Research Square

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Sodium-Glucose Cotransporter-2 Inhibitors and Urinary Outcomes After Holmium Laser Enucleation of Prostate: An Exploratory Retrospective Cohort Analysis

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Abstract

Purpose:

The use of sodium-glucose cotransporter-2 inhibitors (SGLT-2is) has been associated with lower urinary tract symptoms (LUTS), but their effect on urinary outcomes after Holmium Laser Enucleation of the Prostate (HoLEP) is unknown. We explored associations between SGLT-2i use and preoperative positive urine culture, postoperative urinary tract infection (UTI), and International Prostate Symptom Score (IPSS) improvement.

Methods:

We performed a retrospective cohort study comparing SGLT-2i users and non-users from our IRB-approved single-surgeon HoLEP database. Outcomes included preoperative positive urine culture, 30-day postoperative UTI, and longitudinal IPSS change. IPSS was analyzed using linear mixed-effects models; urine culture and UTI outcomes were assessed using univariate analyses. Sensitivity analyses included propensity score matching and exclusion of postoperative UTI cases.

Results:

Of 855 patients, 50 (5.8%) used SGLT-2is. Preoperative positive urine cultures occurred in 25% of users and 29% of controls (OR 0.82, 95% CI 0.33 to 1.84). Postoperative UTI occurred in 4 SGLT-2i users (8.0%) and 24 controls (3.0%) (OR 2.82, 95% CI 0.68 to 8.72; $p = .07$). The overall cohort demonstrated significant improvement in IPSS post-HoLEP ($p < .001$). However, there was no significant difference in longitudinal IPSS improvement between SGLT-2i users and controls at 2 weeks ($p = .2$) or 3 months ($p = .9$).

Conclusion:

We did not detect statistically significant differences in UTI, IPSS recovery, or preoperative positive urine cultures between SGLT-2i users and controls. However, we provide preliminary hypothesis-generating data that warrant further definitive investigation of urinary outcomes in SGLT-2i users undergoing HoLEP.

Introduction

Sodium-glucose cotransporter-2 inhibitors (SGLT-2is) are an increasingly used treatment for type 2 diabetes mellitus (T2DM), heart failure, and chronic kidney disease [1]. The medication primarily acts to prevent glucose reabsorption in the kidney and promote glycosuria [2]. Genitourinary effects of the medication may include lower urinary tract symptoms (LUTS) [3], genital mycotic infections [4], and reduced risk of nephrolithiasis [1]. Recent findings are mixed regarding the risk of urinary tract infection

(UTI) with SGLT-2i use [4, 5], and the effect of SGLT-2i use on UTI risk after urologic surgery remains unclear [6–9].

Holmium laser enucleation of the prostate (HoLEP) has been well characterized to be a safe and effective minimally invasive surgical treatment for benign prostatic hyperplasia (BPH) [10]. Compared to transurethral resection of the prostate, HoLEP offers superior postoperative outcomes including maximum urinary flow rate, post-void residual volume, and qualitative symptom improvement, as well as significantly lower risk of adverse outcomes [11, 12]. HoLEP also offers durable symptom relief independent of prostate size with shorter catheter duration, bladder irrigation time, and hospital stay [13, 14].

Although SGLT-2is have several influences on the genitourinary system, their potential impact on perioperative symptoms after HoLEP has not yet been studied. Like other transurethral procedures, HoLEP may disturb the urethral mucosa and predispose patients to storage symptoms and bacterial infection [8]. We thus hypothesized that the use of SGLT-2is would be associated with increased preoperative positive urine cultures, postoperative UTI and less IPSS improvement post-HoLEP. The objective of our study was to explore the impact of SGLT-2is on these variables and inform future studies.

Methods

Patient Selection

Our institution prospectively maintains a single-surgeon HoLEP database approved by the Institutional Review Board (2111918). We examined a total of 855 patients who underwent HoLEP from July 2020 to May 2026. Patients taking SGLT-2is at the time of surgery were identified (n = 50). Patients dependent on a Foley catheter preoperatively were excluded from the unmatched analysis of preoperative urine cultures due to the high likelihood of microbial colonization (n = 204). An additional 7 patients with missing preoperative urine culture data were excluded, yielding an analytic cohort of 644 patients. In a sensitivity analysis of preoperative urine cultures, patients dependent on clean intermittent catheterization (CIC) were excluded in addition to those dependent on a Foley catheter (n = 186 excluded; 29 SGLT-2i users and 429 controls analyzed after excluding missing data).

Surgical Procedure and Follow-up

Preoperatively, all patients were assessed with a clinical history, physical exam, and IPSS. Age, weight, height, diabetes mellitus, and American Society of Anesthesiologists (ASA) classification were recorded at the time of surgery. If a patient was unable to void spontaneously, their dependence on a Foley catheter or CIC was documented. Prostate size was estimated with transrectal ultrasound, CT, or MRI. All patients were required to provide a clean catch urine sample for urine culture. If urine cultures were positive, appropriate preoperative antibiotics were administered. Per recommendations from the U.S.

Food and Drug Administration and European Society of Anesthesiology and Intensive Care, SGLT-2is were held 3 days prior to surgery and resumed upon return to normal diet [15, 16].

Our surgical technique has been previously described, however most patients undergo en-bloc enucleation with early apical release using a pulse modulated laser and 26 French scope [17]. Patients were observed at follow-up appointments 2 weeks and 3 months postoperatively. At these visits IPSS and Michigan Incontinence Symptom Index (MISI) scores were assessed. Postoperative complications were recorded via the Clavien-Dindo Grading System up to 30 days postoperatively, including UTI. A UTI was recorded if a patient reported UTI symptoms and had a supporting positive urine culture. UTIs diagnosed outside our institution were captured if the patient reported having a postoperative UTI at follow-up and supporting culture documentation was received electronically.

Outcomes and Study Variables

Outcomes were preoperative positive urine culture, 30-day postoperative UTI, and IPSS (absolute and change from baseline). MISI and IPSS voiding and storage subscores were exploratory outcomes because of limited data. The primary study variable was SGLT-2i use.

Statistical Methods

Continuous variables were compared with t-tests or Mann-Whitney U tests and categorical variables with Chi-square or Fisher's exact tests, as appropriate. Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated for binary outcomes. Because SGLT-2i users more frequently had diabetes, we also reported diabetes-only subgroup analysis for preoperative positive culture and UTI.

Longitudinal IPSS was analyzed with a linear mixed-effects model (Python statsmodels, version 0.14.5) to account for correlation in repeated measurements over time for each patient. The model included SGLT-2i use, time of measurement (preoperative, 2 weeks postoperative, and 3 months postoperative), and the interaction between SGLT-2i use and time. The reference categories were no SGLT-2i use and preoperative IPSS. The interaction terms estimate the between-group difference in IPSS change from baseline at each time point. Because IPSS is unreliable in patients with a Foley catheter, preoperative IPSS was excluded for these patients (n = 13 SGLT-2i users and n = 191 controls; 4 and 55 preoperative IPSS values removed, respectively) in both the observed comparisons and the mixed model. Their 2-week and 3-month IPSS values were retained. Missing data were not imputed. Univariate comparisons used all available data (complete-case analysis); the mixed model used all available IPSS observations and is valid if data are missing at random given the model covariates.

Sensitivity analyses excluded patients with postoperative UTI (n = 28) and used 2:1 nearest-neighbor propensity score matching (PSM; caliper 0.2 standard deviations of the logit of the propensity score) on age, body mass index (BMI), ASA class, preoperative Foley status, prostate size, and diabetes. Balance was assessed with standardized mean differences (SMD; < 0.1 indicating balance). To characterize

precision, we calculated the minimum between-group difference in IPSS change detectable with 80% power (two-sided α = 0.05) using the standard error of each SGLT-2i-by-time interaction term. This analysis demonstrated the study had approximately 80% power to detect a minimum between-group difference of 4.4 IPSS points at 2 weeks and 4.9 IPSS points at 3 months post-HoLEP. No adjustment was made for multiple comparisons given the exploratory design; p-values and CIs should be interpreted as descriptive. Significance was set at $p < .05$. Analyses used Python (version 3.11, SciPy 1.17, NumPy 1.26) and R (version 4.5.3). GPT-6 and Claude Opus 5.5 assisted with developing statistical analysis code in Python and R. The authors reviewed, validated, and take full responsibility for the code and the resulting analyses.

Results

Cohort characteristics

Of 855 patients, 50 (5.8%) were taking an SGLT-2i. SGLT-2i patients more often had diabetes (90% vs. 22%, $p < .001$), higher BMI (30.1 vs. 28.4, $p = .03$), and higher ASA class ($p < .001$). Age, prostate size, preoperative Foley and CIC dependence, insulin dependence, preoperative IPSS, and use of alpha-antagonists, finasteride, anticholinergics, or beta-3 agonists did not differ significantly (Tables 1 and 2).

Table 1
Baseline patient characteristics by cohort.

	Baseline Cohort Characteristics		
	SGLT-2i (n = 50)	**No SGLT-2i (n = 805)**	***p*-value**
Mean age (± SD)	70.8 (± 8.1)	70.3 (± 8.0)	.7
Mean BMI (± SD)	30.1 (± 5.0)	28.4 (± 5.3)	.03
ASA 1, n (%)	0 (0%)	5 (0.6%)	< .001
ASA 2, n (%)	10 (20%)	379 (47%)	
ASA 3, n (%)	37 (74%)	410 (51%)	
ASA 4, n (%)	3 (6.0%)	11 (1.4%)	
Median prostate size, mL (Q1 – Q3)	65.5 (38.5–111)	71 (43–108)	.8
Diabetes mellitus, n (%)	45 (90%)	174 (22%)	< .001
Preoperative Foley dependence, n (%)	13 (26%)	191 (24%)	.8
Preoperative CIC dependence, n (%)	7 (14%)	186 (23%)	.2
Alpha-antagonist use, n (%)	41 (82%)	595 (74%)	.3
Finasteride use, n (%)	11 (22%)	198 (25%)	.8
Anticholinergic use, n (%)	6 (12%)	55 (6.8%)	.2
Beta-3 agonist use, n (%)	2 (4.0%)	28 (3.5%)	.7
Insulin dependence, n (%)	0 (0%)	4 (0.5%)	> .9

t-tests: age, BMI. Mann-Whitney U: prostate size. Fisher's exact: ASA, use of anticholinergics, beta-3 agonists, insulin. Chi-square: diabetes, Foley dependence, CIC dependence, use of finasteride, alpha-antagonists.

Table 2
Observed IPSS and mixed-effects estimates of the difference in IPSS change after HoLEP

	Longitudinal IPSS Outcomes Before and After HoLEP						
	Observed IPSS			Mixed-Effects Model			
Time Point	**SGLT-2i**	**No SGLT-2i**	***p*-value**	**SGLT-2i Mean ΔIPSS**	**No SGLT-2i Mean ΔIPSS**	**Estimated difference in ΔIPSS (β) compared to controls (95% CI)**	***p*-value**
Pre-Op (Mean ± SD)	20.5 (± 8.8) (n = 31)	21.2 (± 7.9) (n = 425)	.7	-	-	-	-
2 weeks Post-Op (Mean ± SD)	12.5 (± 7.5) (n = 40)	11.3 (± 7.8) (n = 448)	.4	-7.7	-9.6	+ 1.9 (-1.2, 5.0)	.2
3 months Post-Op (Median (Q1 – Q3))	4.5 (2.0–9.2) (n = 28)	6.0 (3.0–11.0) (n = 422)	.3	-13.6	-13.4	−0.2 (− 3.6, 3.2)	.9

Observed IPSS: mean ± SD (t-test) for preoperative and 2 weeks; median (Q1 – Q3) (Mann-Whitney U) for 3 months. Model: linear mixed-effects, SGLT-2i × time interaction, reference = no SGLT-2i and preoperative IPSS. A positive difference indicates smaller improvement in SGLT-2i users. Preoperative IPSS was excluded for patients with preoperative Foley dependence in both the observed comparison and the model.

Preoperative positive urine cultures

After excluding patients with preoperative Foley catheter dependence or missing preoperative urine culture data, 644 patients were analyzed (608 controls, 36 SGLT-2i users) (Fig. 1). Positive preoperative urine cultures occurred in 9 SGLT-2i users (25%) compared to 176 controls (29%) (OR 0.82, 95% CI 0.33 to 1.84; p = .7; Table 3). Results were consistent in the diabetes-only subgroup (OR 0.50, 95% CI 0.18 to 1.27; p = .2; Table 3). In the sensitivity analysis that also excluded CIC-dependent patients, 458 patients were analyzed (29 users, 429 controls); positive cultures occurred in 4 (13.8%) users and 75 (17.5%) controls (OR 0.76, 95% CI 0.19 to 2.28; p = .8; Table 3), consistent with the primary analysis.

Figure 1. Flow diagram of patient selection into analytic cohorts. Created with Canva.

Table 3
Preoperative positive urine culture and 30-day postoperative UTI by SGLT-2i use.

	Perioperative Outcomes According to SGLT-2i Use			
	SGLT-2i	**No SGLT-2i**	**Odds Ratio (95% CI)**	***p*-value**
Pre-Op Positive Urine Culture	9/36 (25%)	176/608 (29%)	0.82 (0.33, 1.84)	.7
Sensitivity: Pre-Op Positive Urine Culture, excluding CIC-dependent patients	4/29 (13.8%)	75/429 (17.5%)	0.76 (0.19, 2.28)	.8
Post-Op UTI	4/50 (8.0%)	24/805 (3.0%)	2.82 (0.68, 8.72)	.07
Diabetes-Only Subgroup: Pre-Op Positive Urine Culture	8/33 (24.2%)	49/126 (38.9%)	0.50 (0.18, 1.27)	.2
Diabetes-Only Subgroup: Post-Op UTI	4/45 (8.9%)	7/174 (4.0%)	2.32 (0.47, 9.63)	.2

Preoperative positive urine culture analysis: Chi-square; UTI: Fisher's exact. Subgroup analysis was restricted to patients with diabetes. Denominators reflect data availability. The sensitivity analysis excluded patients dependent on a Foley catheter or on CIC.

Postoperative UTI

Postoperative UTI within 30 days occurred in 4 of 50 users (8.0%) and 24 of 805 controls (3.0%) (OR 2.82, 95% CI 0.68 to 8.72; $p = .07$; Table 3). Results were consistent in the diabetes-only subgroup (OR 2.32, 95% CI 0.47 to 9.63; $p = .2$; Table 3).

Postoperative IPSS

IPSS was available for 31 (62%), 40 (80%), and 28 (56%) SGLT-2i users and 425 (53%), 448 (56%), and 422 (52%) controls at the preoperative (excluding Foley-dependent patients), 2-week postoperative, and 3-month postoperative visits, respectively. Observed IPSS did not differ between groups at any time point (Table 2). IPSS improved significantly in the overall cohort at 2 weeks and 3 months ($p < .001$). In the mixed model, the difference in IPSS improvement (positive values indicate less improvement among users) was + 1.9 points at 2 weeks (95% CI − 1.2 to 5.0; $p = .2$) and − 0.2 points at 3 months (95% CI − 3.6 to 3.2; $p = .9$) (Table 2).

Sensitivity and Exploratory Analyses

Excluding the 28 patients with postoperative UTI (4 users, 24 controls) did not change results (Online Resource 1). After matching (49 users, 98 controls), most covariates were balanced (SMD < 0.1); residual imbalance remained for BMI (SMD − 0.13) and preoperative Foley dependence (SMD 0.12). One user had

no control within the caliper and was excluded. Matched results were concordant (Online Resource 1). Exploratory analyses of MISI, which had limited data, and IPSS voiding and storage subscores showed no significant differences (Online Resources 2 and 3) [18].

Discussion

SGLT-2is have been increasingly utilized in recent years due to their established benefits for glycemic control, reduction in adverse cardiac events for patients with heart failure, and slowed progression of chronic kidney disease [19, 20]. While these medications play a role in the genitourinary system and are known to increase LUTS [1–3], their effects on perioperative symptoms after urologic surgery have not been well characterized. Our group was interested in evaluating whether SGLT-2i use was associated with higher rates of preoperative positive urine cultures, postoperative UTI, and bothersome urinary symptoms, all of which are a source of morbidity in the perioperative period for HoLEP. The aim of this study was to perform an exploratory analysis on our retrospective cohort to better inform future studies evaluating the perioperative urologic morbidity of SGLT-2i use surrounding HoLEP. Understanding this impact may help inform perioperative management and patient counseling.

In our cohort, there was no significant association between SGLT-2i use and preoperative positive urine cultures, a finding consistent with the diabetes-only subgroup analysis and CIC-excluded analysis. This is consistent with current literature showing no significant association between SGLT-2i use and asymptomatic bacteriuria [21, 22]. There is currently no clearly defined mechanism for why glycosuria may not directly translate into asymptomatic bacteriuria and UTI. One proposed mechanism is that osmotic diuresis may counterbalance the impact of increased urinary glucose concentration through increased urinary flow, although this mechanism has not been validated [23].

We also found no statistically significant association between SGLT-2i use and postoperative UTI rates. While the SGLT-2i group had a numerically higher postoperative UTI rate (8.0% vs 3.0%), this difference did not achieve statistical significance due to a limited number of UTI events. With four events among users, the CI is compatible with both a reduction and a substantial increase in risk, so a clinically meaningful difference cannot be excluded. Users also more frequently had diabetes and higher ASA class, which independently affect infection risk. However, results were consistent in the diabetes-only subgroup analysis, with no statistically significant difference found between users and controls (8.9% vs. 4.0%). There is no clear consensus on the risk of UTI with SGLT-2i use, with conflicting evidence from recent studies [5, 9]. Evidence on SGLT-2is and UTI after urologic surgery is limited and mixed, and no studies exist for HoLEP [22, 24]. Our exploratory analysis thus provides hypothesis-generating data which warrant further evaluation with prospective and randomized studies.

In this study, SGLT-2i use was not associated with statistically significant differences in longitudinal IPSS post-HoLEP. For the overall cohort, IPSS significantly decreased after surgery compared to patients' preoperative baseline IPSS. However, there was no significant difference found between treated and control groups in the magnitude of postoperative IPSS improvement. This result held true after excluding

patients with a postoperative UTI and propensity score matching for potentially confounding covariates. At 3 months, the between-group difference in IPSS was − 0.2 points (95% CI − 3.6 to 3.2), a range that excludes differences as large as the minimal clinically important difference (MCID) reported by one prior study (5.26 points) [25]. At 2 weeks, the estimated difference was 1.9 points (95% CI − 1.2 to 5.0), which is compatible with no difference and with a delay in early recovery approaching the MCID. Smaller differences, which some patients may still find meaningful, could not be excluded. MCID estimates for IPSS vary across studies, and our study was not designed or powered to establish equivalence.

Exploratory analysis of perioperative MISI as well as IPSS voiding and storage subscores did not suggest significant associations between these outcomes and SGLT-2i use. These findings were limited by missing data and the small number of SGLT-2i users.

These results apply to SGLT-2is held for 3 days before surgery and resumed with a normal diet, not to uninterrupted use. They do not demonstrate harm but cannot exclude modest effects, and so do not support changing current perioperative practice. Future studies should capture hemoglobin A1c, diabetes duration, SGLT-2i agent and dose, and treatment duration.

This study had several limitations. The retrospective and single-surgeon design limits generalizability and statistical precision. Missing patient-reported data reduced an already small sample size, which limited the ability of this study to detect modest between-group differences in our outcomes of interest. IPSS was missing for roughly half of patients at 3 months; we assumed missingness was unrelated to unobserved symptom severity. Of note, postoperative UTI occurred in only 4 patients taking SGLT-2i. Propensity score matching adjusted for measured covariates but could not adjust for confounding in unmeasured covariates or truly replicate the effects of randomization. Further, UTIs diagnosed outside our institution may not have been fully captured if our electronic medical record did not receive supporting culture documentation. Finally, postoperative complications were captured only through 30 days, so UTIs after that period were not tracked. Despite these limitations, this is the first study to our knowledge exploring the use of SGLT-2is and perioperative urologic outcomes after HoLEP.

Conclusion

In this exploratory single-surgeon cohort of patients undergoing HoLEP, we did not detect statistically significant differences in postoperative UTI, longitudinal IPSS improvement, or preoperative positive urine cultures between SGLT-2i users and controls. Given the small number of SGLT-2i users and limited statistical precision, clinically meaningful differences in UTI risk and early symptom recovery cannot be excluded. These findings do not support changes to current perioperative practice but provide preliminary, hypothesis-generating evidence to inform larger prospective studies.

Declarations

Ethical Considerations:

This study is approved by the SUNY Upstate Institutional Review Board (no. 2111918, initial approval 08/24/2024, amendment approved 06/22/2026). This study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

Consent to Participate:

The requirement for informed consent to participate has been waived by the SUNY Upstate Institutional Review Board.

Consent for Publication:

Not applicable.

Competing Interests:

S Wiener: Scientific Advisory Board and holds stock options, Avvio Medical. The nature of this relationship is not related to the subject of this manuscript.

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Author Contribution

S.T.: Writing – original draft, methodology, software, investigation, formal analysis, data curation, conceptualization. A.G.N.: Writing - review & editing, methodology, data curation, conceptualization. M.G.: Data curation. A.U.: Data curation. A.L.: Data curation. E.K.: Data curation. S.W.: Writing – review & editing, methodology, supervision, project administration, conceptualization.

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Data Availability

The research data used for this study contain protected health information and sensitive patient data from our prospectively maintained institutional database. Therefore, this data must remain confidential and cannot be made publicly available. Requests for de-identified data can be sent to the corresponding author upon reasonable request.

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