The Utilization of Benign Prostatic Hyperplasia and Bladder-Related Medications After a Transurethral Prostatectomy

Jeffrey Campbell, Jennifer Reid, Michael Ordon, and Blayne Welk

OBJECTIVE To determine how often prostate- and bladder-specific medications for lower urinary tract symptoms are used following a transurethral prostatectomy (TURP).

METHODS This study utilized several linked, routinely collected datasets from the province of Ontario, Canada to identify men older than 66 years who underwent their first TURP between April 2003 and March 2016. The primary outcome was the probability of using at least 30 days of either prostate-specific alpha blockers (AB), 5-alpha reductase inhibitors (5ARI), or anticholinergics/beta-3 agonists (AC/B3) after their TURP.

RESULTS We identified 58,038 men (median age 75), with a median follow-up of 4.9 years. In the 6 months prior to their TURP, AB, 5ARIs or AC/B3 were used by 62%, 32%, and 6%, respectively. Following a 90-day washout period after TURP, these medications were used by 27%, 20%, and 15% of men, respectively. The cumulative probability of using these medications within the first 10 years after TURP was 38%, 28%, and 20%, respectively. Family physicians prescribed the majority of AB, while urologists prescribed the majority of the AC/B3. Among men on AC/B3 prior to TURP, 46% used them after TURP; in multivariate cox regression analysis age ≥75, diabetes, preoperative use of AC/B3, and no preoperative urinary retention predicted postoperative utilization of AC/B3 medications.

CONCLUSION There is considerable use of AB and 5ARIs despite a lack of evidence for using these medications after a TURP. Given the well-characterized placebo response in BPH patients, this practice should be properly evaluated for clinical efficacy. UROLOGY 130: 126–131, 2019. © 2019 Elsevier Inc.

Benign prostatic hyperplasia (BPH) is a histologic diagnosis for men with progressive enlargement of the prostate gland from proliferation of epithelial and smooth muscle prostate cells.[1] BPH is prevalent in aging men and is a major contributor to lower urinary tract symptoms (LUTS). Fifty percent of men with BPH will have associated LUTS with variable severity.[2] The burden of LUTS secondary to BPH increases with age. Approximately 80% of men over the age of 70 years develop LUTS secondary to BPH.[3]

Early detection and treatment of BPH-related LUTS can improve quality of life outcomes and prevent more serious complications. The current Canadian and American guidelines for treatment of LUTS secondary to BPH include medical management with alpha (α)-blocker (AB) and 5-α reductase inhibitors (5ARI).[4,5] AB cause smooth muscle relaxation and reduced urethral tone by inhibiting α1-adrenoergic receptors in the prostatic stroma which subsequently promotes bladder emptying.[6] Although AB is the first-line therapeutic option for men with symptomatic LUTS secondary to BPH, they do not alter the disease course.[7,8] In contrast, 5ARIs are used for men with evidence of prostate enlargement with the goal of altering the natural history of BPH progression in addition to improving LUTS.[7,8] Anticholinergics and beta-3

Funding Support: *This work was made possible by generous support from the MacMaster Fund for Urology through St. Joseph's Health Care Foundation. This study was supported by the ICES Western site. ICES is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). Core funding for ICES Western is provided by the Academic Medical Organization of Southwestern Ontario (AMOSO), the Schulich School of Medicine and Dentistry (SSMD), Western University, and the Lawson Health Research Institute (LHRI). The opinions, results, and conclusions are those of the authors and are independent from the funding sources. No endorsement by the St. Joseph's Health Care Foundation, ICES, AMOSO, SSMD, LHRI, or the MOHLTC is intended or should be inferred.*

From the Department of Surgery, Western University, London, Ontario, Canada; the Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada; the Department of Surgery, University of Toronto, London, Ontario, Canada; and the Department of Epidemiology and Biostatistics, Western University, London, Ontario, Canada

Address correspondence to: Blayne Welk, M.D., F.R.C.S.C., M.Sc., Division of Urology and Epidemiology and Biostatistics, Western University, Room B4-667, St Joseph's Health Care, 268 Grosvenor Street, London ON N6A 4V2. E-mail: bkwelk@gmail.com

Submitted: February 28, 2019, accepted (with revisions): May 7, 2019

https://doi.org/10.1016/j.urology.2019.05.003
0090-4295

agonists (AC/B3) are used for treating frequency, urgency/urge incontinence, and nocturia associated with BPH.[4,5,9] If medical management fails, or if there are absolute indications for surgical management, the gold-standard surgical treatment is a transurethral prostatectomy (TURP). Unfortunately up to one-third of patients have persistent or de novo LUTS after TURP.[10] There are no guidelines or high-quality studies to direct the management of LUTS after TURP.

While AC/B3 are appropriate for persistent storage symptoms post-TURP, the use of AB and 5ARI in this situation is less clear, and the prevalence and intensity of utilization of these medications has not been well characterized. Our objective was to determine the frequency of AB, 5ARI, and AC/B3 utilization after TURP, and to determine predictors of AC/B3 utilization post-TURP as a marker for persistent overactive bladder symptoms.

METHODS

Design and Setting

We conducted a retrospective, cohort study that utilized several routinely collected datasets from the province of Ontario (Canada); they were linked using unique, encoded identifiers and analyzed at ICES. Ontario has a population of over 13 million people with universal access to a single publicly funded healthcare system, and universal drug coverage for those over 65 years of age. The use of data in this project was authorized under Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. Patient consent was not required.

Data Sources

The administrative data sources which were used for this study include: (1) Registered Persons Database (which contains vital statistics),[11] (2) Ontario drug benefit database (which contains all prescription drug use for patients >65 years of age; previous research has demonstrated a high accuracy for prescribed medications),[12] (3) Canadian Institute for Health Information Discharge Abstract Database and Same Day Surgery (which identifies all inpatient and outpatient procedures),[13] (4) National Ambulatory Care Reporting System (which identifies all emergency room encounters),[14] (5) Ontario Health Insurance Plan (which contains all physician billing codes for patient assessment or treatment),[15] (6) the Ontario diabetes database (which identifies diabetics based on physician visits or hospital admission and has been validated with a specificity 97%,[16] and (7) the ICES Physician Data Base (which identifies physician specialties). All datasets have demonstrated validity and reliability and have been used extensively for research. These databases contain patient-level data in linkable files and are more than 99.5% complete for all study variables.

Patient Population

We constructed a cohort of men older than 66 years who underwent their first TURP between April 2003 and March 2016. Patients undergoing TURP were identified using physician billing codes (S655 or S654). The date of TURP was used as the index date. We excluded men: not living in Ontario, with a prior potential diagnosis of prostate cancer, with a TURP in the prior 10 years, who underwent a simultaneous bladder tumor resection, and those that were <66 years of age at the time of TURP (this was required so that we would have medication utilization data both 1 year before and after the TURP). Further details are shown in eTable 1 in the Appendix.

Study Outcome

Our primary outcome was a patient filling a prescription of >30 days duration for one of the medication classes of interest: AB, 5ARI, or AC/B3. Specific medications included in each of these classes are listed in eTable 2 in the Appendix. We limited our assessment of AB to those specifically indicated for male LUTS (tamsulosin, silodosin, and alfuzosin). We did not consider prescriptions within the first 90 days after TURP in order to give patients an opportunity to discontinue preoperative medications, and to eliminate any prescriptions associated with immediate postoperative symptoms. Total duration of use was the total prescribed doses (regardless of time between prescriptions) between the index date +90 days and the end of the observation period. Cumulative duration of utilization was determined by considering repeat prescriptions within 1.5× the duration of the previous script, similar to our previous work.[17] Men were observed for utilization of a medication of interest from the index date +90 days until censoring; patients were censored at death, radical prostatectomy, emigration from the province, or the end of the study period (March 31, 2017).

Covariates

Common conditions preceding a TURP (hematuria, recurrent infections, and acute urinary retention) were defined by a hospitalization or emergency room visit within 1 year prior to the surgery based on diagnostic codes. Simultaneous bladder stone treatment was identified by physician billing codes for cystolithopaxy at the time of TURP. Similarly, the energy modality of the TURP procedure was classified based on hospital records as either electrocautery, laser, or unknown. Diabetic patients were identified through the Ontario diabetes database (using a 5-year window prior to the index date). Further details are shown in eTable 1 in the appendix.

Statistical Analysis

Baseline characteristics are reported using medians and interquartile ranges (IQR), or number (proportion). Our primary analysis reported percentages, rate of utilization, and cumulative probability of utilization for each of the medication classes based on a life-table method. Cochran-Armitage trend test was used to evaluate AC/B3 usage over time. To determine the significant predictors of utilization of AC/B3 medication post-TURP, we evaluated 4 *a priori* variables (age, preoperative urinary retention, diabetes, and preoperative use of AC/B3); we used a cox proportional hazards model (PROC PHREG, SAS 9.4, SAS institute, Cary, NC) and the assumption of proportionality was confirmed graphically (Schoenfeld residuals) and statistically (time-dependent covariates). When proportionality was violated an interaction term with time was included and a graphical representation of the hazard ratio (HR) over time was provided. HR and 95% confidence intervals are reported; we considered 2-tailed P values <0.05 statistically significant.

RESULTS

Patient Baseline Characteristics

A total of 99,524 patients underwent a TURP procedure during the study period. After application of our exclusion criteria, 58,038 patients remained for analysis (eFigure 1 in the Appendix). The median age was 75 years (IQR 71-81). Patients were followed for a median duration of 4.9 years (IQR 2.5-8.1). A total of 21,420 (36.9%) men were censored at death and 309 (0.5%) at radical prostatectomy. There was a median of 4385 patients (IQR 4186-4801) in each fiscal year. Most TURP procedures were performed in a nonacademic setting (88%, 51,044). An electrical TURP was carried out in 78% (45,285) of the patients, and 11.6% (6715) had a laser-TURP; we could not determine the technique used in the remaining 10.4% (6038) patients. In the year before surgery, patients presented to the hospital or emergency room with acute urinary retention (44%), gross hematuria (24.3%), or a urinary tract infection (4%) (Table 1). In the 6 months prior to their procedure, 49.8% of patients were taking an AB, 31.9% were taking a 5ARI, and 6.0% were taking an AC/B3. Some patients were prescribed multiple medications during this time period (Fig. 1).

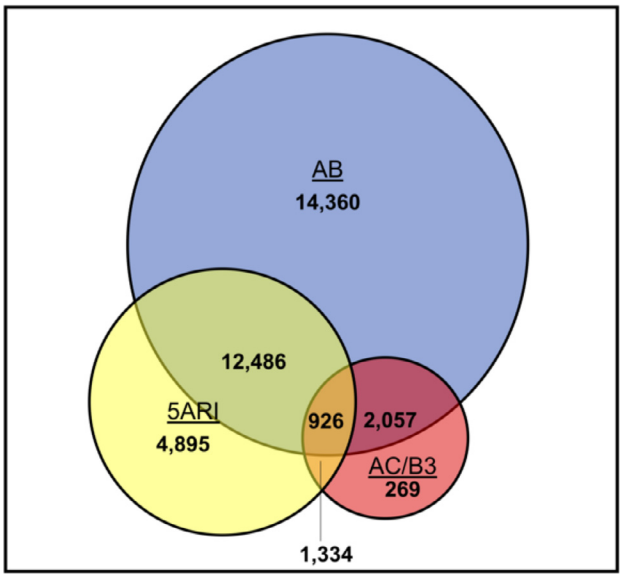

Figure 1. Venn diagram showing the total number of patients taking relevant medications prior to their transurethral prostatectomy (TURP). Numbers in the interlocking circles represent the number of patients taking at least 30 days of combination medical management after their TURP (not necessarily at the same time). AB, alpha-blocker; AC/B3, anticholinergic or β3 agonist; 5ARI, 5-α reductase inhibitor). (Color version available online.)

Primary Outcomes

After the 90-day washout period, 27% of men were prescribed an AB, 20% a 5ARI, and 15% an AC/B3 at some point during follow-up. The cumulative risk of using an AB, 5ARI, or AC/B3 10 years after TURP was 38%, 28%, and 20%, respectively (Fig. 2). Primary care physicians were the most frequent prescribers of AB, whereas urologists prescribed the majority of the AC/B3 (eTable 3 in the Appendix). A total of 10,942,858 AB, 11,477,749 5ARI, and 5,283,283 AC/B3 doses were prescribed post-TURP; in the AC/B3 group, only 11.6% of prescribed doses were for a beta-3 agonist.

The median time to first use was 1.25 years (IQR 0.40-3.87) for AB, but less than a year for both 5ARI (0.83 years, IQR 0.35-3.43) and AC/B3 (0.69 years, IQR 0.34-2.39). The median duration of total use (which accounts for use of the medication in noncontinuous periods) for AB, 5ARI, and AC/B3 was 360 (IQR 101-930), 620 (IQR 210-1,430), and 250 (IQR 71-730) days, respectively. The median duration of continuous use was 93 (IQR 45-150), 35 (IQR 45-163), and 63 (IQR 45-135) days for AB, 5ARI, and AC/B3, respectively.

There was a statistically significant increase in the utilization of AC/B3 prior to TURP over time ($P < 0.01$). Among men on AC/B3 prior to TURP, 46.3% continued use after TURP. Multivariate cox regression analysis demonstrated that age ≥75, diabetes, preoperative use of AC/B3, and no preoperative urinary retention predicted postoperative use of AC/B3 medications (Table 2). The hazard function for preoperative use of AC/B3 violated the proportionality assumption, meaning that it changed over time. Table 2 contains the HR for the immediate period after TURP; this HR decreases with an increased period of time between TURP and first prescription of an AC/B3 (shown in eFigure 2 in the Appendix).

DISCUSSION

We conducted a population-based retrospective cohort study including more than 58,000 men over the age of 65 years who underwent their first TURP over a 14-year period. We observed that 27%, 20%, and 15% of men

Table 1. Baseline Characteristics for Patients that Underwent a TURP

	Number of Patients (%)
Type of hospital for TURP	
Academic	6994 (12.0%)
Nonacademic	51,044 (88.0%)
Presentation to hospital/emergency room in the year prior to TURP for:	
Gross hematuria	14,087 (24.3%)
Urinary tract infection	2281 (3.9%)
Acute urinary retention	25,527 (44.0%)
Type of TURP procedure	
Laser	6715 (11.6%)
Electrical	45,285 (78.0%)
Unknown	6038 (10.4%)
Concomitant bladder stone treatment	5193 (8.9%)
Diabetes	12,867 (22.2%)

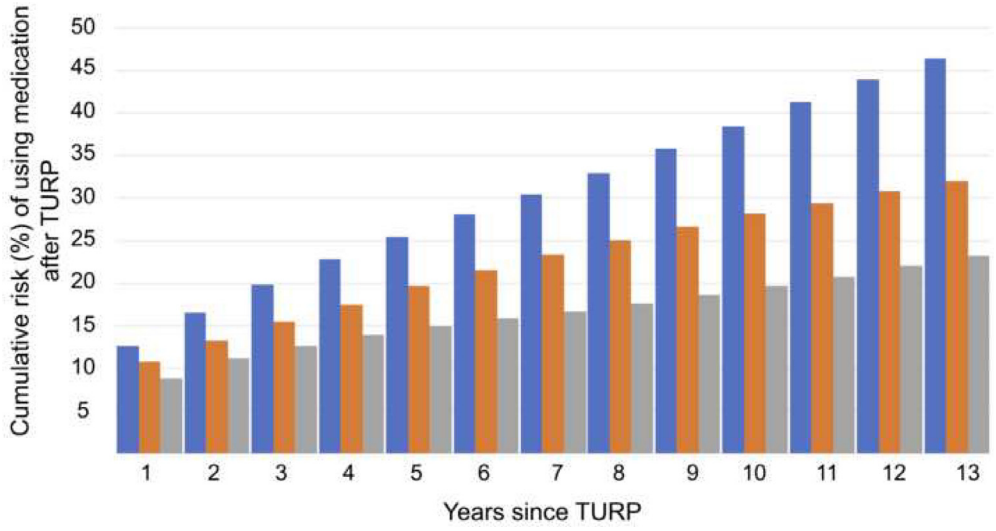

Figure 2. Cumulative risk (%) of using an alpha blocker (AB; blue), 5-alpha reductase inhibitors (5ARI; orange), or anti-cholinergic/β3 agonist (AC/B3; grey) per year after transurethral prostatectomy (TURP). (Color version available online.)

Table 2. Cox Regression Analysis of Covariates Influencing the Use of Anticholinergics or Beta-3 Agonists After Primary TURP

Covariate	Adjusted Hazard Ratio (95% CI)	*P* value
Age (reference < 75 years)	1.16 (1.11-1.21)	<0.01
Pre-TURP urinary retention (reference no)	0.47 (0.45-0.49)	<0.01
Diabetes mellitus (reference no)	1.30 (1.23-1.36)	<0.01
Preoperative use of AC/B3* reference no)	5.83 (5.42-6.26)	<0.01

* Proportionality assumption was violated for this covariate, and the model was adjusted with an interaction with time covariate. This HR represents the HR immediately after TURP, and the HR decreases with time from TURP (see eFigure 2 in the Appendix for more details)

used an AB, 5ARI, and/or AC/B3, respectively, post-TURP. These values are consistent with the anecdotally high number of patients seen for post-TURP LUTS. Persistent LUTS after TURP are bothersome, reduce quality of life outcomes, and occur in 20-50% of patients.[10] Despite several new technologies that have been developed for TURP, the prevalence of LUTS does not appear to vary significantly between methodologies.[18] The lack of guidelines for the use of these medications post-TURP may contribute to the high rates of medication therapy despite trivial clinical evidence.

A quarter of men were prescribed an AB after TURP, and the median total duration of use was longer than a year; the continuous usage was considerably short, suggesting many of these men were trialed on ABs multiple times after TURP. These medications primarily act on α-adrenergic receptors in the bladder neck and prostatic stroma to initiate smooth muscle relaxation and promote bladder emptying.[6] After TURP, the bladder neck and prostatic stromal tissue have presumably been resected and therefore these medications do not have a clear mechanism by which they would improve urinary symptoms. α-Adrenergic receptors are also found in the internal urethral sphincter and bladder mucosa,[19] and it is possible that these residual receptors could help reduce LUTS post-TURP. A small clinical trial evaluated the use of AB after TURP[20]; men were randomized to Tamsulosin, Tamsulosin plus Solifenacin, or placebo for 8 weeks immediately following TURP. There was no clinical improvement in symptoms or quality of life scores. In fact, there was an increase in postoperative postvoid residual volume in both groups treated with an AB after TURP.[20] Similarly, a Russian study showed that AB therapy immediately following TURP did not improve postsurgical symptoms or improve voiding volumes.[21] The large scale Medical Therapy of Prostatic Symptoms trial evaluated AB, and in the placebo arm there was improvement in symptoms scores and flow rate (of 1.4 mL/s)[8]; there may be a similar placebo response in patients post-TURP. The extended use of AB after TURP represents a significant, nonevidence-based cost in a publicly funded healthcare system: over 10 million doses of AB were provided to patients post-TURP (with an estimated cost of more than $5 million dollars). Primary care physicians were found to be the most common prescribers of AB in our patient population. Several reasons could explain this phenomenon including a reflexive prescription for men with LUTS, a lack of understanding of the mechanism of action, or an inadequate history of prior surgeries. The highest risk of requiring medical management for LUTS after a TURP is within the first few years, which suggests

that urologists should be following these patients to ensure adequate treatment of post-TURP LUTS.

The inhibition of the 5α-reductase enzyme leads to a decrease in the conversion of testosterone to dihydrotestosterone and a resulting reduction in prostate volume in men with BPH.[22] 5ARIs decrease the risk of urinary retention, improve urinary symptoms, and reduce the risk of TURP.[8,22] In addition, 5ARI treatment has been observed to prevent hematuria secondary to BPH and reduce the risk of bleeding and blood transfusion during TURP.[23,24] The benefit of a 5ARI for symptom management after TURP is unclear. There has been one multicenter study from China that randomized patients with prostates >80 g to treatment with a 5ARI or placebo for 3 years after TURP.[25] After a 3-year treatment period, patients taking a 5ARI did not have any significant change in symptom scores, quality of life measures, postvoid residual, or rate of repeat TURP. 5ARI treatment did appear to reduce post-TURP hematuria, and reduce prostate volume, which suggests there may be a clinical benefit in select patient populations. In our patient cohort, urologists were the most common prescriber of 5ARI after TURP, which may represent a surgeon awareness of incomplete resection, treatment of patients at continued risk of bleeding or an attempt at avoiding repeat TURP.[26] In large glands when residual tissue is noted at the completion of the procedure, urologist may be selectively starting (or continuing) men on 5ARI to reduce the risk of prostatic regrowth and promote a further reduction in prostate volume.

Most studies report that storage symptoms have the highest bother in men suffering from LUTS after TURP.[18] Several structural and functional changes occur in the detrusor muscle after prolonged bladder outlet obstruction, which result in persistent and often de novo overactivity.[27] Elevated pressures in the bladder secondary to bladder outlet obstruction can lead to detrusor ischemia and underactivity, and chronic obstruction results in bladder muscle hypertrophy, collagen deposition, and subsequent reduced capacity and compliance.[18,27] Given this bladder remodeling and the high prevalence of storage symptoms after TURP, one would predict AC/B3 would be commonly used to treat LUTS post-TURP; however, we found only 15% of patients were trialed on an AC/B3 after TURP. A recent randomized controlled trial found that postoperative tolterodine, when compared to placebo, alleviates storage symptoms and improves quality of life after TURP.[28] Primary care physicians and other specialists likely still have reservations about utilizing an AC/B3 medication in men with a history of BPH due to the risk of urinary retention. Although this is a commonly discussed side effect of these medications, multiple studies have demonstrated AC/B3 are safe to use in patients with BPH as long as there is no clinically meaningful elevated postvoid residual.[9,29] The rate of AC/B3 utilization after TURP increased over time, which does demonstrate an increasing comfort with these medications. Age ≥75 years, a preexisting diagnosis of diabetes mellitus, preoperative use of AC/B3, and no history of urinary retention predicted postoperative utilization of AC/B3 medications. These factors also predict abnormal detrusor function and therefore not surprisingly are associated with AC/B3 use after TURP.[30] Further studies to evaluate the efficacy of this post-TURP are warranted.

Strengths and Limitations

To our knowledge, this is the first population-based cohort study that explores the frequency of medical management for LUTS after TURP. Strengths of our analysis include the Ontario Drug Benefit database, which has high accuracy, and Ontario's universal healthcare system, which limits selection bias. We accounted for a washout period post-TURP and had a median 5-year follow-up period post-TURP to describe medication utilization. Limitations of our work include generalizability to those less than 66 years of age, who may have different utilization patterns post-TURP. We could not determine the exact indication for the prescription, however the study medications are relatively specific to urologic indications; other reasons to use medications, for example ABs for medical expulsive therapy for ureteral stones would not be expected to persist past 30 days in most cases. There are clinical variables (such as the preexisting degree of urinary urgency) which were not available, and which may have accounted for the usage of the AC/B3 medications. Our exploration of risk factors for use of AC/B3 was based on variables which were readily available in the administrative data; there are other relevant variables which are also likely to be significant predictors of AC/B3 usage post-TURP. We did not include nonselective ABs as we could not determine if they were started for LUTS or for another indication such as hypertension; therefore, an even greater percentage of men may have been treated with ABs for their post-TURP LUTS. Mirabegron was not available throughout the entire study period, and therefore the usage pattern of this medication post-TURP may be different from what was observed among men in this study who were predominately treated with anticholinergics. Finally, we could only capture filled prescriptions, not medication compliance; we attempted to address this limitation by defining our outcome as greater than 30 days of medication usage to try and capture patients who refilled their medication at least once. While patient compliance may have been lower than suggested by our results, these medications were still prescribed by a physician despite the limited evidence for AB and 5ARIs post-TURP.

CONCLUSION

LUTS are common after TURP; however, the medical management of these symptoms is not well studied. Despite a lack of evidence to support their use, our study demonstrated that after a median follow-up of almost 5 years, AB, 5ARI, and AC/B3 are prescribed after a TURP to 27%, 20%, and 15% of men, respectively.

Randomized trials are needed to justify the high rates of AB and 5ARI utilization post-TURP, particularly if these findings are also seen other medical systems.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.05.003.

References

1. Auffenberg GB, Helfand BT, McVary KT. Established medical therapy for benign prostatic hyperplasia. *Urol Clin N Am*. 2009;36:443–459. v-vi. https://doi.org/10.1016/j.ucl.2009.07.004.
2. Park HJ, Won JE, Sorsaburu S, et al. Urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) and LUTS/BPH with erectile dysfunction in Asian men: a systematic review focusing on Tadalafil. *World J Men's Health*. 2013;31:193–207. https://doi.org/10.5534/wjmh.2013.31.3.193. Accessed December 24, 2013.
3. Egan KB. The epidemiology of benign prostatic hyperplasia associated with lower urinary tract symptoms: prevalence and incident rates. *Urol Clin N Am*. 2016;43:289–297. https://doi.org/10.1016/j.ucl.2016.04.001.
4. Nickel JC, Méndez-Probst CE, Whelan TF, et al. 2010 Update: guidelines for the management of benign prostatic hyperplasia. *Can Urol Assoc J*. 2010;4:310–316.
5. McVary KT, Roehrborn CG, Avins AL, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol*. 2011;185:1793–1803. https://doi.org/10.1016/j.juro.2011.01.074. Accessed March 21, 2011.
6. Furuya S, Kumamoto Y, Yokoyama E, et al. Alpha-adrenergic activity and urethral pressure in prostatic zone in benign prostatic hypertrophy. *J Urol*. 1982;128:836–839.
7. Roehrborn CG, Siami P, Barkin J, et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. *Eur Urol*. 2010;57:123–131. https://doi.org/10.1016/j.eururo.2009.09.035. Accessed September 19, 2009.
8. McConnell JD, Roehrborn CG, Bautista OM, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med*. 2003;349:2387–2398. https://doi.org/10.1056/NEJMoa030656.
9. Roehrborn CG, Kaplan SA, Jones JS, et al. Tolterodine extended release with or without tamsulosin in men with lower urinary tract symptoms including overactive bladder symptoms: effects of prostate size. *Eur Urol*. 2009;55:472–479. https://doi.org/10.1016/j.eururo.2008.06.032. Accessed June 17, 2008.
10. Chughtai B, Simma-Chiang V, Kaplan SA. Evaluation and management of post-transurethral resection of the prostate lower urinary tract symptoms. *Curr Urol Rep*. 2014;15:434. https://doi.org/10.1007/s11934-014-0434-1.
11. Jha P, Deboer D, Sykora K, et al. Characteristics and mortality outcomes of thrombolysis trial participants and nonparticipants: a population-based comparison. *J Am Coll Cardiol*. 1996;27:1335–1342.
12. Levy AR, O'Brien BJ, Sellors C, et al. Coding accuracy of administrative drug claims in the Ontario Drug Benefit database. *Can J Clin Pharmacol*. 2003;10:67–71.
13. Williams J, Young W, et al. Appendix I: a summary of studies on the quality of health care administrative databases in Canada.. In: Goel V, Williams JI, Anderson GM, eds. *Patterns of Health Care in Ontario: the ICES Practice Atlas*. 2nd ed. Canadian Medical Association; 2000:339–347.
14. Gibson D, Richards H, Chapman A. The national ambulatory care reporting system: Factors that affect the quality of its emergency data. *Int J Inform Qual*. 2008;2:97–114.
15. Raina P, Torrance-Rynard V, Wong M, et al. Agreement between self-reported and routinely collected health-care utilization data among seniors. *Health Serv Res*. 2002;37:751–774.
16. Hux JE, Ivis F, Flintoft V, et al. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care*. 2002;25:512–516.
17. Welk B, McArthur E, Fraser LA, et al. The risk of fall and fracture with the initiation of a prostate-selective α antagonist: a population based cohort study. *BMJ*. 2015;351:h5398. https://doi.org/10.1136/bmj.h5398. Accessed October 26, 2015.
18. Kim SJ, Al Hussein Alawamlh O, Chughtai B, et al. Lower urinary tract symptoms following transurethral resection of prostate. *Curr Urol Rep*. 2018;19:85. https://doi.org/10.1007/s11934-018-0838-4. Accessed August 20, 2018.
19. Yamaguchi O. Latest treatment for lower urinary tract dysfunction: therapeutic agents and mechanism of action. *Int J Urol*. 2013;20:28–39. https://doi.org/10.1111/iju.12008. Accessed November 28, 2012.
20. Shin YS, Zhang LT, You JH, et al. Efficacy and safety of tamsulosin hydrochloride 0.2 mg and combination of tamsulosin hydrochloride 0.2 mg plus solifenacin succinate 5 mg after transurethral resection of the prostate: a prospective, randomized controlled trial. *Clin Interv Aging*. 2016;11:1301–1307. https://doi.org/10.2147/CIA.S115042. Accessed September 19, 2016.
21. Ergakov DV, Martov AG. Combination therapy in the management of urinary disorders after transurethral resection of the prostate. *Urologiia*. 2018:62–70.
22. McConnell JD, Bruskewitz R, Walsh P, et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. Finasteride Long-Term Efficacy and Safety Study Group. *N Engl J Med*. 1998;338:557–563. https://doi.org/10.1056/NEJM199802263380901.
23. Bansal A, Arora A. Transurethral resection of prostate and bleeding: a prospective, randomized, double-blind placebo-controlled trial to see the efficacy of short-term use of finasteride and dutasteride on operative blood loss and prostatic microvessel density. *J Endourol*. 2017;31:910–917. https://doi.org/10.1089/end.2016.0696-rev. Accessed June 26, 2017.
24. Ren J, Lai S, Jiang Z, et al. A systematic review and meta-analysis of the effects on dutasteride treatment for reducing surgical blood loss during transurethral resection of the prostate. *Urol Int*. 2017;98:456–465. https://doi.org/10.1159/000453669. Accessed December 23, 2016.
25. Qian X, Yu G, Qian Y, et al. Efficacy of 5α-reductase inhibitors for patients with large benign prostatic hyperplasia (>80 mL) after transurethral resection of the prostate. *Aging Male*. 2015;18:238–243. https://doi.org/10.3109/13685538.2015.1068750. Accessed July 30, 2015.
26. Rubin MA, Kantoff PW. Effect of finasteride on risk of prostate cancer: how little we really know. *J Cell Biochem*. 2004;91:478–482. https://doi.org/10.1002/jcb.10787.
27. Mirone V, Imbimbo C, Longo N, et al. The detrusor muscle: an innocent victim of bladder outlet obstruction. *Eur Urol*. 2007;51:57–66. https://doi.org/10.1016/j.eururo.2006.07.050. Accessed August 14, 2006.
28. Tehranchi A, Rezaei Y, Shojaee R. Tolterodine to relieve urinary symptoms following transurethral resection of the prostate: a double-blind placebo-controlled randomized clinical trial. *Korean J Urol*. 2014;55:260–264. https://doi.org/10.4111/kju.2014.55.4.260. Accessed April 10, 2014.
29. Kim HJ, Sun HY, Choi H, et al. Efficacy and safety of initial combination treatment of an alpha blocker with an anticholinergic medication in benign prostatic hyperplasia patients with lower urinary tract symptoms: updated meta-analysis. *PLoS One*. 2017;12: e0169248. https://doi.org/10.1371/journal.pone.0169248. Accessed January 10, 2017.
30. Luo F, Sun HH, Su YH, et al. Assessment of noninvasive predictors of bladder detrusor underactivity in BPH/LUTs patients. *Int Urol Nephrol*. 2017;49:787–792. https://doi.org/10.1007/s11255-017-1539-5. Accessed February 15, 2017.