Opioid prescribing patterns following surgical interventions for benign prostatic hyperplasia

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Cite as: Gressler LE, Sze C, Punyala A, et al. Opioid prescribing patterns following surgical interventions for benign prostatic hyperplasia. *Can Urol Assoc J* 2025 January 14; Epub ahead of print. http://dx.doi.org/10.5489/cuaj.8958

Published online January 14, 2025

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ABSTRACT

Introduction: This study aimed to analyze opioid prescribing behavior following surgical interventions for benign prostatic hyperplasia (BPH), focusing on differences in postoperative opioid prescribing practices between patients who undergo surgical procedures in operative room (OR) settings vs. non-operative room (non-OR) settings.

Methods: A retrospective cohort study was conducted using a 10% random sample of the IQVIA PharMetrics® Plus for Academics database, including men who

KEY MESSAGES

- Patients undergoing BPH surgeries in OR settings are more likely to receive opioid prescriptions postoperatively compared to those in non-OR settings.
- Despite higher prescription rates in OR settings, cumulative days and morphine equivalent daily dose of opioid use do not significantly differ between OR and non-OR groups.
- The findings suggest potential overprescription of opioids for minimally invasive procedures, highlighting the need for improved pain management strategies.

underwent surgical interventions for BPH from 2015–2020. Propensity score analysis and inverse probability treatment weighting were employed to adjust for potential confounders. Primary outcomes included opioid receipt, cumulative days of opioid use, and morphine equivalent daily dose (MEDD).
Results: Among the included men (n=6022), those undergoing procedures in OR settings were more likely to receive opioid prescriptions postoperatively compared to those in non-OR settings (42.78% vs. 28.00%, p<0.001). While cumulative days and MEDD of opioid prescriptions did not significantly differ between groups, there was a statistically significant difference in the distribution of opioid receipt duration (p=0.0128). The adjusted model showed significantly higher odds of opioid prescription for men undergoing OR procedures (odds ratio 1.922, 95% confidence interval 1.690–2.185).
Conclusions: Men undergoing BPH surgeries in OR settings were more likely to receive opioid prescriptions postoperatively, suggesting potential overprescription. Despite similar cumulative opioid use, differences in prescription rates indicate a need for improved postoperative pain management strategies, possibly using non-opioid alternatives. Future research should focus on optimizing pain control, characterizing actual opioid consumption, and considering patient-specific factors in surgical decision-making.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a chronic condition that afflicts more than 50% of the aging male population.[1] Patients diagnosed with BPH experience a variety of symptoms that contribute to a decreased quality of life, including urinary hesitancy, urge incontinence, nocturia, and increased rates of anxiety and/or depression.[2] Treatment options for BPH range from lifestyle modifications to pharmacologic and surgical interventions depending on the severity of symptoms and their impacts on the patient's quality of life.

Surgical procedures widely vary in their post-operative pain profiles, and opioids are the current mainstay for management of pain post-surgery.[3] While post-operative pain is expected to subside within a few weeks for most patients, this post-surgery period nonetheless represents a time where patients are susceptible to excessive opioid exposure.[4] Furthermore, opioid prescribing recommendations for chronic pain have been non-specific, and there is thus great variation in treatment of post-surgical pain, even between patients under the same institution or surgeon.[5] Therefore, postoperative opioid use is a growing concern for urologists concerned with patients' quality of life. Given the range of serious adverse events associated with prolonged opioid use such as drug dependence, overdose, and death, careful monitoring of opioid administration is vital to ensuring positive patient outcomes post-surgery.[6]

Despite this need, however, there is a lack of real-world data pertaining to opioid prescribing behavior following surgical interventions for BPH. We sought to address this by analyzing enrollees in the IQVIA PharMetrics® Plus for Academics database for the incidence of opioid prescription, the duration of opioid administration, and the morphine equivalent daily dose (MEDD) following various surgical options for BPH, with the aim of characterizing and improving post-operative opioid prescribing practices and the selection of appropriate surgical procedure.

METHODS

Study design

A retrospective cohort was derived from a 10% random sample of enrollees within the IQVIA PharMetrics® Plus for Academics database from 2015 to 2020. The final cohort was comprised of men who received a surgical intervention for BPH and who were continuously enrolled for the180 days following the BPH intervention.

Data source

IQVIA PharMetrics® Plus for Academics is a health plan claims database comprised of fully adjudicated medical and pharmacy claims for more than 117 million unique enrollees since 2006. Data contributors to the database are largely commercial health plans. It is representative of the commercially insured US national population. It contains a longitudinal view of inpatient and outpatient services, prescription and office/outpatient administered drugs, costs, and detailed enrollment information. Medical claims include information on diagnoses using the International Classification of Diseases, Tenth Revision Clinical Modification codes (ICD-10-CM) and performed clinical procedures identified using Current Procedural Terminology, fourth revision (CPT®-4) and ICD-10 Procedure Coding System (ICD-10-PCS) codes. Pharmacy claims encompass prescription medications dispensed in an outpatient pharmacy and are recorded using National Drug Codes (NDC). The pharmacy claims also provide details regarding the date of medication dispensed, quantity dispensed, and the days' supply provided.

Study cohort

Men over the age of 18 who underwent surgical intervention for BPH treatment from October 1st, 2015, to September 30th, 2020, were included in the cohort. Patients included in the cohort were enrolled and followed in the database for at minimum 180 consecutive days following the receipt of a BPH procedure to ensure that outcomes could be continuously and equivalently tracked across the cohort.

Exposure

Individuals were classified as exposed and unexposed depending on whether the BPH procedure received is generally performed in an operative room (OR) setting. Exposed individuals received a BPH procedure in an OR setting. These procedures included include transurethral resection of the prostate (TURP), aquablation, laser surgery, and transurethral incision of the prostate (TUIP). Unexposed individuals received a BPH procedure in non-operative room (non-OR) setting.

These procedures included Rezum water vapor therapy, prostatic urethral lift (Urolift), transurethral microwave thermotherapy (TUMT), and transurethral needle ablation (TUNA). The index date was considered to be the date of the surgical intervention.

Covariates
Patient-level baseline characteristics were collected in the year preceding the index date. Demographic characteristics included age and US census region. Medical conditions that are highly prevalent and/or associated with the receipt of a BPH procedure and/or opioid use were identified. More specifically, this included pain-related conditions, urologic conditions, mental health conditions, substance use disorders, and other highly common comorbidities. Medication-specific covariates related to the treatment of BPH, its symptoms, or opioid use were identified and included prior alpha-1 blocker, psychotropic, and opioid use.

Outcomes
The primary outcomes of interest were the receipt of an opioid (binary outcome), cumulative days of opioids received (continuous outcome), and morphine equivalent daily doses (MEDD; continuous outcome).[7] These were examined from 14-180 days following the index date to mitigate the potential misclassification of post-surgical acute pain.[8]

Statistical analysis
Descriptive and bivariate analyses, including chi-squared tests for categorical variables and t-tests for continuous variables, were used to compare patient characteristics across the OR and non-OR study group. Primary outcomes and overall incidence were calculated for both study groups.

Propensity score analysis using a multivariable logistical regression model was used to account for any identified imbalances between the OR and non-OR group. The selection of potential covariates for inclusion in the propensity score model was based on empirical observations using bivariate chi-squared analyses. Variables with observed significant associations with the outcome alone or the outcome and exposure simultaneously were identified. Covariates with a p-value ≤ 0.2 in bivariate analysis were considered for inclusion in the model. Inverse Probability Treatment Weighting (IPTW) was utilized to determine the average effect across the entire population.[9] Individuals in non-overlapping areas of the propensity score distributions were excluded from the analysis. The remaining individuals were then assigned a weight. The weight for each individual was calculated as the inverse of the probability of receiving the OR procedure. Stabilized IPTWs were calculated using the mean propensity score divided by (1 - individual propensity score). After applying the weighting, standardized mean differences (SMD) were calculated for all covariates to address confounding imbalances. Covariates with an absolute SMD > 0.2 were considered indicative of residual confounding and imbalance.

Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CI) of receiving an opioid for both unadjusted and IPTW-adjusted models. A generalized linear regression was used to estimate the association between cumulative days prescribed and "exposed" surgical procedures (OR procedures). All analyses were performed on SAS 9.4 with a significance level of 5%. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[10] The study was determined to be exempt by the local Institutional Review Board.

Sensitivity analysis

Propensity score methods operate under the assumption that there is no unmeasured confounding.[11] To assess the robustness of the results regarding this assumption, sensitivity analyses quantifying the minimum strength of association required between the unmeasured confounders and the exposure and the outcome that would be necessary to invalidate the observed risk estimate were calculated.

RESULTS

Sample characteristics

A total of 7,445 (0.17%) of the 4,338,117 men enrolled within the 10% random sample of IQVIA PharMetrics® Plus for Academics had a claim for surgical intervention for BPH from 2015-2020. Applying the exclusion criteria, 6,022 (80.9%) of the 7,445 men remained (Appendix Figure 1). Of the included men, most (n = 4549; 75.5%) underwent procedures in the OR (exposed group), while 1473 (24.5%) patients received procedures in a non-OR setting (unexposed group). Baseline characteristics prior to and after IPTW weighting are included in Appendix Table 1. The distribution of propensity scores prior to and following the removal of non-overlapping regions of the propensity scores are shown in Appendix Figure 1 and Appendix Figure 2. The SMD of the IPTW weighting demonstrated good balance, with absolute SMD < 0.2 across all covariates (Appendix Table 2).

Opioid prescribing following surgery for BPH

Following the procedures in the IPTW-restricted population, 42.78% men in the exposed OR setting group received an opioid compared to 28.00% of men in the unexposed non-OR setting group ($p < 0.001$; Table 1). Long-term opioid use, defined as use for more than 90 days, was observed in 18.19% of men in the non-OR group and 12.24% in the OR group. Mean cumulative days of opioids prescribed was lower in the exposed OR setting group compared to the unexposed non-OR setting group, but this difference was not statistically significant (72.63 days vs. 112.25 days, $p = 0.0523$). Similarly, MEDD (43.64 vs. 35.06, $p = 0.5985$) and average number of opioid prescriptions (43.64 vs. 6.24, $p = 0.6833$) were higher in the exposed OR setting group, yet not statistically significant. When stratifying by number of days of opioids received into four groups, a statistically significant difference in distribution was observed ($p = 0.0128$). Results of the unadjusted and adjusted multivariate analyses are detailed in Table 1. In

the IPTW-adjusted model, men undergoing a BPH procedure requiring an OR (exposed) had significantly higher odds of receiving an opioid prescription compared to men in the unexposed non-OR setting group (OR 1.922; 95%CI: 1.690-2.185). The generalized linear regression model did not find that mean cumulative days of opioids prescribed or MEDD were statistically significantly different between groups in either the unadjusted or IPTW-adjusted models.
The bias analysis (Appendix Table 3) indicates that an unmeasured confounder with an odds ratio of 4.0 or higher with the exposure or 2.0 or higher with the outcome, which is not already considered in the model, would be required to nullify the findings of the adjusted analysis. It is highly improbable to have an unmeasured confounder of such magnitude that is not already accounted for among the measured covariates.

DISCUSSION

The findings indicate that men who received a surgical intervention for BPH in OR settings were more likely to receive prescriptions for opioids post-operatively compared to those in non-OR settings. Despite the non-OR procedures being generally minimally invasive and well-tolerated, the cumulative days and MEDD of opioid prescriptions did not differ significantly between the groups. This difference in the number of prescriptions was unlikely to be explained by any unidentified confounders, per our bias analysis. This suggests potential over-prescription of opioids, particularly for minimally invasive therapies performed outpatient or in-office, where non-opioid alternatives could likely be used instead. Another notable finding is that over 40% of men received an opioid prior to their BPH procedure. This may be due to factors such as chronic pain conditions, BPH-related discomfort, pre-existing comorbidities, limited access to non-opioid alternatives, preoperative pain management protocols, or provider-specific prescribing habits.

The postoperative period is crucial as patients are susceptible to complications and often overexposed to opioid pain control. Patients tend to use fewer opioid pills than prescribed, with one study reporting that patients receiving radical prostatectomy did not use 77% of prescribed opioids.[12] Moreover, patients often escalate their consumption to match the prescribed amount, with each additional pill prescribed leading to 0.5 pill higher consumption.[13] Postoperative pain management strategies vary widely, increasing opioid exposure, with even greater variability in teaching hospitals compared to non-teaching hospitals.[14] An estimated 6-6.2% of opioid-naïve patients report persistent opioid use following urologic surgery, with no significant difference between minor and major procedures, indicating significant patient-level predictors . Reducing initial opioid exposure not only decreases misuse but also prevents diversion and substance abuse.

Evidence supports that minimizing prescribed opioid doses can maintain patient satisfaction and avoid additional appointments. A multicenter study evaluating ketorolac versus oxycodone for outpatient urologic procedures found similar improvements in pain scores, despite higher pill consumption in the oxycodone group. Patients in the oxycodone group were also more likely to retain medication surpluses (61.3% vs. 38.7%).[18] Studies show that using nonsteroidal anti-inflammatory drugs (NSAIDs) and other non-opioid medications for pain control is associated with a lower risk of persistent opioid use, with patients using an average of 4-10 opioid pills post-procedure.[19–22]

A prospective randomized controlled trial by Donahue et al. followed 47 patients undergoing TURP, comparing standard care (SOC) with a multimodal experimental group (MMG) that included adding ibuprofen, teaching about opioid use, and discharging without opioids.[23] The MMG group had non-inferior pain control and used significantly fewer MEDDs after discharge (0 vs. 4.1), with comparable satisfaction and adverse event profiles. These findings suggest that multimodal protocols favoring NSAIDs for TURPs could reduce adverse events without impacting pain control.

Other strategies that have been tested to reduce opioid prescribing. Preoperative education about expected levels of postoperative pain, opioid side effects, and non-opioid options led to lower and shorter-lasting pain scores, a high (90%) rate of declining an opioid prescription, and earlier opioid cessation if used.[24,25] Intraoperative and inpatient pain control such as dorsal penile nerve block and transversus abdominis plane (TAP) block is also associated with lower need for medication postoperatively following radical cystectomy and robotic surgery.[26,27] Electronic prescribing requirements for opioids have been shown to reduce institution-wide prescribing by over half, and reducing default prescription quantities on EMR systems has yielded similar results.[28]

This study has limitations. First, TUNA is no longer supported by the American Urological Association for BPH treatment. While TUNA data in the non-OR group are no longer applicable to best clinical practice, they provide insight into outpatient prescribing patterns and pain control strategies. Second, claims data typically do not capture individual drugs administered in inpatient settings, particularly during perioperative periods and readmissions. Only dispensed prescriptions are tracked, and actual patient consumption may vary, with studies noting behaviors with retained, returned, or wasted pills. The classification of individuals as exposed or unexposed was based on whether the BPH procedure is typically performed in an OR setting, as the dataset did not provide explicit information on the actual procedure location. Pre-existing opioid prescriptions or persistent use was stratified as a cofactor within the IPTW model, but this binary variable cannot account for dose or pattern of preoperative use, leading to varied opioid use, pain control requests, and pain scores among patients. A more granular assessment by specific procedure was not possible due to sample size limitations. Lastly, patient characteristics and relevant medical data are limited to enrolled months, potentially omitting covariates crucial to this study, such as prior surgical intervention, prostate volume, anatomical variation, symptom history, surgeon and facility experience, anesthesia requirements, and prior pain history. These factors, which affect clinical decision-making, might introduce selection bias when assigning patients to OR versus non-OR procedures. However, our bias analysis suggested that unmeasured confounders were unlikely to explain our findings.

A complementary study could follow differences in patient behaviors and actual opioid consumption across the same groups (OR vs. non-OR setting), with patients recording daily pill consumption and reporting unused pills. The current study's data generalizes to commercially insured men; however, Original Medicare claims data would help generalize findings to a larger population. Elderly men, who are common recipients of BPH surgery, may be covered by Medicare and might receive different surgical options and pain management. Extending the dataset to include Medicare claims data is relevant and could potentially reveal important differences.

CONCLUSIONS

Urologists can increasingly offer minimally invasive BPH procedures in-office and/or without general anesthesia. While men receiving procedures outside of the OR are less likely to be prescribed opioids, similar dosages or cumulative prescription durations suggest possible overprescription; this effect could not be accounted for with covariates. Future studies are needed to determine optimal pain control, characterize actual opioid consumption, and account for potential confounders such as anatomical variation or prior surgical outcomes in this population.

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FIGURES AND TABLES

Table 1. Description and weighted frequency of demographics and outcomes in the IPTW restricted population and beta coefficients and odds ratio of opioid use and cumulative opioid prescribing in the OR group compared to the non-OR group within 14–180 days after the procedure

	Non-OR procedure	**OR procedure**	**p**
Total sample, n	1463	4473	
Age, n (%)			0.9973
18–45	14 (0.97%)	42 (0.94%)	
46–55	91 (6.25%)	269 (6.02%)	
56–65	424 (28.98%)	1298 (29.01%)	
>65	933 (63.79%)	2864.5 (64.04%)	
Individuals with any opioid prescription, %	28.00	42.78	<0.001
Cumulative days of opioids prescribed mean (SD)	112.25 (490.33)	72.63 (338.72)	0.0523
Duration of prescription categories, %			0.0128
1 and 30 days	73.46	79.74	
31 and 60 days	5.14	4.75	
61 and 90 days	3.20	3.26	
>90 days (long-term use)	18.19	12.24	
Morphine equivalent daily dose, mean, median (SD)	35.06, 30.00, (26.66)	43.64, 30.00, (322.68)	0.5985
Number of opioid prescriptions, mean (SD)	6.24 (17.48)	6.71 (21.64)	0.6833

	Estimate	**Standard error**	**p**	**OR**	**95% CI**
Any opioid prescription					
Unadjusted	0.7267	0.0662	<0.0001	2.068	1.816–2.355
IPTW-adjusted	0.6532	0.0656	<0.0001	1.922	1.690–2.185
Cumulative days of opioids prescribed					
Unadjusted	-39.62	20.41	0.0523		
IPTW-adjusted	-31.99	20.05	0.1107		
Morphine equivalent dose					
Unadjusted	8.58	16.29	0.5985		
IPTW-adjusted	9.00	15.96	0.5726		

CI: confidence interval; IPTW: inverse probability treatment weighting OR: odds ratio; SD: standard deviation.