00001$). Similarly, a significantly increased risk of retrograde ejaculation was observed after TUVP (RR 55.75; 95% CI 17.96–173.05, $p < 0.00001$), HoLEP (RR 8.13; 95% CI 2.05–32.17, $p = 0.003$) and PVP (RR 24.88; 95% CI 8.66–71.50, $p < 0.0001$). For HoLEP and PVP, no significant difference from baseline erectile function was identified based on International Index of Erectile Function-5 scores. In this meta-analysis, studies of PUL, PAE, and aquablation were scarce. However, no change in retrograde ejaculation rates was observed after PUL or PAE, whereas one study reported a significantly higher rate after aquablation. Overall, newer minimally invasive surgical therapies were associated with a lower risk of retrograde ejaculation. (Manfredi et al., 2022)

In another systematic review and network meta-analysis of erectile function, PUL resulted in an improvement in erectile function at 24 months compared with M-TURP; however direct evidence of this was lacking. M-TURP, B-TURP, PVP, HoLEP/EEP, OP, laparoscopic simple prostatectomy, and aquablation showed no significant differences in erectile function at up to 60 months of follow-up. (Light et al., 2021) In a Cochrane review including six studies with 640 participants, the effects of minimally invasive treatments (Rezūm, PUL, PAE) on erectile function remained uncertain. In the same review, the effect on ejaculatory function, based on eight studies with 461 participants, was likewise uncertain. (Franco et al., 2022)

Standard procedures for treating LUTS have been developed primarily with efficacy as the main outcome, rather than the preservation of ejaculatory function, which naturally reflects on the results following surgery. The incidence of retrograde

ejaculation after TURP is considerably lower when attempts are made to preserve ejaculatory function. (Gross & Netsch, 2022) Ejaculation-preserving TURP generally involves preserving approximately 1 cm of tissue proximal to the verumontanum, with or without sparing the bladder neck (Sokolakis et al., 2022).

In a small study of 60 patients, half underwent ejaculation-sparing TURP in which the supramontanal region and the lissosphincter were spared. This approach resulted in a significant preservation of antegrade ejaculation postoperatively (ejaculation projection score 3.77 vs 0; $p < 0.001$) (Ramachandran et al., 2024). Similarly, PVP can be performed in a more ejaculation-preserving manner by sparing the same structures. Nevertheless, patients should be informed that ejaculation-preserving modifications do not guarantee maintenance of antegrade ejaculation.

With respect to EEP, ejaculatory preservation may be achieved by placing the initial incision 1.5 cm cranial to the verumontanum. (Sokolakis et al., 2022) For OP, the Madigan technique, which preserves the prostatic urethra, has been described and subsequently adapted to RASP (Simone et al., 2019). PAE may preserve normal ejaculatory function, as it does not involve direct tissue ablation, similarly to PUL (Sokolakis et al., 2022).

In principle, preservation of ejaculatory function should be easier to achieve with tissue ablation performed under direct visual control. The Rezūm system has shown promising results in terms of sexual function preservation; still, RCTs comparing Rezūm with TURP or other reference techniques are lacking (Gross & Netsch, 2022; Sokolakis et al., 2022). Ejaculatory preservation rates of 81–98% have been reported after aquablation have been reported, but independent studies without manufacturer involvement remain scarce (Gross & Netsch, 2022). Examples of reported rates of retrograde ejaculation and erectile dysfunction are presented in Table 13.

Table 13. Ejaculatory and erectile dysfunction rates identified in the review of the literature.

Operation type	Source	Design	N	Time frame	Sexual dysfunction	
					Ejaculatory dysfunction (%)	Erectile dysfunction (%)
TURP	Gill et al., 2024	Meta-analysis	918*†	2 y	59.2	
TUIP	Lourenco et al., 2010	Systematic review	145*		27.6	
			119*			3.4
	Madersbacher & Marberger, 1999	Review	270*		18.2	
TUVP	Madersbacher & Marberger, 1999	Review	189*		85	
PVP	Gill et al., 2024	Meta-analysis	839*†	2 y	44.6	
RASP/MISP	Mariano et al., 2006	Prospective study	60	6 m	68.3	100
PUL	Sønksen et al., 2015	Prospective randomized multinational study	45	1 y	0	0
	McNicholas et al., 2013	Retrospective analysis	102	1 y	0	
Aquablation	Gilling et al., 2020	Double-blind, multicenter prospective study	117	> 3 y	11.3	3.4
	Bach et al., 2020	Prospective multicenter study	178		8.4	0.6
	Desai et al., 2020	Prospective multicenter study	101	2 y	16.8	1.0
Rezūm	Roehrborn et al., 2017	Randomized controlled trial	135	1–2 y	1.9	
PAE	Ray et al., 2018	Observational study	216	12 m	24.1	
TUMT	Madersbacher & Marberger, 1999	Review	98*		0–22	
TUNA	Madersbacher & Marberger, 1999	Review	117*		0	

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

2.6.3.5 Reoperation

The primary goal of surgery for BPH/LUTS is to relieve symptoms that impair QoL. Consequently, long-term efficacy is a central consideration in surgical management. Also, the increasing incidence of LUTS, together with economic constraints, further emphasises the importance of durable treatment outcomes (Reich et al., 2006). Reoperation after surgery for BPH/LUTS may be required due to regrowth of prostatic tissue, leading to recurrent BOO and LUTS. Reoperation may also result from long-term postoperative complications, such as urethral stricture or BNS causing LUTS.

In a systematic review and meta-analysis by Cornu et al., the overall reoperation rate at 12 months after TURP was low. The reoperation rates at 12 months were also similar between M-TURP (7.4%) and B-TURP (6.5%) (OR 0.66, 95% CI 0.25–1.72). The same study concluded that HoLEP may offer favourable long-term efficacy; however, this conclusion was based on only two studies, and reoperation rates were not available in the meta-analysis. In addition, in the same meta-analysis, PVP appeared to be associated with a higher reoperation rate for BPO recurrence (PVP 5.6% vs M-TURP 1.5%, OR 3.87, 95% CI 1.06–14.04). These findings should be interpreted with caution, as the pooled sample sizes were small (N = 196 for PVP and N = 197 for TURP), making the results more susceptible to confounding factors. (Cornu et al., 2015)

Regarding minimally invasive treatments, a meta-analysis estimated that PUL has a yearly surgical reintervention rate of 6.0% (95% CI 3.0–8.9). In one study with a maximum follow-up of 5 years, the overall surgical reintervention rate after PUL was 22.9% (32 of 140 patients) (Miller et al., 2020). In a Cochrane review of minimally invasive treatments, the retreatment rates of PUL and PAE compared with TURP were considered uncertain. In contrast, TUMT appeared to result in higher retreatment rates, while Rezūm was not included in the analysis due insufficient long-term results (Franco et al., 2022).

In a large retrospective study of over 43,000 patients, the 5-year reoperation rate for LUTS was 8.2% after TURP (used as reference), 3.3% after OP (HR 0.38, 95% CI 0.31–0.46, $p < 0.001$), 12.5% after PVP (HR 1.52, 95% CI 1.35–1.72, $p < 0.001$), and 7.1% after EEP (HR 0.84, 95% CI 0.63–1.14, $p = 0.3$) (Gilfrich et al., 2021).

In an analysis of the Austrian nationwide database including over 21,000 patients, the re-TURP rate after 8 years of follow-up was 8.3% for TURP and 4.3% for OP, while the overall endourological reintervention rates were 12.7% and 8.8%, respectively (Eredics et al., 2018). These findings were comparable to rates reported a decade earlier in Austria, where re-TURP and overall endourological reintervention rates were 7.4% and 14.7% after TURP, and 3.4% and 9.5% after OP (Madersbacher et al., 2005).

In a more recent retrospective analysis of 155,874 patients, the 5-year probability of re-invention was 18.7% for PUL (95% CI 16.8–20.5), 19.6% for PAE (95% CI 16.1–22.9), 7.7% for TUIP (95% CI 7.0–8.4), 6.9% for PVP (95% CI 6.1–7.6), 5.6% for TURP (95% CI 5.5–5.8), 5.5% for TUVP (95% CI 4.8–6.3), and 3.5% for both HoLEP (95% CI 3.1–3.8) and OP (95% CI 2.3–4.7) (Page et al., 2025).

In another retrospective population-based cohort study of urethral strictures using Medicare and commercial claims data, 5-year retreatment rates were 7.0% for TURP (476 of 6,748 patients), 8.9% for PVP (348 of 3,922 patients), and 11.6% for PUL (34 of 293 patients). Interestingly, retreatment was most commonly performed with using the same procedure as the index operation during 1-year and 5-year follow-up, whereas TURP was the second most common reoperation across all other procedure types. (Kaplan et al., 2024) Some of the reoperation rates reported in the current literature are shown in Table 14.

Table 14. Reoperation rates identified in the review of the literature.

Operation type	Reoperation				
	Source	Design	N	Time frame	Rate (%)
Open	Varkarakis et al., 2004	Contemporary patient series	151	3.5 y	3.9
	Gilfrich et al., 2021	Retrospective register study	3,651	5 y	5.5
	Kuntz et al., 2007	Randomized controlled trial	60	5 y	6.7
	Page et al., 2025	Retrospective register study	1,147	5 y	3.5
	Gilfrich et al., 2016	Retrospective register study	8,376	1 y	2.99
TUIP	Lourenco et al., 2010	Systematic review	196*		18.4
	Page et al., 2025	Retrospective register study	6,581	5 y	7.7
	Madersbacher & Marberger, 1999	Review	270*		15.9
TUVP	Ahyai et al., 2010	Meta-analysis	186*		2.4
	Geavlete et al., 2011	Prospective study	170	1.5 y	3.5
	Page et al., 2025	Retrospective register study	4,305	5 y	5.5
	Madersbacher & Marberger, 1999	Review	189*		0

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

Operation type	Reoperation				
	Source	Design	N	Time frame	Rate (%)
TURP	Ahyai et al., 2010	Meta-analysis	440*B 954*M		0.4 0.6
	Gill et al., 2024	Meta-analysis	918*†	2 y	9.8
	Al-Ansari et al., 2010	Randomized controlled trial	60	3 y	1.8
	Geavlete et al., 2011	Prospective study	170B 170M	1.5 y	9.4 8.8
	Cornu et al., 2015	Systematic review and meta-analysis	613B 625M 218B 232M	1 y 2–5 y 	6.5 7.4 16 13
	Tascı et al., 2011	Retrospective register study	3,589	3.5 y	4.4
	Gilfrich et al., 2021	Retrospective register study	34,526	5 y	12.1
	Bachmann et al., 2015	Randomized controlled trial	142	1 y	0.8
	Kaplan et al., 2024	Retrospective register study	22,649	5 y	7.0
	Gilfrich et al., 2016	Retrospective register study	78,192	1 y	6.21
	Mordasini et al., 2018	Randomized controlled trial	126	5 y	11.9
	Page et al., 2025	Retrospective register study	114,820	5 y	5.6
HoLEP/EEP	Capogrosso et al., 2023	Single center prospective study	243	1 y	2.4
	Ahyai et al., 2010	Meta-analysis	363*		0
	Page et al., 2025	Retrospective register study	15,895	5 y	3.5
	Elmansy et al., 2011	Retrospective analysis	949	10 y	0.7
	Gilfrich et al., 2021	Retrospective register study	1,814	5 y	10.4
	Elzayat & Elhilali, 2007	Retrospective analysis	118	4 y	4.2
	Page et al., 2025	Retrospective register study	15,895	5 y	3.5
	Gilfrich et al., 2016	Retrospective register study	2,600	1 y	5.22
	Kuntz et al., 2007	Randomized controlled trial	60	5 y	5.0

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type. B = B-TURP. M = M-TURP

Operation type	Reoperation				
	Source	Design	N	Time frame	Rate (%)
PVP	Ahyai et al., 2010	Meta-analysis	142*		5.6
	Gill et al., 2024	Meta-analysis	839*†	2 y	11.3
	Al-Ansari et al., 2010	Randomized controlled trial	60	3 y	11
	Cornu et al., 2015	Systematic review and meta-analysis	196*	1 y	5.6
	Gilfrich et al., 2021	Retrospective register study	3,050	5 y	15.5
	Elshal et al 2012	Longitudinal study	288	3.3 y	2
	Elshal et al., 2013	Randomized controlled trial	52	5.8 y	7.7
	Bachmann et al., 2015	Randomized controlled trial	139	1 y	2.2
	Ruszat et al., 2008	Single center prospective study	500	5 y	6.8
	Kaplan et al., 2024	Retrospective register study	11,392	5 y	8.9
	Mordasini et al., 2018	Randomized controlled trial	128	5 y	14.3
	Page et al., 2025	Retrospective register study	6	5 y	6.9
	Gilfrich et al., 2016	Retrospective register study	6,409	1 y	10.13
RASP/MISP	Lucca et al., 2015	Systematic review and meta-analysis	764*†		3.5
PUL	Sønksen et al., 2015	Prospective randomized multinational study	45	1 y	7
	Lambertini et al., 2024	Systematic review	291*†		10.9
	Kaplan et al., 2024	Retrospective register study	7,529	5 y	11.6
	Page et al., 2021	Retrospective register study		2 y	11.9
	McNicholas et al., 2013	Retrospective analysis	102	1 y	6.5
	Page et al., 2025	Retrospective register study	4,606	5 y	18.7
	Raizenne et al., 2022	Retrospective register study	1,362	2 y	8.5
Aquablation	Gilling et al., 2020	Double-blind, multicenter prospective study	117	> 3 y	4.3
	Desai et al., 2020	Prospective multicenter study	101	2 y	2.0
Rezūm	Page et al., 2025	Retrospective register study	1,145	1 y	2.4
	Kaplan et al., 2024	Retrospective register study	1,597	1 y	6.2
	Roehrborn et al., 2017	Randomized controlled trial	135	1–2 y	4.3

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

Operation type	Reoperation				
	Source	Design	N	Time frame	Rate
PAE	Ray et al., 2018	Observational study	216	1 y	19.9
	Minore et al., 2024	Retrospective register study	426		3.3
	Raizenne et al., 2022	Retrospective register study	335	2 y	28.5
	Page et al., 2025	Retrospective register study	1,879	5 y	19.6
	Müllhaupt et al., 2024	Randomized controlled trial	48	5 y	41.7
TUMT	Stenmark et al., 2022	Retrospective register study	570	11 y	23
	Madersbacher & Marberger, 1999	Review	98*		3–11
TUNA	Madersbacher & Marberger, 1999	Review	117*		2

* = Pooled N. † = N for whole meta-analysis, not spesific for complication type.

2.6.4 Non-urological complications

2.6.4.1 Major Adverse Cardiovascular Event

Men with moderate-to-severe LUTS appear to have an increased risk of major adverse cardiovascular events (MACE), defined as acute coronary syndrome, other chronic ischaemic heart disease, transient ischaemic attack, or cerebrovascular accident (Gacci et al., 2016). Surgery to treat LUTS may increase this risk. Early studies suggested higher long-term mortality after TURP compared with OP, primarily due to a higher mortality from acute myocardial infarction. (Malenka et al., 1990) Proposed explanations for this historic difference include patient selection bias and potential cytotoxic effects of glycine on the myocardium (Madersbacher et al., 2005).

In a nationwide retrospective study published in 2005 including 23,123 patients in Austria, the annual incidence of myocardial infarction in the general population increased gradually from 0.3% in men aged 50–59 years to 1.1% in those older than 80 years. In contrast, the respective annual incidence after TURP increased from 0.9% (50–59 years) to 2.3% (80+ years), while after OP it remained relatively stable at around 2.5% across the age groups. The 8-year cumulative incidence of hospital admission for myocardial infarction was 4.8% after TURP and 4.9% after OP. (Madersbacher et al., 2005) Overall, the incidence of MACE appears higher than in the general population; however, this may reflect

the association between LUTS and cardiovascular disease. (Gacci et al., 2016; Madersbacher et al., 2005)

In an earlier study by Hahn et al., both TUMT and TURP were associated with a 20–30% increased risk of acute myocardial infarction, expressed as a ratio of observed to expected number of cases of 1.25 (95% CI 1.01–1.54). This finding was consistent with the increased risk of cardiovascular disease in patients with BPH. While overall mortality from MACE was not significantly higher than expected in these groups, mortality following acute myocardial infarction was increased after TUMT due to very high case-fatality rate. (Hahn et al., 2000)

In a population-based analysis of 44,939 patients undergoing transurethral surgery, 0.8% (365) experienced a MACE within 30 days postoperatively. The incidence was 0.9% after TURP (reference), 0.7% after PVP (OR 0.7, 95% CI 0.6–0.9, p = 0.017), and 0.6% after EEP (OR 0.7, 95% CI 0.4–1.1, p = 0.181). (Marchioni et al., 2019) Similarly, in a cohort of 7,359 men, reported cardiovascular and thromboembolic complication rates were 0.7% after TURP, 0.5% after tissue vaporisation, and 0% after enucleation (Bhojani et al., 2014). In a study focusing on perioperative MACE after 180-W PVP, 1.9% of the 923 patients experienced a MACE (Marchioni et al., 2018). With regard to HoLEP, the incidence of acute myocardial infarction was 0.4% (one patient) in an early (published 2007) series of 280 patients and ranged from and 0.1% to 1.2% in earlier reports (Shah et al., 2007).

The increasing use of anticoagulants and antithrombotic agents, together with decisions regarding discontinuation before transurethral surgery, highlights the dural concern of bleeding risk and the risk of MACE after surgery for BPH/LUTS (Marien & Shah, 2013). Retrospective studies have shown that aspirin withdrawal precedes up to 10.2% of acute cardiovascular syndromes (Burger et al., 2005), and therefore the balance between bleeding risk and risk of MACE must be considered carefully.

A review published in 2013 concluded that withdrawal of OAC or antithrombotic medication reduces the risk of bleeding in exchange for a higher risk of MACE, especially in men receiving these medications for secondary prevention (Marien & Shah, 2013). However, there are some discrepancies in the literature. In an earlier retrospective series of 305 men undergoing TURP, no significant differences were observed between patients whose OAC was discontinued preoperatively, those not receiving OAC, and those who continued taking aspirin (Raj et al., 2011). This may be explained by the relatively small sample size in relation to the overall risk of MACE in the general population.

In a more recent study published in 2024, TURP patients in whom OAC medication was withheld preoperatively (82% for AF, 14% for pulmonary embolism/deep vein thrombosis and 3.5% for mechanical cardiac valve prosthesis)

had a significantly higher perioperative stroke risk compared with patients not receiving OAC (0.4% in 513 non-OAC patients vs 2.7% in 113 OAC patients, p = 0.01) (Kuo et al., 2024).

In contrast, a meta-analysis of TURP – including three studies in which OAC was continued and one using bridging therapy – reported a pooled thromboembolic event rate of 2.6% after TURP, which did not differ significantly from that of the control group (Fa et al., 2020). MACE rates reported in the current literature, stratified by surgical modality, are presented in Table 15.

2.6.5 Mortality

In earlier studies, patients undergoing transurethral prostatectomy appeared to have an increased risk of mortality even years after the operation. The risk of dying up to 5 years postoperatively was 1.58-fold (95% CI 1.07–2.33) higher than after OP (Malenka et al., 1990). However, evidence from studies published in the 21st century suggests that this difference has diminished over time, and EAU guidelines conclude that the mortality risk of both TURP and OP has decreased significantly (Cornu et al., 2025).

In nationwide analyses of mortality rates in Austria, patients who underwent TURP or OP between 1992–1996 (N = 23,123) and 2002–2006 (N=21,674) had 90-day mortality rates of 0.7% and 0.5% for TURP and 0.9% and 0.4% for OP. Similarly, the 8-year incidence of in-hospital mortality decreased over time, from 20.0% and 20.9% for TURP and OP in the earlier period, to 16.7% and 17.2% in the later period. (Eredics et al., 2018; Madersbacher et al., 2005)

Bhojani et al. reported an overall perioperative mortality of 0.4%, with no significant difference between TURP (0.4%; OR reference), tissue vaporisation (0.3%; OR 0.68, 95% CI 0.29–1.62, p = 0.4), or enucleation (0.0%; OR 0.00, 95% CI 0.00–0.00, p = 0.9) (Bhojani et al., 2014).

In a study of 95,577 cases from a nationwide German health insurance database, the overall 30-day mortality rate was 0.36%. The 30-day mortality rate was 0.32% after TURP (reference), 0.58% after laser vaporisation (OR 1.81, 95% CI 1.27–2.59, p < 0.01), 0.27% after EEP (OR 0.85, 95% CI 0.39–1.86, p = 0.678), and 0.51% after OP (OR 1.59, 95% CI 1.14–2.20, p < 0.01) (Gilfrich et al., 2016).

The effect of urologist caseload volume and in-hospital mortality has also been studied at the national level in Taiwan. The overall in-hospital mortality rate of 9,539 TURP cases during 2003 was 1.83%. Urologists who had a high annual caseload (≥56 procedures) had a mortality rate of 1.16%, while urologists with medium (27–55) or low (<27) caseload volumes had mortality rates of 1.97% and 2.37%. Even after adjusting for comorbidities, age, and hospital characteristics, the likelihood of in-hospital mortality was statistically significantly higher when treated by a urologist

with a low (OR 1.835, 95% CI 1.198–2.812, $p < 0.01$) or medium caseload (OR 1.606, 95% CI 1.052–2.452, $p < 0.05$) (Chen & Lin, 2008).

In a prospective multicentre evaluation of 10,654 patients operated on during 2002–2003, the 30-day mortality rate of TURP was 0.10%. Reich et al. also reported that the mortality rate increased with increasing resection weight (greater than 60 g vs ≤30 g; OR 7.90, 95% CI 2.12–29.51). (Reich et al., 2008)

In the same year, in Bavaria, the 30-day mortality rate of 902 OP patients was 0.2% (Gratzke et al., 2007). Regarding 180-W PVP, the 30-day mortality rate was 0.3% (Cindolo et al., 2018). In slightly more recent studies, the 90-day postoperative mortality rates after laparoscopic simple prostatectomy (N=843) and RASP (N=487) were 0% and 0.2% respectively (Autorino et al., 2015).

In a 10-year retrospective study of 155,847 patients undergoing surgical interventions for BPE, the overall 30-day mortality rate was 0.2%. Mortality rates of individual procedure types were not provided. (Page et al., 2025) In a study of complications and device failures associated with PUL, 11 deaths within a 90-day period were reported (Juliebø-Jones et al., 2023).

Mortality is arguably the most significant complication after surgery performed to improve QoL. However, it is rarely reported in RCTs studying traditional surgical procedures or newer minimally invasive treatment modalities. One reason for this lack of data might be that cohort sizes are too small to reliably detect mortality events. Large nationwide cohort studies are therefore needed accurately assess mortality after surgery for LUTS, but recent studies reporting such outcomes are scarce. Mortality rates available in the current literature are presented in Table 15.

Table 15. Mortality and major adverse cardiovascular event rates identified in the review of the literature.

Operation type	Source	Design	N	Time frame	MACE (%)	Mortality (%)
Open	Varkarakis et al., 2004	Contemporary patient series	232		0.4	0
	Gratzke et al., 2007	Prospective multicenter study	902	30 d		0.2
	Kuntz et al., 2007	Randomized controlled trial	60	90 d		3.3
	Gilfrich et al., 2016	Retrospective register study	8,376	30 d		0.51
TURP	Rassweiler et al., 2005	Review			0–1.5	0–0.25
	Reich et al., 2008	Prospective multicentre study	10,654	30 d		0.1
	Gilfrich et al., 2016	Retrospective register study	78,192	30 d		0.32
	Bhojani et al., 2014	Retrospective register study	4,794	30 d	0.7	0.4
	Patel et al., 2015	Retrospective register study	4,968	30 d	0.6	0.62
	Labban et al., 2022	Retrospective register study	38,399	30 d		0.3
	Marchioni et al., 2019	Retrospective register study	29,854		0.9	
PVP	Cindolo et al., 2018	Retrospective register study	813	30 d	1.0	0.1
	Gilfrich et al., 2016	Retrospective register study	6,409	30 d		0.58
	Bhojani et al., 2014	Retrospective register study	2,439	30 d	0.5	0.3
	Patel et al., 2015	Retrospective register study	2,853	30 d	0.4	0.46
	Labban et al., 2022	Retrospective register study	19,121	30 d		0.2
	Elshal et al., 2012	Longitudinal study	288		0.4	
	Marchioni et al., 2018	Retrospective register study	923		1.9	
	Marchioni et al., 2019	Retrospective register study	12,822		0.7	

Operation type	Source	Design	N	Time frame	MACE (%)	Mortality (%)
HoLEP/EEP	Gilfrich et al., 2016	Retrospective register study	2,600	30 d		0.27
	Bhojani et al., 2014	Retrospective register study	126	30 d	0.0	0.0
	Labban et al., 2022	Retrospective register study	3,797	30 d		0.1
	Kuntz et al., 2007	Randomized controlled trial	60	90 d		0
	Riveros et. al 2023	Retrospective register study	3,489	30 d	0.2	0.1
	Marchioni et al., 2019	Retrospective register study	2,263		0.6	
	Shah et al., 2007	Retrospective register study	280		0.4	
RASP/MISP	Pokorny et al., 2015	Retrospective study	67	30 d		0
	Autorino et al., 2015	Retrospective register study	1,330	90 d		0.1
PUL	Page et al., 2021	Retrospective register study	2,942	30 d		0.1
Aquablation	Bach et al., 2020	Prospective multicenter study	178		2.8	
	Desai et al., 2020	Prospective multicenter study	101	90 d	5.0	

3 Aims

This thesis is an investigation into the contemporary surgical landscape for the management of benign prostatic hyperplasia and lower urinary tract symptoms in Finland. It aims to address critical gaps in understanding procedural outcomes, safety, and utilisation patterns. The main purpose of the substudies is to provide evidence to support clinical decision-making, guideline development, and healthcare policy, especially in a context where the prevalence of BPH and, consequently, LUTS is escalating globally due to demographic shifts. This thesis offers generalisable findings, drawing on nationwide registry data.

The specific aims for the current study were:

1. To investigate changing utilisation trends of surgical treatments for BPH/LUTS.
2. To compare the short- and long-term risks of photoselective vaporisation of the prostate and transurethral resection of the prostate.
3. To investigate postoperative mortality rates and risk factors for mortality associated with transurethral resection of the prostate, laser vaporisation of the prostate, and open prostatectomy.

4 Materials and Methods

4.1 Data sources and permissions

The cohorts for all three studies were obtained from the National Institute for Health and Welfare of Finland, including the Care Register for Healthcare (CRHF) registry data and the Finnish Cancer Registry. The mortality data and causes of death were obtained from Statistics Finland. These are mandatory national registries and cover the entire Finnish population. The combined database includes data on patients' admission and discharge from inpatient care, procedural codes, and reported diagnoses during admission, time and cause of death, as well as date and type of cancer diagnosis (Kytö et al., 2021). Procedures were classified using the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCSP) and reported diagnoses using the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). All three modalities of PVP and both M-TURP and B-TURP were represented in the data.

These studies received approval from the National Institute for Health and Welfare of Finland (permission number: THL/2245/5.05.00/2019) and Statistics Finland (reference number: TK-53-484-20). The legal foundation for the processing of personal data was grounded in public interest and scientific research, as stipulated under the European Union General Data Protection Regulation 2016/679 (Articles 6(1)(e) and 9(2)(j)) and the Data Protection Act (Sections 4 and 6). Given the retrospective nature of the study design, the requirement for informed consent was waived, and no contact was made with the participants.

4.2 Study Cohorts

4.2.1 Study I

In Study I, procedures were classified as TURP (KED22), OP (KED00, KED10), PVP (KED52), TUIP (KED33), TUMT (KED72), TUNA (KED62), TUVP (KED76) and Other (KED96, KED98). Study I observed procedures performed annually between 2004 and 2018 and included only the first operation per patient per study year. If multiple operational codes were recorded during the same hospital

admission, the most clinically significant procedure was included. The hierarchy of procedural significance was determined by author consensus as follows: Other < TUVP < TUMT < TUNA < TUIP < TURP < PVP < OP. Emergency operations, patients with non-specific operational coding, patients under 40 years of age, and patients with malignancy or neoplasm of the urinary system were excluded. The exclusion of urological malignancies was warranted because, during the treatment or diagnosis of a urinary system neoplasm, a prostate sample might be obtained, potentially resulting in the assignment of a KED procedure code without an actual KED procedure being performed. The exclusion criteria and corresponding numbers are provided in Table 16.

4.2.2 Study II

In Study II, transurethral resection of the prostate (KED22) and photoselective vaporisation of the prostate (KED52) were examined. The data encompassed all three generations of PVP, as well as both bipolar and monopolar TURP. The study period extended from 1 January 2006 to 30 September 2018, and there was a 2-year "washout" period prior to second study, excluding patients who underwent operations between 2004 and 2005. Only the first elective procedure performed during the study period was included in the study population, while later procedures and those performed as an emergency operations were excluded. Study II aimed to compare TURP and PVP, and to reduce confounding, patients with a PCA diagnosis were excluded. Patients diagnosed with urological or genital malignancy, or with an unspecified tumour of the urinary tract, were excluded, based on the same rationale as in Study I. Patients with operative coding for both PVP and TURP, those with non-specific operational coding during the index procedure, patients under 40 years of age, or those lost to follow-up were excluded from the study (Table 16).

4.2.3 Study III

In Study III, the procedures considered were open prostatectomy (KED00, KED10), transurethral resection of prostate (KED22, KED33, KED76), and laser vaporisation of the prostate (KED52). TUIP and TUVP operational codes were included in the TURP group, since the primary objective of this study was to compare laser surgery with open surgery and conventional electrosurgical modalities. In Study III, procedures were performed between 2004 and 2014, and only the first procedure within the study period was included in the study population. The Study III population consisted of elective patients admitted for surgery from home. Patients arriving from institutional care and those with missing data on housing status were excluded from the analysis. In contrast to previous studies, Study III aimed to

examine the role of a PCA diagnosis in postoperative mortality following elective surgery for LUTS. This decision was justified by the exclusion of emergency operations and patients arriving from institutional care; thus, the study population was restricted to men undergoing elective surgery, and the risk of including palliative operations was minimised. Patients diagnosed with non-prostatic malignancy or neoplasm of the urinary system were excluded based on the same rationale as in Studies I and II. The exclusion criteria and corresponding numbers are provided in Table 16.

Table 16. Exclusion criteria in the substudies

Study I	**N**
Assessed for eligibility	*64,117*
Non-specific operational coding	1,554
Urological malignancy or neoplasm	8,784
Emergency operation	2,707
Age under 40 years	107
Study population	*52,761*
Study II	
Assessed for eligibility	*27,408*
Urological malignancy or neoplasm of the urinary tract	5,085
Non-specific operational coding	749
Operational codes for both TURP and PVP	130
Lost to follow-up	23
Age under 40 years	12
*Original study population**	*21,869*
Study III	
Assessed for eligibility	*45,134*
Emergency operation	1,697
Non-prostate malignancy or neoplasm of urinary system	1,436
Patients arrive from institutional care	1,144
Multiple/other operational codes	241
Missing housing condition information	27
Missing mortality data	25
Study population	*39,320*

*Population before inverse probability of treatment weighting balancing

4.3 Outcome definitions

4.3.1 Study I

Study I investigated national trends in surgical procedures for the treatment of BPO/LUTS. The primary outcome was the annual number of procedures, and secondary outcomes were procedure incidence, postoperative length of stay, and mean patient age. In Study I, the patient population was stratified into the following age categories: 40–49, 50–59, 60–69, 70–79, 80–89, and ≥90 years. The postoperative length of hospital stay was defined as a minimum of 1 day, encompassing both same-day discharges and outpatient procedures within this metric.

4.3.2 Study II

Study II examined short- and long-term risks comparing TURP and PVP. Short-term risks were defined as postoperative mortality, MACE (defined as myocardial infarction, stroke, or cardiovascular death), and reoperation for bleeding within 90 days postoperatively. Long-term risks were reoperations for BPE, urethral stricture, or BNS within 12 years of the index operation. Long-term reoperations were further categorised as reoperations of the prostatic urethra or distal urethra. Risks were assessed using NCSP coding alongside ICD-10 codes recorded in the CRHF. Comorbidities were identified using ICD-10 coding, as described previously (Palomäki et al., 2021).

4.3.3 Study III

The primary outcome of Study III was 90-day mortality, and the secondary outcomes were mortality within 1 year of the index operation, cause of death (cardiac, respiratory, genitourinary, vascular, gastrointestinal, infection, malignancy, miscellaneous), and excess mortality. Patients' comorbidity burden was quantified using the CCI, calculated from ICD-10 codes (Charlson et al., 1987; Quan et al., 2005), and an ICD-10 diagnosis of atrial fibrillation (AF) was used as a surrogate marker for use of OAC. Operating centres were categorised into three groups based on annual surgical volume (<50, 50–100, >100). Causes of death were classified as underlying (the disease or injury that initiated the sequence of pathological events leading to death) or immediate (the final disease, injury, or complication directly causing death), as both are mandatory entries on the Finnish death certificate.

4.4 Statistical analysis

4.4.1 Study I

In Study I, the mean operation incidence, specific to each age group and year, was determined by dividing the total number of procedures within a given age cohort by the corresponding same-aged male population in Finland. This was predicated on the assumption that the entire male population was at risk throughout the study duration. The overall mean operation incidence was computed by dividing the aggregate number of procedures by the total male population in Finland aged 40 years or older over the study period. The relative proportion of specific operation types was ascertained by dividing the count of each procedure type by the total number of operations performed during the same timeframe. Temporal trends in incidence were evaluated using the two-sided Cochran-Armitage test. Trends in hospital stay duration and patient age were assessed through linear regression analysis. Statistical significance was established as p-value <0.05. Statistical analyses were performed using SAS version 9.4.

4.4.2 Study II

In Study II, inverse probability of treatment weighting (IPTW) was used to balance baseline differences between the TURP and PVP treatment groups to reduce confounding (Austin & Schuster, 2016). IPTW is a propensity score-based method that weights individuals in an observational study according to the inverse of their probability of receiving the treatment they actually received, given a set of observed covariates. The method creates a pseudo-population in which the distribution of confounders is independent of treatment assignment, thereby mimicking randomisation in an RCT. IPTW addresses selection bias by adjusting for measured confounders and thus enables unbiased estimation of treatment effects.

In Study II, propensity scores based on age, AIDS/HIV, alcohol abuse, anaemia, atrial fibrillation, cerebrovascular disease, chronic pulmonary disease, coagulopathy, dementia, diabetes, heart failure, heart valve disease, hypertension, liver disease, non-prostate cancer, metastatic cancer, paralysis, peripheral vascular disease, prostate cancer, prior myocardial infarction, psychotic disorder, rheumatic disease, renal failure, place of procedure (high-volume vs intermediate- or low-volume centre), and calendar year of operation were generated using logistic regression. These were used for the IPTW calculations. To improve balance, the IPTW was stabilised, resulting in treatment weights ranging from 0.47 to 2.96 (Austin & Schuster, 2016). This adjustment resulted in well-balanced treatment groups.

Subgroup analyses were performed in patients aged <70 years and ≥70 years, and in patients with or without AF, with separate propensity scoring and IPTW adjustments. The age threshold of 70 years in the subgroup analyses was selected to facilitate analyses in a clinically relevant population with increasing comorbidity burden. In Study II, differences between the study cohorts were assessed using the chi-squared, Jonckheere-Terpstra, and t test. The effect sizes of baseline characteristics of the cohorts were evaluated using standardised mean differences (SMD). Risks were evaluated using the Kaplan-Meier method and Cox regression. Proportional hazard assumptions were validated through Schoenfeld residuals. Patients were censored at the time of death during the assessment of non-mortality risks. Regression models were weighted using stabilised IPTW, and the number needed to treat was computed as outlined previously (Altman & Andersen, 1999). The magnitude of unmeasured confounding was estimated using the E-value (VanderWeele & Ding, 2017). Results were reported as means, medians, percentages, SMDs, HRs with 95% CI, interquartile ranges (IQR), or standard deviations (SD). As in Study I, statistical significance was established as $p < 0.05$, and all statistical computations were executed using SAS version 9.4.

4.4.3 Study III

In Study III, differences between the study cohorts were assessed using the t test and chi-squared test. Outcomes were analysed through a modified Poisson regression model incorporating robust error variances (Zou, 2004). Clinically predetermined variables were incorporated into the multivariable models. Excess postoperative mortality was determined by subtracting the baseline all-cause mortality rates, adjusted for age, sex, and calendar year, of the general Finnish population from postoperative all-cause mortality rates (Kytö et al., 2021). Results were reported as means, medians, percentages, or RR with 95% CI. Statistical significance was established as a $p < 0.05$, as in Studies I and II. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

5 Results

5.1 Study I

The purpose of Study I was to investigate national trends in the surgical treatment of BPO/LUTS in Finland. Between 2004 and 2018, a total of 64,117 surgical procedures were conducted in Finland. After applying the exclusion criteria outlined previously, a study population of 52,761 patients was established for analysis. The baseline characteristics, as well as the results of this cohort, are detailed in Table 17. Over the study period, the procedures included 39,333 TURP, 6,220 PVP, 4,499 TUIP, 1,204 OP, 742 TUVP, 580 TUMT, 65 TUNA, and 118 other partial excisions of the prostate. TURP remained the most frequently performed procedure across all age categories. During this timeframe, the relative proportion of TURP declined from 80% to 72%. At the same time, the proportion of PVP rose from 0.1% to 16%, peaking at 18% in 2013. Conversely, the relative proportion of TUNA decreased from 0.8% to 0.2%, TUVP from 3.6% to 0.5%, TUMT from 2.7% to 0.6%, OP from 3.3% to 2.0%, and other partial excisions from 0.2% to 0.0%. The proportion of TUIP procedures initially dropped from 9.7% in 2004 to 7.4% in 2007 and 2008, subsequently recovering to 8.8% by 2018. The temporal trends in annual procedure volumes are illustrated in Figure 4.

The mean operation incidence rate across the population from 2004 to 2018 was 263 per 100,000 (standard deviation [SD] 12.2). No significant variation in the overall operation incidence rate was observed over the study period (trend $p = 0.5044$). However, a significant decline in incidence was noted for TURP, OP, TUVP, TUMT, TUNA, and other partial excisions of the prostate (trend $p < 0.05$), while the incidence of PVP exhibited a significant increase (trend $p < 0.0001$). Operation incidence also decreased significantly across all age groups except for men aged 40–49 and those aged over 90 years. The highest operation incidence rates during the study period were observed in the age groups of 70–79 (737 per 100,000) and 80–89 (739 per 100,000). The lowest rate was observed in the age group of 40–49 (11 per 100,000). Trend *p*-values for incidence are provided in Table 17. Age-specific annual operation incidence rates per 100,000 are depicted in Figure 5.

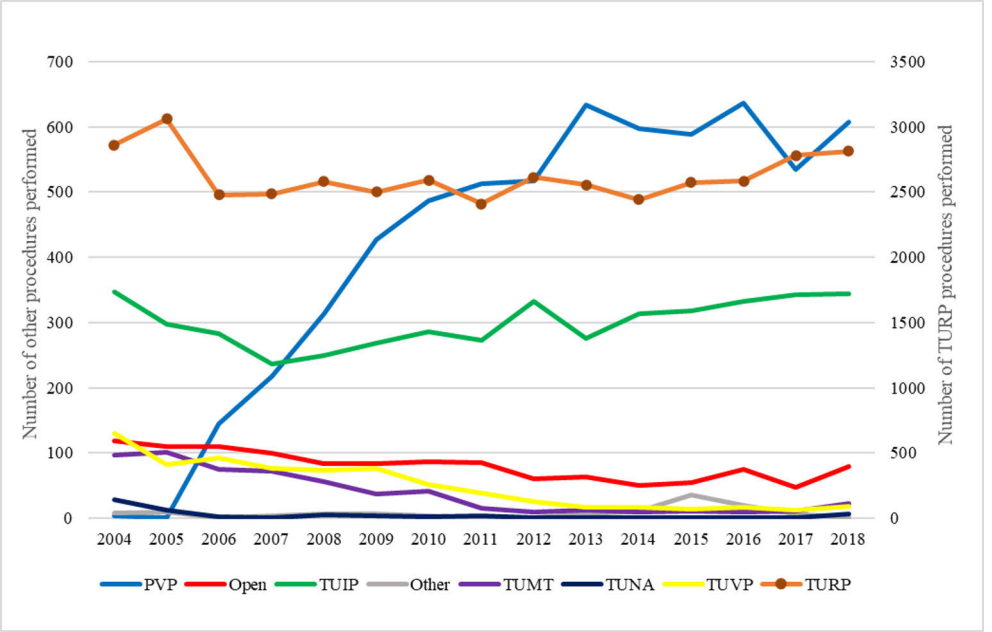
The duration of postsurgical hospital stay shortened significantly across all procedure types and age groups over the study period ($p < 0.05$). Patients undergoing

OP experienced the longest mean hospital stay at 8.1 days (SD 3.0), whereas those receiving TUMT had the shortest at 1.1 days (SD 0.2). The mean hospital stay following TURP was 4.0 days (SD 2.1), and after PVP it was 2.3 days (SD 1.5). Among patients aged over 90 years, the mean hospital stay decreased from 7.0 days (SD 3.2) in 2004 to 3.2 days (SD 1.6) in 2018. The shortest hospital stays were recorded in the age group of 40–49, with the mean duration declining from 3.6 days (SD 1.7) in 2004 to 2.4 days (SD 1.1) in 2018. Trends in mean hospital stay duration for procedures with N > 1,000 across all age groups are presented in Figure 6. *P*-values, and parameter estimates for postsurgical length of stay, are available in Table 17.

The mean age of all operated patients increased significantly from 69.6 years (SD 9.1) in 2004 to 71.8 years (SD 8.5) in 2018 ($p < 0.0001$). This age increment was significant for all procedure types except for TUVP. The oldest mean age was observed in the TUMT group at 75.3 years (SD 8.9), while the youngest was in the TUNA group at 64.4 years (SD 11.1). The mean ages of different procedure types, as well as *p*-values and parameter estimates of linear regression for mean age, are provided in Table 17.

Table 17. Baseline characteristics, mean age and postsurgical length of stay of patients treated surgically for BPO/LUTS in Finland between 2004 and 2018 in Study I.

Total number of patients			Mean age			Mean postsurgical length of stay		
	N	Trend *p*-value for incidence	Years (SD)	*P*-value	Parameter Estimate	Days (SD)	*P*-value	Parameter Estimate
All operation types	52,761	0.50	70.7 (8.8)	<.0001	0.14	3.8 (2.3)	<.0001	-0.19
TURP	39,333	<.0001	70.9 (8.5)	<.0001	0.13	4.0 (2.1)	<.0001	-0.19
OP	1,204	<.0001	72.6 (7.3)	0.014	0.12	8.1 (3.0)	<.0001	-0.23
PVP	6,220	<.0001	70.6 (8.6)	<.0001	0.27	2.3 (1.5)	<.0001	-0.043
TUIP	4,499	0.13	67.5 (11.0)	<.0001	0.28	3.2 (2.2)	<.0001	-0.16
TUVP	742	<.0001	72.4 (8.5)	0.25	0.10	4.0 (2.9)	<.0001	-0.16
TUMT	580	<.0001	75.3 (8.9)	<.0001	0.65	1.1 (0.2)	0.01	-0.007
TUNA	65	<.0001	64.4 (11.1)	0.03	0.70	3.0 (1.8)	0.02	-0.12
Other	118	0.002	71.8 (9.0)	0.008	0.51	4.2 (2.4)	<.0001	-0.26
40–49	587	0.52				3.1 (3.8)	0.0004	-0.13
50–59	4,936	<.0001				3.3 (1.7)	<.0001	-0.16
60–69	17,819	<.0001				3.5 (1.9)	<.0001	-0.18
70–79	20,713	<.0001				3.9 (2.3)	<.0001	-0.21
80–89	8,215	<.0001				4.4 (2.7)	<.0001	-0.23
90–	491	0.10				4.7 (4.0)	<.0001	-0.27



The primary y-axis on the left-hand side represents the scale for PVP, Open, TUIP, Other, TUMT, TUNA, and TUVP. The secondary y-axis on the right-hand side represents the scale for TURP.

Figure 4. Annual number of surgical procedures for benign prostatic obstruction in Study I (first published in Scandinavian Journal of Urology, 2024)

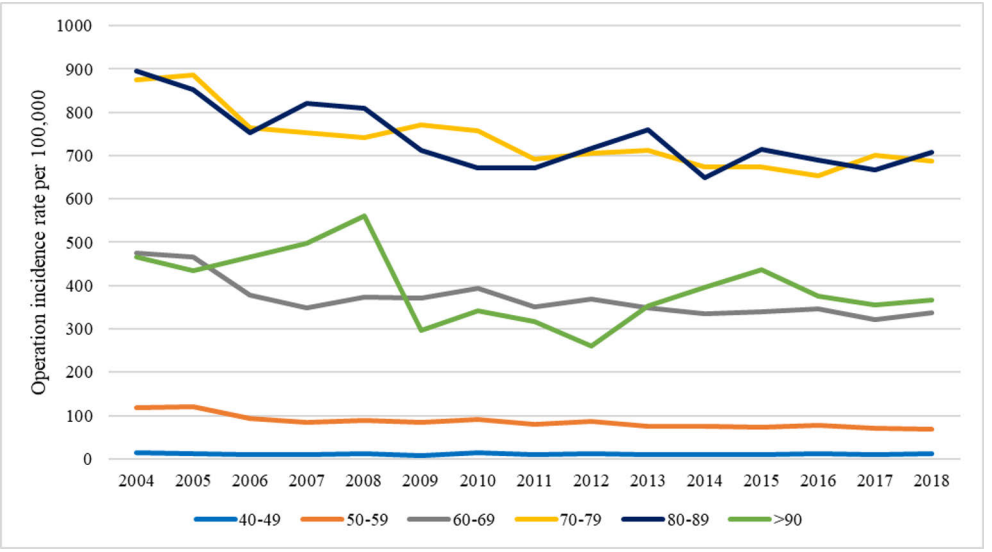


Figure 5. Annual operation incidence rate per 100,000 men in Study I (first published in Scandinavian Journal of Urology, 2024).

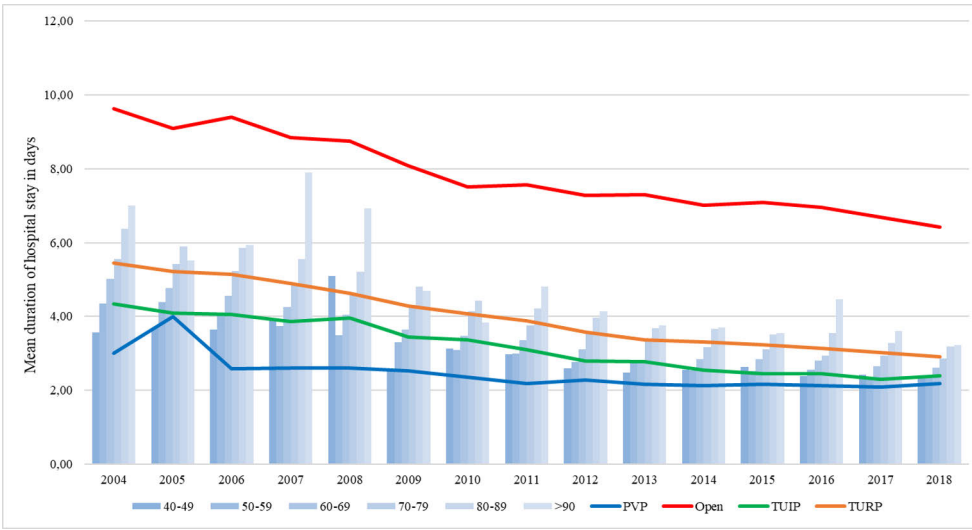


Figure 6. Mean duration of hospital stay in days in Study I (first published in Scandinavian Journal of Urology, 2024).

5.2 Study II

The objective of Study II was to further compare short- and long-term risks of PVP and TURP. A total of 27,408 TURP or PVP procedures were conducted between 2006 and 2018 across 20 surgical centres. Following the application of the aforementioned exclusion criteria, the study cohort comprised 5,331 patients who underwent PVP and 16,538 patients who underwent TURP (Figure 7). The conversion rate from PVP to TURP was 2.2%. The baseline characteristics of the initial cohort and the weighted study population are presented in Table 18. Within the unadjusted population, individuals treated with PVP exhibited a higher prevalence of AF, vascular disease, and heart failure compared to those treated with TURP. In addition, individuals treated with PVP had a slightly younger mean age. Application of IPTW effectively balanced these baseline disparities, yielding a weighted cohort of 5,342 PVP and 16,587 TURP patients.

The short-term postoperative mortality and complication risks are presented in Table 19. The overall 90-day postoperative mortality rate across all operated patients was 0.6%. This accounted for 125 deaths, with specific rates of 0.4% for PVP and 0.6% for TURP. Additionally, 427 patients experienced MACE, and 256 required reoperation for bleeding within 90 days of the index procedure. Statistical analysis revealed no significant differences in 90-day postoperative mortality or MACE incidence between the PVP and TURP groups. However, reoperation for bleeding was significantly less frequent following PVP (0.9%) than TURP (1.3%), with a HR of 0.72 (95% CI 0.53–0.99; p = 0.042). Subgroup analyses indicated that older

patients (aged ≥70 years) and those with AF were more prone to reoperation for bleeding compared to their younger counterparts and those without AF.

Long-term reoperation risk outcomes are presented in Table 20. The median follow-up duration over the 12-year cumulative period was 4.3 years. Overall, the total reoperation rate was higher following PVP than TURP, a trend consistent across age groups and irrespective of the presence of AF. This elevated reoperation rate after PVP was predominantly driven by a greater incidence of prostatic urethral interventions, including resection or vaporisation of residual adenoma and bladder neck incision (Figure 8(a)). Conversely, reoperations involving the distal urethra were less common after PVP than after TURP (Figure 8(b)). The E-value for any reoperation across the entire cohort was estimated at 1.69 (95% CI 1.40–1.95), indicating robustness of the findings to potential unmeasured confounding.

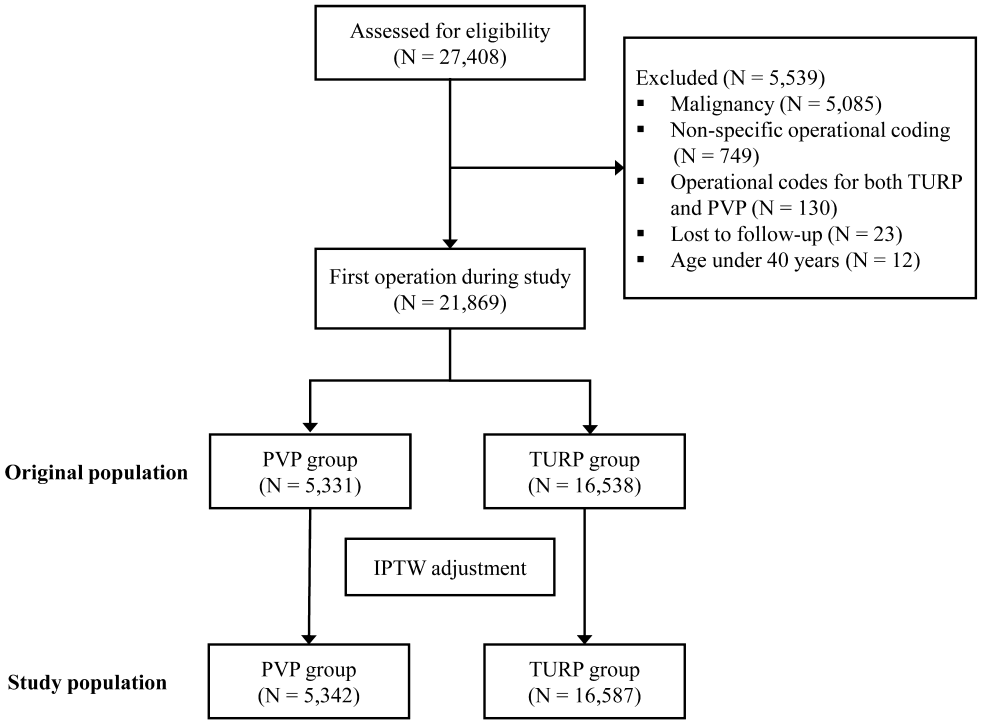


Figure 7. Study II flowchart (first published in Annals of Medicine, 2023).

Table 18. Baseline features of benign prostatic hyperplasia patients treated with PVP or TURP in Study II, first published in Annals of Medicine 2023. Features of all patients and inverse probability weight-balanced cohort. SMD = standardized mean difference.

Variable	Original study population				Weighted study population			
	PVP N = 5,331	TURP N = 16,538	*P*-value	|SMD|	PVP N = 5,342	TURP N = 16,587	*P*-value	|SMD|
Age, years (SD)	70.3 (8.6)	70.6 (8.5)	0.008	0.042	70.5 (8.5)	70.5 (8.7)	0.790	0.004
AIDS/HIV	0.1%	0.1%	0.106	0.023	0.1%	0.1%	0.973	0.001
Alcohol abuse	2.0%	2.6%	0.020	0.038	2.5%	2.5%	0.906	0.002
Anaemia	1.3%	1.5%	0.356	0.015	1.4%	1.4%	0.856	0.003
Atrial fibrillation	17.7%	12.1%	<0.0001	0.159	13.5%	13.5%	0.995	0.0001
Cerebrovascular disease	11.7%	9.6%	<0.0001	0.070	10.0%	10.1%	0.770	0.005
Chronic pulmonary disease	8.4%	8.8%	0.354	0.015	8.4%	8.7%	0.557	0.009
Coagulopathy	0.6%	0.4%	0.085	0.026	0.4%	0.4%	0.919	0.002
Dementia	3.1%	3.0%	0.817	0.004	3.1%	3.0%	0.810	0.004
Diabetes	12.2%	11.6%	0.213	0.020	11.6%	11.7%	0.802	0.004
Heart failure	8.1%	6.4%	< 0.0001	0.064	6.8%	6.8%	0.837	0.003
Heart valve disease	5.8%	4.1%	< 0.0001	0.078	4.6%	4.6%	0.972	0.001
Hypertension	27.9%	25.6%	0.001	0.052	25.8%	26.1%	0.670	0.007
Liver disease	1.0%	0.9%	0.607	0.008	0.9%	0.9%	0.984	0.0003
Neurological disease*	4.6%	4.8%	0.170	0.022	4.7%	4.6%	0.779	0.004
Cancer**	8.3%	8.2%	0.840	0.003	8.1%	8.2%	0.684	0.006
Metastatic	0.2%	0.3%	0.906	0.002	0.2%	0.3%	0.934	0.001
Paralysis	0.3%	0.6%	0.021	0.039	0.5%	0.5%	0.555	0.009
Peripheral vascular disease	5.5%	4.7%	0.011	0.039	4.8%	4.9%	0.745	0.005
Prior myocardial infarction	7.0%	5.9%	0.004	0.044	6.3%	6.2%	0.719	0.005
Psychotic disorder	0.8%	1.3%	0.001	0.054	1.2%	1.2%	0.990	0.0002
Rheumatic disease	2.5%	2.9%	0.146	0.023	2.8%	2.8%	0.925	0.001
Renal failure	2.7%	3.0%	0.276	0.017	2.9%	2.9%	0.940	0.001
University hospital***	51.3%	43.5%	< 0.0001	0.157	44.5%	44.5%	0.293	0.017
Year of operation			< 0.0001	0.246			0.954	0.009

*Other than cerebrovascular disease **Patients with urogenital cancer were excluded ***As the surgical centre

Table 19. Short-term postoperative mortality, MACE, and major bleeding rates among patients with benign prostatic hyperplasia treated with PVP or TURP (reference group) in Study II (first published in Annals of Medicine, 2023). HR = hazard ratio. NNT = number needed to treat.

Short-term risks	Adjusted %		Adjusted HR		NNT
	PVP	TURP	HR (95 % CI)	*P*-value	
Postoperative mortality					
All patients	0.4 %	0.6 %	0.72 (0.46–1.12)	0.144	583.0
< 70 years	0.1 %	0.2 %	0.48 (0.14–1.61)	0.235	782.2
≥ 70 years	0.7 %	0.9 %	0.75 (0.46–1.24)	0.263	434.9
Atrial fibrillation	0.2 %	0.1 %	1.15 (0.61–2.18)	0.660	-497.7
No atrial fibrillation	0.3 %	0.5 %	0.54 (0.28–1.01)	0.051	431.1
MACE					
All patients	1.8 %	2.0 %	0.87 (0.69–1.10)	0.253	386.1
< 70 years	0.9 %	1.1 %	0.86 (0.54–1.35)	0.503	664.5
≥ 70 years	2.5 %	2.8 %	0.88 (0.67–1.15)	0.337	301.4
Atrial fibrillation	3.5 %	4.3 %	0.83 (0.55–1.23)	0.351	140.6
No atrial fibrillation	1.5 %	1.7 %	0.90 (0.69–1.18)	0.440	599.8
Reoperation due to bleeding					
All patients	0.9 %	1.3 %	0.72 (0.53–0.99)	0.042	284.8
< 70 years	1.1 %	1.3 %	0.83 (0.55–1.26)	0.379	441.4
≥ 70 years	0.7 %	1.2 %	0.58 (0.36–0.94)	0.028	199.1
Atrial fibrillation	1.3 %	2.9 %	0.44 (0.24–0.81)	0.009	61.1
No atrial fibrillation	0.9 %	1.0 %	0.86 (0.60–1.23)	0.411	721.0

Table 20. Long-term (up to 12 years) reoperations among patients with benign prostatic hyperplasia treated with PVP or TURP (reference group) in Study II (first published in Annals of Medicine, 2023). HR = hazard ratio. NNT = number needed to treat.

Long-term risks	Adjusted %		Adjusted HR		NNT
	PVP	TURP	HR (95 % CI)	*P*-value	
Reoperation, overall					
All patients	23.5 %	17.8 %	1.20 (1.09–1.31)	<0.0001	-31.7
< 70 years	25.3 %	17.3 %	1.29 (1.14–1.47)	<0.0001	-22.5
≥ 70 years	19.4 %	17.8 %	1.31 (1.00–1.39)	0.058	-20.6
Atrial fibrillation	31.0 %	16.3 %	1.69 (1.34–2.14)	<0.0001	-10.3
No atrial fibrillation	22.8 %	17.9 %	1.15 (1.04–1.27)	0.006	-41.8
Reoperation of prostatic urethra					
All patients	21.3 %	13.2 %	1.66 (1.41–1.72)	<0.0001	-12.9
< 70 years	23.2 %	13.4 %	1.67 (1.45–1.92)	<0.0001	-12.6
≥ 70 years	17.2 %	12.6 %	1.48 (1.28–1.71)	<0.0001	-18.3
Atrial fibrillation	28.5 %	11.2 %	2.24 (1.72–2.93)	<0.0001	-8.2
No atrial fibrillation	20.7 %	13.4 %	1.49 (1.34–1.66)	<0.0001	-17.0
Reoperation of distal urethra					
All patients	4.4 %	6.0 %	0.64 (0.53–0.77)	<0.0001	47.4
< 70 years	4.5 %	5.2 %	0.66 (0.51–0.86)	0.002	57.6
≥ 70 years	4.2 %	6.9 %	0.63 (0.49–0.81)	0.0003	40.0
Atrial fibrillation	6.3 %	6.9 %	1.07 (0.70–1.63)	0.760	-216.4
No atrial fibrillation	4.2 %	6.0 %	0.60 (0.49–0.73)	<0.0001	42.6

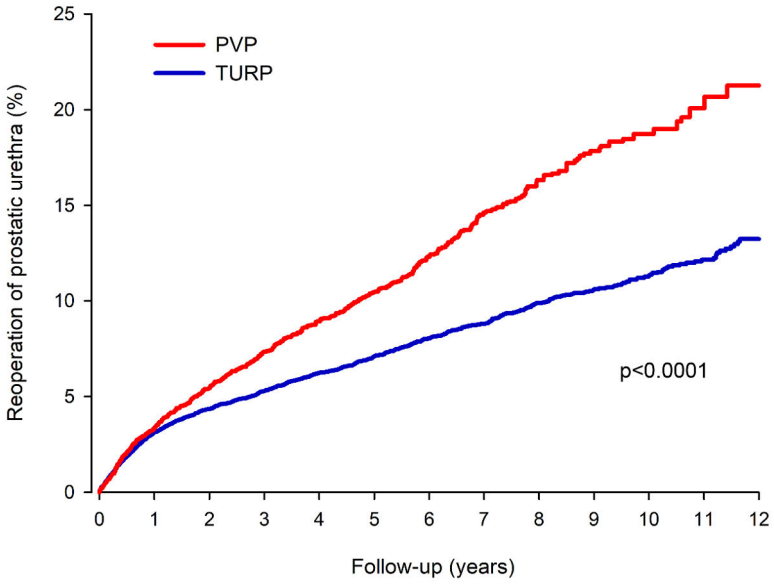


Figure 8 A. Cumulative incidence of prostatic urethral reoperation after PVP and TURP in Study II (first published in Annals of Medicine, 2023).

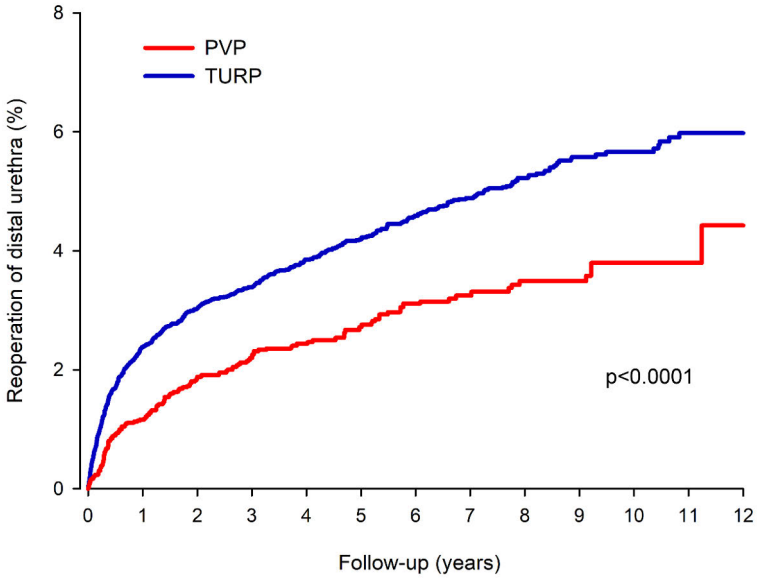


Figure 8 B. Cumulative incidence of distal urethral reoperation after PVP and TURP in Study II (first published in Annals of Medicine, 2023).

5.3 Study III

The purpose of Study III was to investigate postoperative mortality rates and risk factors for mortality associated with TURP, PVP, and open prostatectomy. During the period 2004–2014, a total of 45,134 procedures were conducted on 41,168 patients in 60 surgical centres. Following the exclusion criteria delineated earlier, a refined cohort of 39,320 patients was included for analysis (Figure 9). The demographic and clinical characteristics of this cohort are summarised in Table 21. During the study period, the distribution of procedures comprised 34,558 TURP (87.9%), 3,715 PVP (9.4%), and 1,047 OP (2.7%). TURP emerged as the predominant procedure across all age groups. The majority of patients (70%) exhibited a CCI score of 0, indicating minimal comorbidity burden, while a smaller proportion (7%) were diagnosed with AF and 9% with prostate cancer. Most of the surgeries were performed in high-volume centres, defined by annual operating volume exceeding 100 procedures.

The associations between various factors and 90-day postoperative mortality are outlined in Table 22. Among the 39,320 patients undergoing surgery to treat BPH/LUTS, 431 deaths were recorded within 90 days, corresponding to a mortality rate of 1.10%. Patients who underwent TURP exhibited a mortality rate of 1.16%, which was significantly higher compared with the 0.59% rate observed in those receiving PVP, with statistical significance confirmed in both univariable ($p = 0.002$) and multivariable analyses ($p = 0.035$) (Table 22). The 90-day postoperative mortality following OP was recorded at 0.67%. Additional independent predictors of increased mortality included advancing age, elevated CCI scores, the presence of AF, and procedures performed in earlier years of the study period.

In the univariable analysis, patients with PCA demonstrated a markedly higher mortality rate of 3.66% ($p < 0.0001$). However, this association was attenuated in the multivariable model when adjusted for other covariates, suggesting that PCA diagnosis alone did not independently increase the 90-day mortality risk. Furthermore, the annual surgical volume of the operating centre was not found to be an independent determinant of mortality outcomes.

During the 90-day postoperative period, the most frequent underlying causes of death were malignancy (35.5%) and cardiac disease (30.9%). The 1-year postoperative mortality rate was 4.6%, with malignancy (45.8%) and cardiac disease (23.2%) remaining the leading causes. Comparative analysis of baseline and postoperative mortality across age groups revealed an age-dependent increase in excess mortality. This remained below 0.5% within 90 days and under 2% within 1 year across all age categories. Detailed categorisations of causes of death are presented in Table 23. Baseline and BPH treatment-related excess mortality data are provided in Table 24.

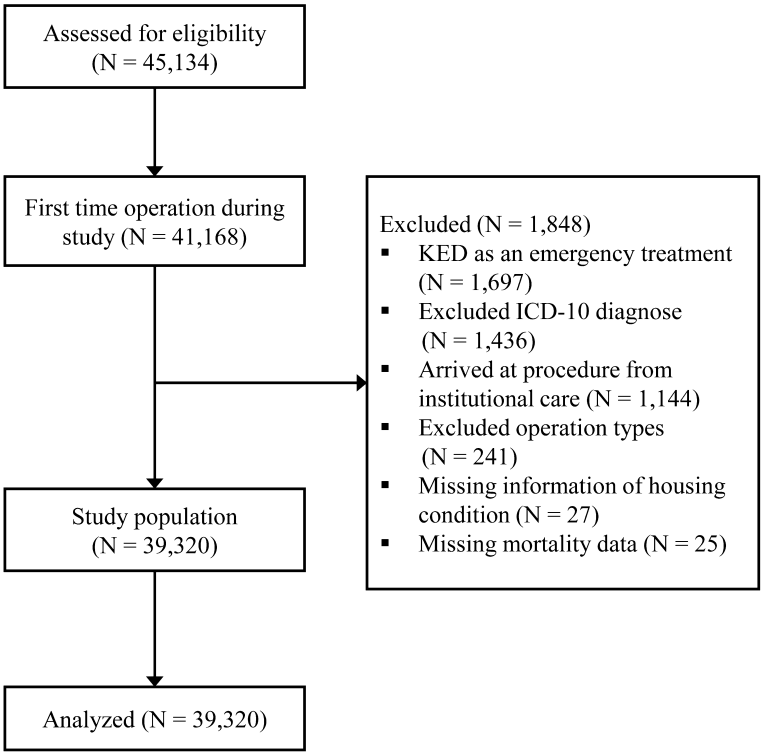


Figure 9. CONSORT flow diagram of Study III (first published in World Journal of Urology, 2022).

Table 21. Baseline characteristics of patients in Study III (first published in World Journal of Urology, 2022).

Variable	All-patients N (%)	Baseline features Age-group (years) <60 N (%)	60-69 N (%)	70-79 N (%)	≥80 N (%)	*P*-value*
Number of patients	39,320	4,284 (10.9)	13,015 (33.1)	15,233 (38.7)	6,788 (17.3)	
CCI score						<0.0001
0	27,660 (70.4)	3,669 (85.6)	10,159 (78.1)	10,181 (66.8)	3,651 (53.8)	
1	4,520 (11.5)	275 (6.4)	1,238 (9.5)	1,956 (12.8)	1,051 (15.5)	
2	5,200 (13.2)	268 (6.3)	1,209 (9.3)	2,273 (14.9)	1,450 (21.4)	
3	1,201 (3.1)	45 (1.1)	239 (1.8)	520 (3.4)	397 (5.9)	
≥4	739 (1.9)	27 (0.6)	170 (1.3)	303 (2.0)	239 (3.5)	
Atrial fibrillation	2,732 (7.0)	67 (1.6)	575 (4.4)	1,278 (8.4)	812 (12.0)	<0.0001
Prostate cancer	4,284 (9.2)	141 (3.3)	680 (5.2)	1,575 (10.3)	1,207 (17.8)	<0.0001
Operation type						<0.0001
TURP	34,558	3,812 (89.0)	11,269 (86.6)	13,444 (88.3)	6,033 (88.9)	
PVP	3,715	402 (9.4)	1,431 (11.0)	1,297 (8.5)	585 (8.6)	
OP	1,047	70 (1.6)	315 (2.4)	492 (3.2)	170 (2.5)	
Annual operation volume of operating centre						0.044
<50	6,561	774 (18.1)	2,186 (16.8)	2,524 (16.6)	1,077 (15.9)	
50-100	7,977	851 (19.9)	2,651 (20.4)	3,137 (20.6)	1,338 (19.7)	
>100	24,782	2,659 (62.1)	8,178 (62.8)	9,572 (62.8)	4,373 (64.4)	

*Indicating the value of $p < 0.05$

Table 22. Univariable and multivariable analysis of a total of 431 deaths and 1.1% 90-day postoperative mortality rate in study III (first published in World Journal of Urology, 2022).

		90-day mortality			
		Univariate		Multivariate	
Variable	**Mortality (%)**	**RR (95% CI)**	***P*-value**	**RR (95% CI)**	***P*-value**
Age group			<0.0001		<0.0001
<60	0.26	1 (reference)		1 (reference)	
60-69	0.47	1.83 (0.96-3.47)	0.066	1.59 (0.84-3.02)	0.154
70-79	1.13	4.40 (2.39-8.08)	<0.0001	3.03 (1.64-5.60)	0.0004
≥80	2.75	10.73 (5.85-19.68)	<0.0001	5.83 (3.13-10.88)	<0.0001
CCI score				<0.0001	
0	0.50	1 (reference)		1 (reference)	
1	1.44	2.90 (2.16-3.89)	<0.0001	2.34 (1.73-3.17)	<0.0001
2	2.79	5.63 (4.47-7.10)	<0.0001	3.75 (2.81-4.99)	<0.0001
3	4.08	8.24 (5.98-11.36)	<0.0001	5.16 (3.51-7.57)	<0.0001
≥4	4.74	9.56 (6.65-13.76)	<0.0001	6.20 (4.15-9.27)	<0.0001
Atrial fibrillation					
No	0.98	1 (reference)		1 (reference)	
Yes	2.60	2.64 (2.05-3.40)	<0.0001	1.53 (1.18-1.99)	0.001
Prostate cancer					
No	0.84	1 (reference)		1 (reference)	
Yes	3.66	4.38 (3.58-5.36)	<0.0001	1.20 (0.92-1.57)	0.170
Operation type			<0.0001		0.029
TURP	1.16	1 (reference)		1 (reference)	
PVP	0.59	0.51 (0.33-0.78)	0.002	0.63 (0.41-0.97)	0.035
OP	0.67	0.57 (0.27-1.21)	0.145	0.72 (0.34-1.51)	0.382
Annual operation volume of operating centre			0.288		0.586
<50	0.93	0.83 (0.63-1.10)	0.200	0.88 (0.67-1.16)	0.367
50-100	1.18	1.06 (0.83-1.34)	0.635	1.03 (0.81-1.29)	0.834
>100	1.11	1 (reference)		1 (reference)	
Study era					
2004-2009	1.20	1 (reference)		1 (reference)	0.001
2010-2014	0.97	0.83 (0.60-1.13)	0.238	0.72 (0.59-0.88)	

Table 23. Causes of death in Study III (first published in World Journal of Urology, 2022).

	90-day mortality		1-year mortality
	Underlying cause of death	Immediate cause(s) of death	Underlying cause of death
Cause of death	**N (%)**	**N (%)**	**N (%)**
Cardiac			
Ischemic	116 (26.9)	109 (15.0)	370 (20.3)
Non-ischemic	17 (3.9)	125 (17.1)	52 (2.9)
Total	133 (30.9)		422 (23.2)
Respiratory	11 (2.6)	43 (5.9)	32 (1.8)
Genitourinary	19 (4.4)	84 (11.5)	26 (1.4)
Vascular			
Stroke	27 (6.3)	25 (3.4)	127 (7.0)
Other	13 (3.0)	34 (4.7)	51 (2.8)
Total	40 (9.3)		178 (9.8)
Gastrointestinal	18 (4.2)	22 (3.0)	45 (2.5)
Infection	12 (2.8)	106 (14.5)	64 (3.5)
Malignancy	153 (35.5)	48 (6.6)	834 (45.8)
Miscellaneous	45 (10.4)	133 (18.2)	220 (12.1)
Total	**431**	**729**	**1,821**

Table 24. Baseline and excess mortality in Study III (first published in World Journal of Urology, 2022).

Age group (years)	90-day mortality (%)			1-year mortality (%)		
	Baseline	Postoperative	Excess	Baseline	Postoperative	Excess
< 60	0.20	0.26	0.06	0.8	1.12	0.32
60–69	0.40	0.47	0.07	1.63	2.01	0.38
70–79	0.92	1.13	0.21	3.73	5.01	1.28
≥ 80	2.29	2.75	0.46	9.29	11.03	1.74

* Excess postoperative mortality was calculated by subtracting the baseline all-cause mortality of the corresponding age-, sex-, and calendar year-specific groups in the total Finnish population from postoperative all-cause mortality. Mortality was weighted within age groups according to the age distribution of the study population.

6 Discussion

6.1 Main results and discussion of the substudies

The surgical management of BPH/LUTS has evolved considerably over the past two decades, driven by advancements in surgical techniques, shifting demographic profiles, and a growing emphasis on patient-centred outcomes. This thesis, encompassing three nationwide cohort studies conducted in Finland, provides a comprehensive examination of temporal trends in surgical utilisation. It also explores comparative risks between photoselective vaporisation of the prostate (PVP) and transurethral resection of the prostate (TURP) and examines postoperative mortality after surgery for BPH/LUTS. By integrating these findings, this discussion elucidates the interplay between procedural safety, efficacy, and adoption patterns, while drawing evidence-based conclusions to inform clinical practice and future research in urology. It should be noted that, during the long study period, several key factors, such as perioperative care, surgical technique, and associated learning curves, have most certainly evolved. Due to the nature of the analyses, many factors are treated as static baseline characteristics. These time-dependent, uncontrollable variables might influence the outcomes and should therefore be acknowledged before interpreting the results.

6.1.1 Trends in the surgical management of benign prostatic hyperplasia

In the population-based analysis of Study I, encompassing 52,761 patients, the objective was to evaluate the evolving utilisation patterns of diverse surgical interventions for BPO in Finland. Over the study period from 2004 to 2018, TURP consistently ranked as the most prevalent surgical approach for BPO (72–80% of procedures annually). Concurrent with the introduction of PVP, the relative proportion of TURP diminished by 7.3%, alongside reductions in the use of minimally invasive surgical therapies, TUVP, and OP, while the proportion of TUIP procedures remained stable. The overall incidence of surgical interventions for BPO showed no significant variation (263 per 100,000, SD 12.2, trend p = 0.0544).

However, the duration of hospital stays decreased, and the average age of patients undergoing surgery increased by 2 years.

During this time frame, an initial surge of enthusiasm for PVP was observed which subsequently plateaued, with procedure numbers stabilising at approximately 600 annually after 2013. The debut of the first-generation (80-W) PVP in Finland in 2006 was marked by its recognition as a safe technique with superior haemostatic properties. However, its capacity for tissue removal was deemed inadequate (Te et al., 2006). In its inaugural year, 145 PVP procedures were performed, followed by a steady rise until 2013. This growth coincided with the introduction of the second-generation 120-W high-performance system in 2007 and the third-generation 180-W XPS laser system in 2010. The 120-W system offered enhanced intraoperative and early postoperative outcomes but was associated with increased storage bladder symptoms compared to TURP (Al-Ansari et al., 2010; Zang et al., 2016). The 180-W XPS laser, now the current standard for PVP, provides shorter operative durations while achieving prostate volume reductions and functional outcomes comparable to TURP (Brunken et al., 2015; Cornu et al., 2025).

Nonetheless, early reports highlighting elevated reoperation rates and suboptimal prostate volume reductions likely tempered the initial excitement surrounding PVP (Al-Ansari et al., 2010; Bachmann et al., 2005; Hermanns et al., 2014; Teng et al., 2013). It should be noted that temporal changes in the utilisation patterns of different procedures do not, in themselves, imply superiority of any specific procedure type. Instead, they reflect the combined influence of multiple clinical, technological, systemic, and marketing factors.

Similar, though more pronounced, trends were noted in Australia and France. In Australia, between 2008 and 2014, Patel and Bariol documented a decline in TURP from 96% to 73%. During the same time period, there was a rise in PVP from 3.4% to 20%, followed by a slight decrease in PVP over the subsequent 3 years. (Patel & Bariol, 2019) Morton et al. reported a reduction in incidence of TURP from 81% to 61% (from 118/100,000 to 90/100,000 men), and an increase in PVP use between 2009 and 2018 (from 4.8/100,000 to 25.0/100,000 men). The use of TUIP remained stable (2000–2018, from 13.5/100,000 to 13.7/100,000), while the already low incidence of OP declined further (2000–2018, from 1.4/100,000 to 0.8/100,000). (Morton et al., 2020) These results mirror our findings.

In France, Peyronnet et al. observed a stable total number of BPO procedures (61,993 in 2005 and 60,184 in 2014). However, there was a dramatic increase in PVP use from 0.2% to 23%, accompanied by a 34% reduction in TURP (from 52,828 to 40,436) and OP (from 9,069 to 5,948) between 2005 and 2014. (Peyronnet et al., 2015) Comparable patterns have also been noted in the United States (US) and Canada (LaBossiere et al., 2019; Malaeb et al., 2012; Schroeck et al., 2012). The 7.3% reduction in the relative proportion of TURP in our study is modest compared

with these international figures; nevertheless, TURP retained its dominant role across all studies, including ours (LaBossiere et al., 2019; Malaeb et al., 2012; Morton et al., 2020; Patel & Bariol, 2019; Peyronnet et al., 2015; Schroeck et al., 2012).

The initially low occurrence and subsequent decline in minimally invasive therapies and TUVP may partly reflect the adoption of PVP, alongside the broader evolution of BPO treatment options. The declines in the use of TUVP (3.6% to 0.5%, from 130 to 18 annual operations), TUMT (2.7% to 0.6%, from 97 to 23 annual operations), and TUNA (0.8% to 0.2%, from 28 to 6 operations) in the current study are likely to reflect guideline shifts away from less efficacious modalities (Oelke et al., 2013). It could be said that Finland was either ahead of its time or particularly responsive to changing attitudes towards these minimally invasive treatments. After adopting the Grading of Recommendations Assessment, Development, and Evaluation approach in 2019 (Speakman et al., 2019), TUMT and TUNA were removed from the EAU Guidelines.

Between 2004 and 2013, the Urologic Diseases in America Project reported that 13.5% of patients in the Medicare cohort received TUMT and 4.9% TUNA, whereas in the Optum Clinformatics Data Mart cohort the corresponding proportions were 21.3% and 12.3%, respectively (Welliver et al., 2020). TUVP as a standalone procedure has increasingly become obsolete due to its suboptimal mid-term effectiveness (Cornu et al., 2025). However, it may still serve a valuable role in achieving haemostasis after TURP.

The mean operation incidence rate observed in our study (263 per 100,000 men from 2004 to 2018) exceeds that reported in Australia (106 to 147 per 100,000 from 2000 to 2018) (Morton et al., 2020). However, it is comparable to more recently reported rates of 234.2 per 100,000 in 2000 and 232.2 per 100,000 in 2019, also from Australia (Shin et al., 2025). The operation incidence rate in Study I falls below US figures, where Malaeb et al. noted a peak of 1,078 per 100,000 in 2005. The operation incidence rate in the US declined by 15.4% to 912/100,000 in 2008. (Malaeb et al., 2012)

Despite an increase in the total number of procedures from 3,591 to 3,893 annually in Study I, the operation incidence remained stable, likely influenced by demographic shifts. Finland's male population aged over 40 years grew by approximately 150,000 during the study period, with declining operation incidence trends in the age groups 50–59, 60–69, 70–79, and 80–89, but not in those aged 40–49 or over 90 years. Disparities in reported operation incidence across studies may stem from differences in data sources; Morton et al. and Malaeb et al. relied on private or Medicare datasets that excluded public in-hospital data (Malaeb et al., 2012; Morton et al., 2020), whereas our study was based on a comprehensive, validated nationwide registry (Sund, 2012). Assuming a LUTS incidence of 15 per

1,000 men reported in the Triumph Project (Verhamme et al., 2002), approximately 18% of Finnish LUTS patients received surgical treatment, which is slightly below the 21% reported in Korea (Lee et al., 2016).

Across all procedure types and age groups, postsurgical hospital stays shortened significantly between 2004 and 2018. However, the mean hospital stay after TURP (4.0 days, SD 2.1) and OP (8.0 days, SD 3.0) appeared unexpectedly prolonged compared with PVP (2.3 days, SD 1.5) and TUMT (1.1 days, SD 0.2), the latter being the only true outpatient procedure in the population of Study I. The mean difference in hospital stay between TURP and PVP aligns with a prior report by Thangasamy et al. (mean difference 1.91 days, 95% CI 1.47–2.35, $p < 0.00001$) (Thangasamy et al., 2012). However, the observed hospital stay after TURP exceeded the range reported in Treharne et al.'s meta-analysis (2.87 days for B-TURP and 3.43 days for M-TURP) (Treharne et al., 2018).

In the US, most TURP procedures involved hospital stays, although a gradual shift was observed, with 31.9% of TURP procedures (12,370/39,092) performed in outpatient care by 2008. Simultaneously, 69.4% of laser vaporisation procedures (20,784/29,955) were performed as outpatient procedures. (Malaeb et al., 2012) Reducing the length of hospital stay offers economic benefits and may have fuelled initial PVP enthusiasm (Thangasamy et al., 2012). Nevertheless, cost-effectiveness analyses should also account for complications and reoperation rates. The trend towards same-day discharge for select BPH patients is gaining traction, supported by emerging safety data (Garden et al., 2022). In the United Kingdom (UK), the day-case rate of BOO surgery increased from 8.3% to 21.0% between 2017 and 2022; during this period, 4.5% of TURP procedures (3,367/71,436) and 22.5% of laser surgeries (4,013/13,852, all endoscopic laser prostate surgeries) were performed as day cases (John et al., 2024).

The mean age of operated patients increased by 2 years to 71.8 years by 2018, rising across all procedures except TUVP. Malaeb et al. reported that the highest BPO procedure rates occurred in the age group of 70 –75 years (1,132 per 100,000) (Malaeb et al., 2012), while another study identified the 70–79 age group as having the highest annual incidence (~4 per 10,000). In contrast, in the Finnish cohort, operation incidence was nearly identical in the 70–79 and 80–89 age groups (737 per 100,000 and 739 per 100,000, respectively).

6.1.2 Comparative risks of photoselective laser vaporisation of the prostate and transurethral resection of the prostate

In the population of Study II, the analysis demonstrated the superiority of PVP in reducing 90-day bleeding reoperations (0.9% vs 1.3% for TURP; HR 0.72, 95% CI

0.53–0.99, $p = 0.042$). This aligns with the proposed haemostatic advantages of PVP, attributed to haemoglobin acting as the primary tissue chromophore (Bach et al., 2012; Kuntzman et al., 1996). However, long-term reoperation rates were significantly higher following PVP (23.5% vs 17.8% for TURP; HR 1.20, 95% CI 1.09–1.31, $p < 0.0001$), predominantly driven by prostatic urethral interventions. Distal urethral reoperations, conversely, favoured PVP (4.4% vs. 6.0% for TURP; HR 0.64, 95% CI 0.53–0.77, $p < 0.0001$).

In the literature, reoperations are more common after PVP (Gilfrich et al., 2021). This might be explained by the predominance of earlier-generation laser systems in historical cohorts, which were associated with poorer prostate volume reduction (Bachmann et al., 2005; Hermanns et al., 2014). By contrast, prostatic urethral interventions related to urethral stricture formation are more frequent after TURP. This is possibly due to the larger diameter of instrumentation (Günes et al., 2015), thermal injury to the urethral mucosa due to current leakage, longer operative duration, or prolonged postoperative catheterisation (Pirola et al., 2022).

The hypothesis that laser procedures for bladder outlet obstruction represent lower-risk alternatives and are therefore preferentially used in older men receives only partial support from our data in Study III. Although a statistically significant association between age and procedure type was observed, the differences were modest, and laser procedures were not predominantly performed in the oldest patients. More critically, Study III demonstrated that men undergoing laser procedures experienced significantly lower 90-day postoperative mortality compared to those treated with TURP (0.59% vs 1.16%, RR 0.51, 95% CI 0.33–0.78, $p = 0.002$).

6.1.2.1 Reoperation risks

These findings on cumulative reoperation rates at 12 years, with a median follow-up of 4.3 years, extend the evidence derived from RCTs, such as the GOLIATH trial. In that study, equivalent overall reoperation rates were observed between PVP and TURP (9.0% vs 7.6% respectively), with no statistically significant difference at 2-year follow-up (log-rank $p = 0.7$) (Thomas et al., 2016). Similarly, a longer-term study of 238 patients with 5-year follow-up reported overall reoperation rates of 14.3% after 80-W PVP and 11.9% after M-TURP ($p = 0.9$) (Mordasini et al., 2018). Consistent with these findings, an earlier RCT by Ruszat et al. reported a 14.8% overall reoperation rate following 80-W PVP in a cohort of 500 procedures (Ruszat et al., 2008).

More closely aligned with the present results, a large retrospective nationwide cohort study including a mixed population treated with 80–180-W PVP (N = 3,050) and M- TURP and B-TURP (N = 34,526) reported 5-year overall reoperation rates

of 15.5% after PVP and 12.1% after TURP (HR 1.31, 95% CI 1.17–1.46, $p < 0.001$) (Gilfrich et al., 2021).

While comparative data beyond 5 years remain limited, these findings align with those of the present investigation. In the short term, the efficacy of PVP and TURP appears comparable, as evidenced by equivalent improvements in objective parameters such as Qmax and IPSS (Bachmann et al., 2014; Brunken et al., 2015). However, by 5 years postoperatively, patients initially treated with PVP exhibit higher reoperation rates (Gilfrich et al., 2021; Mordasini et al., 2018). Importantly, the current data reveal that this disparity further intensifies with extended follow-up, with 23.5% of PVP patients requiring reoperation by 12 years compared to 17.8% of those undergoing TURP (HR 1.20, 95% CI 1.09–1.31, $p < 0.0001$). These results underscore potential limitations in the long-term durability of PVP.

By contrast, in a recently published US study of BPH surgery performed between 2015 and 2021, the lowest 5-year retreatment rates were after TURP (7.0%, 476/6,748 procedures), with no statistically significant difference between PVP (8.9%, 348/3,922 procedures) and PUL (11.9%, 34/293 procedures) (Kaplan et al., 2024). Although these retreatment rates probably reflect outcomes of newer generation techniques (B-TURP and 180-W PVP), they are surprisingly similar to those reported earlier. The 5-year retreatment rate attributable solely to adenoma regrowth has earlier been reported as 6.8%–12.5% for PVP (Gilfrich et al., 2021; Mordasini et al., 2018; Ruszat et al., 2008) and 4.8%–8.2% for TURP (Gilfrich et al., 2021; Mordasini et al., 2018). Further studies with a substantially longer follow-up are therefore required to fully assess the long-term efficacy of these procedures.

Regarding clinically significant distal urethral strictures necessitating operative intervention, our data suggest a superiority of PVP over TURP (4.4% vs 6.0%; HR 0.64, 95% CI 0.53–0.77, $p \leq .0001$, NNT 47.4). This difference may be attributable to the smaller diameter of PVP instrumentation, although further research is required to substantiate this finding. Interestingly, this advantage was not observed in patients with AF (6.3% vs 6.9%, $p = 0.760$). The underlying mechanism remains unclear, as operative times for OAC patients in the literature do not appear to differ significantly from those of controls (Fa et al., 2020; Ruszat et al., 2007), making associations with prolonged procedures or increased bleeding unlikely. In addition, recurrent or chronic bleeding from previously treated prostatic surfaces may also be an indication for reoperation during long-term follow-up. Such bleeding-related interventions are challenging to distinguish in registry-based data and were therefore not considered in Study II. Consequently, it remains possible that some bleeding-related long-term reoperations were coded as repeat procedures regardless of the underlying indication.

Whether incidental PCA diagnosis affects the retreatment rate after surgery for LUTS remains unresolved. In Study II, patients with an established PCA diagnosis at the time of treatment were excluded from the analysis; however, patients who

received a subsequent PCA diagnosis during the study period were included. The rate of incidental PCA detected after surgery for LUTS appears to be rising, which may reflect changes in clinical practice and PCA screening strategies. Enucleation-based procedures generally afford greater tissue retrieval and are therefore associated with higher rates of incidental PCA detection compared with TURP. (Capogrosso et al., 2018) In contrast, patients undergoing PVP typically yield no tissue for histopathological examination due to vaporisation. Future studies are therefore warranted to elucidate the prognostic significance of incidental PCA with respect to retreatment risk following surgery for LUTS.

6.1.2.2 Major adverse cardiovascular events and bleeding risk

In Study II, within our large national cohort of consecutively operated BPH patients, no significant differences were observed in the incidence of MACE between PVP and TURP (1.8% vs 2.0%, $p = 0.253$). Intriguingly, the incidence of cardiovascular and thromboembolic complications reported by Bhojani et al. was notably lower (35/4,794 = 0.7% for TURP and 13/2,439 = 0.5% for tissue vaporisation) compared with our cohort (Bhojani et al., 2014). This discrepancy may be attributed to methodological variations, as Bhojani et al. assessed complications within 30 days, whereas our study extended the observation window to 90 days. Alternative explanations for this involve the inclusion of cardiovascular deaths in the risk profile and possible differences in patient inclusion/exclusion criteria, all of which might have influenced the observed outcomes.

The MACE rates observed in the current study were more comparable to those reported by Marchioni et al., who examined perioperative MACE following 180-W PVP and reported an incidence of 1.9%, (18 of 923 patients) (Marchioni et al., 2018). In another study assessing perioperative MACE among 44,939 patients, MACE occurred in 0.9% of TURP patients, 0.7% of PVP patients, and 0.6% of enucleation patients. They reported that PVP was associated with a significantly lower risk of MACE compared with TURP (OR 0.7, 95% CI 0.6–0.9, $p = 0.017$), whereas no statistically significant difference was observed between enucleation and TURP (OR 0.7, 95% CI 0.4–1.1, $p = 0.181$). (Marchioni et al., 2019)

The ongoing debate regarding the discontinuation of OAC prior to TURP merits attention. In the literature, patients on OAC face an elevated risk of perioperative bleeding, whereas cessation, particularly for secondary prevention, is linked to heightened cardiovascular and cerebrovascular complications (Burger et al., 2005; Taylor et al., 2011). In Study II, the risk of MACE was 3.5% after PVP and 4.3% after TURP in patients with AF (HR 0.83, 95% CI 0.55–1.23, $p = 0.351$). By contrast, the risk of MACE was 1.5% after PVP and 1.7% after TURP in patients without AF (HR 0.90, 95% CI 0.69–1.18, $p = 0.440$). Study III confirmed AF as an independent

risk factor for increased mortality (2.60%, RR 1.53, 95% CI 1.18–1.99, $p = 0.001$). Although AF was used to identify patients at potentially increased bleeding risk, the diagnosis does not directly correspond to OAC use. Furthermore, in Study II, a possible advantage of continuing OAC medication in preventing MACE was not observed among patients with AF. Consistent with this, MACE rates in the AF group did not differ significantly between the operative techniques, as noted above.

Current understanding of the safety profile of PVP in individuals at heightened bleeding risk predominantly stems from case series, as these patients are frequently excluded from RCTs (Cornu et al., 2025). This poses a challenge, given that urologic surgeries are typically classified as high-risk in procedural bleeding risk assessments (Shaw et al., 2020; Spyropoulos et al., 2016). This potentially necessitates the discontinuation of OAC therapy, which is often employed to mitigate thromboembolism in patients with AF (Hindricks et al., 2021). Additionally, risks such as transurethral resection syndrome and irrigation fluid absorption remain pertinent concerns for these procedures (Hermanns et al., 2015; Ortner et al., 2022; Tokas et al., 2021). Although these adverse events were not evaluated in the present study, they warrant consideration when planning BPH surgeries.

In Study II, PVP demonstrated a reduced likelihood of reoperation for bleeding (0.9% vs 1.3%), with a hazard ratio of 0.72 (95% CI 0.53–0.99, $p = 0.042$) and NNT of 285 across the entire study population. This benefit was particularly pronounced among patients with AF, where the NNT decreased to 61. This suggests that PVP offers substantial advantages for individuals who might be at elevated bleeding risk. Postoperative bleeding following TURP is a well-documented complication (Rassweiler et al., 2006), with perioperative OAC therapy exacerbating this risk. Nevertheless, bleeding complications after PVP have also been noted (Fa et al., 2020).

The overall reoperation rate for bleeding in our study exceeds previously reported figures, reflecting the real-world, all-inclusive design of our analysis. In contrast, Reich et al. observed no postoperative bleeding in their cohort of 66 high-risk patients (26 on OAC) (Reich et al., 2005), while Ruszat et al. and Sandhu et al. reported no bleeding complications requiring transfusions or reoperations in their studies of 116 and 24 high-risk patients, respectively (Ruszat et al., 2007; Sandhu et al., 2005). Existing literature consistently indicates a higher incidence of bleeding complications with TURP compared with PVP (Ahyai et al., 2010; Al-Ansari et al., 2010; Fa et al., 2020). However, significant bleeding during PVP may compromise visibility, occasionally necessitating conversion to TURP. Other causes of conversion include early fibre defects and, in cases of large prostates, inadequate de-obstruction with the primary fibre (Ruszat et al., 2008). The conversion rate in Study II was 2.2%, which is lower than the reported range of 3.5%–5.2% (Ahyai et al., 2010; Ruszat et al., 2008).

Emerging endoscopic enucleation techniques are increasingly supplanting PVP and TURP to address the relatively high reoperation demand following these procedures. While enucleation methods appear safe, evidence regarding their safety in anticoagulated patients remains limited (Cornu et al., 2025). Future investigations should therefore focus on validating the safety and efficacy of EEP techniques in anticoagulated populations, compared with traditional standards like PVP and TURP.

6.1.3 Short-term postoperative mortality

In Study III the excess mortality attributable to surgery remained low (< 0.5% at 90 days), aligning with the perception of BPH interventions as low risk in elective settings. The leading causes of death were malignancy (35.5%) and cardiac disease (30.9%), highlighting the influence of underlying comorbidities rather than procedural complications per se. However, Study III revealed an overall 90-day postoperative mortality rate of 1.10%, with TURP (1.16%) exhibiting a statistically significantly higher rate than PVP (0.59%; univariable: RR 0.51, 95% CI 0.33–0.78, $p = 0.002$). The mortality rate after OP was 0.67%, with no statistically significant difference compared with TURP (RR 0.57, 95% CI 0.27–1.21, $p = 0.145$). This disparity between TURP and PVP persisted despite adjustments for confounders, underscoring the potential safety advantage of PVP in the short term (multivariable: RR 0.63, 95% CI 0.41–0.97, $p = 0.035$). Nonetheless, it should be noted that, in registry-based studies, the absence of granular clinical data may influence outcomes. Although differences between operation types were observed at the population level, these findings advocate for individualised treatment strategies. The results of Study III underscore the importance of preoperative risk assessment regardless of the choice of surgical technique.

The 90-day postoperative mortality rate following TURP in this study, at 1.16%, exceeds the 0.5% cumulative incidence rate reported recently by Eredics et al. in a nationwide assessment of BPH-related mortality (Eredics et al., 2018). This discrepancy may be explained by methodological differences, as Eredics et al. restricted their analysis to in-hospital mortality, whereas our study utilised the Finnish Causes of Death Registry, thereby capturing all deaths irrespective of location during the study period. Study III shares similarities with the extensive 2016 study by Gilfrich et al., which examined 95,577 cases from a German nationwide health insurance database. A key methodological distinction is the follow-up window: Gilfrich et al. focused on 30-day postoperative mortality, whereas our study extended the period to 90 days. Despite this difference, the postoperative mortality rates reported by Gilfrich et al. for laser vaporisation (37 of 6,409 men, 0.58%) and

OP (43 of 8,376 men, 0.51%) (Gilfrich et al., 2016) closely mirror the findings of our study, suggesting consistency across differing observation periods.

Bhojani et al., using data from the American College of Surgeons National Surgical Quality Improvement Program (2006–2011), compared TURP with laser procedures and observed reduced blood transfusion rates, shorter hospital stays, and fewer reinterventions with laser vaporisation. However, no significant difference in perioperative mortality was detected between TURP (0.4%) and laser (0.3%; OR 0.68, 95% CI 0.29–1.62, $p = 0.4$). Advanced age (OR 1.10, 95% CI 1.00–1.19, $p = 0.01$) emerged as an independent risk factor for increased mortality, while normal preoperative albumin and higher preoperative haematocrit levels (>30%) were associated with fewer complications and lower perioperative mortality. (Bhojani et al., 2014)

Similarly, Patel et al., leveraging the same American database (2006–2011), quantified complication rates across urological procedures and reported the highest mortality after TURP (31 of 4,968 men, 0.62%), compared with lower rates after photoselective vaporisation (13 of 2,853 men, 0.46%), radical retropubic prostatectomy (8 of 2,279 men, 0.35%), and laparoscopic radical prostatectomy (9 of 8,381 men, 0.11%) (Patel et al., 2015). Since Patel et al. assessed morbidity irrespective of surgical indication, their cohort likely included patients with PCA. The observed 0.22% disparity in 30-day postoperative mortality between the studies by Patel et al. and Bhojani et al. may therefore be attributable to differing inclusion/exclusion criteria, particularly regarding the handling of PCA cases (Bhojani et al., 2014; Patel et al., 2015).

The Finnish context, with universal healthcare and comprehensive registry linkage, likely captures a more representative spectrum of outcomes, including non-hospital deaths. However, it should be noted that in Study III the postoperative mortality rate reflects the patient profile and treatment selection at least as much as the inherent safety of the operative treatment itself. Independent risk factors identified in Study III, including advancing age and elevated CCI, echo prior findings, where frailty predicts perioperative adversity (Guo et al., 2016; Mandal et al., 2013; Patel et al., 2015). The diagnosis of atrial fibrillation was also identified as an independent risk factor for mortality, which may be explained by an increased risk of bleeding and MACE associated with the possible use of OAC (Marien & Shah, 2013). The risk of mortality decreased significantly in the later study era, confirming improvement in perioperative care and patient selection over the past decade in Finland, as was earlier observed in Austria in a nationwide analysis of reoperation rates and mortality (Eredics et al., 2018).

The disparity in 90-day postoperative mortality between TURP and PVP in Study III differs from the results of the aforementioned large retrospective cohort studies in America, Germany, and Austria (Bhojani et al., 2014; Eredics et al., 2018;

Gilfrich et al., 2016). However, this disparity was statistically absent in Study II. After balancing the study population for confounding factors, Study II reported a lower overall 90-day mortality (0.6%), with no significant difference between PVP (0.4%) and TURP (0.6%; HR 0.72, 95% CI 0.46–1.12, $p = 0.144$). These findings are more consistent with the existing literature. This temporal decline in 90-day postoperative mortality observed in Study II may reflect procedural refinements, such as the adoption of bipolar TURP and improved perioperative care, associated with the later study period (Study III: 2004–2014 vs Study II: 2006–2018).

The absence of a statistically significant mortality disparity in Study II, despite the lower bleeding reoperation rate observed after PVP (0.9% vs 1.3%; HR 0.72, 95% CI 0.53–0.99, $p = 0.042$), suggests that while PVP mitigates haemostatic risks, broader cardiovascular events may dominate short-term mortality. Integrating these findings with Study I, the increasing utilisation of PVP (from 0.1% to 16%, trend $p < 0.0001$), completion of the learning curve, and adoption of higher-power laser systems may partly explain the reduced mortality in later cohorts (Study III: 0.59%, Study II: 0.4%).

However, mortality rates from Studies II and III cannot be directly compared, as Study II employed inverse probability of treatment weighting to balance confounding factors between the study populations. Consequently, patient selection is a likely contributor to the mortality disparity observed in Study III. Another distinction between Studies II and III is the inclusion of patients with established PCA in Study III. Although the decision is justified by the frequent coexistence of BOO due to BPH in these individuals, the two conditions are not mutually exclusive. Moreover, Crow et al. have suggested that TURP in patients with PCA does not appear to result in excess postoperative mortality or complications (Crow et al., 2002).

Although the likelihood of detecting incidental PCA has declined to 5.2%–6.4% in the era of PSA testing (Capogrosso et al., 2018; Jones et al., 2009; Zigeuner et al., 2003), the proportion of PCA patients in Study III was higher (9.2%, 4,284 of 39,320 patients), reflecting the inclusion of men with a known diagnosis of PCA. This increased the risk of higher observed mortality in the cohort, particularly after TURP, due to inadvertent inclusion of palliative procedures. The 90-day postoperative mortality following palliative TURP has been estimated to be 3.4% (two of 137 patients) (Pelletier et al., 2018), and was similarly elevated in Study III (3.66%; RR 4.38, 95% CI 3.58–5.36, $p < 0.0001$) compared with the overall mortality rate (1.10%). Nevertheless, PCA was not identified as an independent risk factor for elevated postoperative mortality in the multivariate analysis (RR 1.20, 95% CI 0.92–1.57, $p = 0.170$) and therefore does not fully explain the observed disparity between TURP and PVP.

6.1.4 Strengths, limitations, and implications

The primary limitation of the substudies stems from their retrospective design and lack of detailed clinical information, which introduces several inherent shortcomings. In Study II, the absence of granular clinical data prevented assessment of pretreatment prostate size and variations in PVP or TURP techniques, all of which may have influenced outcomes. Surgeon's experience is another important missing variable. The implementation of PVP occurred during the study period, and although its utilisation plateaued in 2013, the procedure is likely still concentrated among a relatively small number of specialised surgeons. In contrast, TURP is more widely performed by a heterogeneous group of operators, including residents. Differences in operator expertise cannot be captured in registry data may therefore have influenced the observed outcomes.

The NCSP coding system did not allow differentiation between PVP generations, nor did it enable distinction between B-TURP and M-TURP. Coding inaccuracies, such as misclassification between BNS, urethral stricture, and residual adenoma, as well as possible underreporting of medical histories, are additional concerns. The use of AF as a surrogate for OAC is validated (Kytö et al., 2021), but it may not capture all anticoagulated patients. Therefore, findings in AF subgroups should not be interpreted as direct evidence of outcomes in OAC patients.

In a subgroup analysis of Study II, the age threshold of 70 years was selected to facilitate clinically relevant comparisons in populations with increasing comorbidities. However, age is a continuous variable, and frailty rather than chronological age alone may be a more appropriate determinant of surgical risk. In addition, although the maximum follow-up in Study II extended to 12 years, the median follow-up was approximately 4.3 years. Consequently, patients with the longest follow-up were predominantly those treated in the early years of the study period, often with earlier-generation PVP systems.

Furthermore, although there was no statistically significant difference in 90-day postoperative mortality between PVP and TURP in Study II, the 95% confidence interval (0.46–1.12) does not exclude a clinically meaningful difference. Retrospective power calculations suggest that, to demonstrate a statistically significant difference between the observed mortality rates of 0.4% and 0.6%, a sample size at least three times larger would have been required (around 68,000 rather than 22,000 patients). This highlights the inherent difficulty of detecting differences in rare outcomes.

In Study III, we were unable to identify or grade postoperative complications that directly contributed to death. For this reason, application of the Clavien-Dindo Classification was not feasible, although its use may have provided additional clinical insight. Emerging techniques, including minimally invasive simple prostatectomy, aquablation, prostatic artery embolisation, convective water vapour

energy ablation, and prostatic urethral lift (Cornu et al., 2025), were excluded because they were not practised in Finland during the study period. EEP procedures were also not included, as they are not commonly performed in Finland and no specific NCSP code exists to reliably identify them.

Nevertheless, these three studies leveraged a combination of nationwide, legally mandated, and previously validated registries (Sund, 2012), with follow-up extending up to 12 years in the second study. In Study II, the analyses were adjusted for a wide array of potential confounders. The use of propensity scoring and IPTW represents a robust approach for confounding control in registry-based studies, producing results akin to randomised trials and with bias reduction that is at least non-inferior to multivariable regression (Deb et al., 2016).

An advantage of IPTW over matching is its ability to retain the full study data, although it may be more susceptible to propensity model misspecification and extreme propensity-score values (Austin & Schuster, 2016; Deb et al., 2016). To mitigate this, stabilised IPTW was applied to minimise the impact of extreme weights. However, several key clinical determinants of treatment selection, such as LUTS severity, prostate volume, and baseline functional status, were not available in the registry data. Consequently, IPTW-adjusted comparisons should be interpreted as associations rather than estimates of causal treatment effects. Residual confounding by indication is therefore likely to persist despite statistical adjustment.

Based on the E-value analysis, the observed higher reoperation rate after PVP could be explained by unmeasured confounders associated with both treatment modality and the need for reoperation, with risk ratios of 1.7 or greater, beyond the measured covariates, whereas weaker confounding would be insufficient to account for the observed association (VanderWeele & Ding, 2017).

7 Summary and Conclusions

The evolving surgical landscape, marked by the enduring dominance of TURP and the rise of PVP, alongside declines in less effective modalities, indicates a cautious adoption of minimally invasive techniques within an aging population. The stable incidence despite rising procedure numbers suggests that effective medical management delays surgical intervention. Meanwhile, shortened hospital stays reflect increasing economic and logistical efficiencies. Surgical treatment for LUTS was deemed safe for all age groups, as excess postoperative mortality was found to be low. Aging, CCI score, and a diagnosis of AF were identified as independent risk factors for higher postoperative mortality. In contrast, PCA diagnosis and annual surgical volume of the operating centre did not independently influence mortality. These findings highlight a low, but clinically relevant, mortality risk in elective settings, driven primarily by patient frailty rather than procedural volume.

The lower mortality observed after PVP in Study III, together with the reduced risk of bleeding-related reoperations in Study II, positions PVP as a suitable alternative for high-risk individuals. However, substantially higher long-term reoperation risk underscores limitations in the durability of PVP, especially for reoperations of prostatic urethra (adenoma regrowth, BNS). It should be noted that, in registry-based studies, the absence of granular clinical data, such as operator-related factors, indication for surgery, and temporal evolution of perioperative care, may influence outcomes. Nevertheless, based on these results, clinicians may individualise treatment strategies, favouring TURP for durable symptom relief in younger and fitter cohorts, and PVP for frailer elderly individuals with elevated bleeding risk and a low likelihood of requiring reoperation. Although differences between operation types were observed at the population level, these findings advocate for individualised treatment strategies. The preoperative risk assessment appears at least as important as the choice of surgical technique, as highlighted by malignancy and cardiac disease being the leading causes of 90-day mortality in Study III. The findings of these studies should not be interpreted as prescriptive guidance, and treatment selection should remain grounded in patient-specific clinical factors. The outcomes presented underscore the need for continued research to optimise surgical management of LUTS in an aging demographic.

Based on these studies and the review of the literature, mortality following surgery for LUTS is uncommon, yet it remains a clinically meaningful complication. Only a limited number of large-scale studies based on nationwide registers exist, and mortality is largely underreported or overlooked in most investigations. This is likely attributable to its low incidence, which necessitates very large cohorts, often comprising thousands of patients, to reliably capture postoperative mortality rates. As newer and less invasive techniques emerge, high-quality studies providing national real-world evidence on long-term efficacy, safety, mortality risk, and utilisation trends are essential. Further academic research is therefore required to provide robust, evidence-based recommendations before the widespread adoption of novel surgical techniques into the Current Care Guidelines.

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