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Opiate Exposure and Predictors of Increased Opiate Use After Ureteroscopy

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Abstract

Objective: Kidney stone formers are at risk for opioid dependence. The aim of this study is to describe opiate exposure and determine predictors of prolonged opiate use among kidney stone formers after surgery.
Materials and Methods: A retrospective review was performed among patients who underwent ureteroscopy for upper tract stone disease. Prescription data were ascertained from a statewide prescribing database. Demographic data and surgical factors were collected from the electronic medical record. Predictors of additional postsurgery prescriptions filled within 30 days and persistent opiate use 60 days after ureteroscopy were determined.
Results: Among 208 patients, 127 (61%) had received preoperative opiate prescriptions within 30 days before surgery. Overall, 12% ($n=25$) of patients required an additional opiate prescription within 30 days after ureteroscopy, and 7% ($n=14$) of patients continued to use opiate medications more than 60 days postoperatively. Patients continuing to use opiates long-term were not chronic opiate users. For both outcomes, preoperative opiate exposure, including number of prescriptions, days prescribed, and unique providers had significant associations (all $p<0.05$). Additionally, younger age ($p=0.049$) was associated with obtaining an additional opiate prescription within 30 days. Lower BMI ($p=0.02$) and higher ASA score ($p=0.03$) were predictors of continued opiate use more than 60 days after ureteroscopy.
Conclusions: The majority of stone formers have had opiate exposure before surgery, often from multiple providers. Approximately 1 in 8 stone formers who undergo ureteroscopy require additional opiate prescriptions within 30 days. A small but significant population receive opiates beyond the immediate postoperative period.

Keywords: opiate, ureteroscopy, nephrolithiasis

Introduction

Kidney stone disease is prevalent and a common urologic disorder.[1] When symptomatic, the condition can cause significant pain requiring analgesic medications. Specifically, in current practice, opiates are commonly prescribed for symptomatic stones.[2] Although the intent of these medications is to ameliorate postoperative pain, rates of opiate misuse and abuse have risen dramatically.[3]

There is increasing concern that repeated exposure to opiates, particularly for kidney stone patients undergoing surgery, leads to opiate dependence or overdose.[4] These patients often have had multiple encounters with providers for symptom relief before intervention,[4] and after intervention may have symptoms related to the procedure or ureteral stenting.[5] A prior study of opioid dependence and overdose after urologic procedures identified younger age, inpatient surgery, longer length of stay, noninsured or Medicare/Medicaid insurance status, and several comorbidities as risk factors.[4] Specifically, the incidence after stone surgery was 0.15% within 1 year.[4] However, the overall incidence is likely higher, as these outcomes were ascertained by administrative coding.

To date, patterns of opiate exposure among kidney stone formers and predictors of prolonged opiate use after surgery are not well described in this high-risk population. In this study, we sought to describe opiate prescribing patterns and opiate exposure among kidney stone patients using our statewide opiate prescribing database. We identified risk factors for increased opiate use after ureteroscopic stone surgery in two ways: additional opiate prescribing within 30 days postsurgery and persistent opiate exposure 60 days postsurgery.

Materials and Methods

Patients who underwent ureteroscopy for renal or ureteral stone treatment at our institution from January to June 2017 were retrospectively identified using current procedure terminology codes (52351, 52352, 53353, and 52356). Patients

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who underwent staged procedures were included but opiate prescribing data were collected based on final-stage ureteroscopy to allow follow-up of medication use. All patients undergoing ureteroscopy at our institution have a postoperative visit at 6–8 weeks with a renal ultrasound. Only primary residents of Tennessee at the time of surgery were included to enable for linkage to the Tennessee Controlled Substance Monitoring Database (TN CSMD) for opiate prescribing data. In accordance with the Controlled Substance Monitoring Act of 2002 and the Tennessee Prescription Safety Act of 2016, all health care providers who dispense controlled substances (Schedule II, III, IV, & V) in Tennessee for more than 15 days per year are required to register to monitor the dispensing of controlled substances. Local Institutional Review Board approval was obtained before data collection.

Demographic data collected included age, sex, race, BMI (body mass index; calculated by weight/height^2, kg/m^2), American Society of Anesthesiologists (ASA) score, past stone surgery, and documented diagnosis of psychiatric disorder. Surgical and stone variables collected included operative time, presence of stent preoperatively, laterality, postoperative stent duration, ureteral access sheath use, and stone diameter.

Prescribing data was categorized by preoperative and postoperative prescriptions, and then further classified by opiate and nonopiate medications. Prescription data from the CSMD provide the quantity and dose of opiate medication received by a patient from a pharmacy along with prescriber information. Preoperative opiate data included chronic opiate use (defined as more than two opiate prescriptions dispensed 60 days before surgery) and the following variables 30 days before surgery: number of opiate prescriptions dispensed, number of providers prescribing opiates, and morphine equivalent dose (MED) of the prescriptions dispensed. As a reference, 100 MED is equivalent to 100 mg of hydrocodone or 67 mg of oxycodone. Nonopiate preoperative prescription data within 30 days before surgery were assessed. Postoperative prescription data collected included the number of days of postoperative opiates prescribed at the time of surgery, total MED provided to the patient, and nonopiate medications prescribed to patients.

The two outcomes evaluated in this study were (1) obtaining an additional opiate prescription within 30 days after ureteroscopic stone surgery, and (2) continued opiate use 60 days after surgery as ascertained by the TN CSMD. We chose the 30- and 60-day time points to capture pain complaints or complications before or after routine 6-week postoperative follow-up visit.

Univariate analyses were performed to determine associations with obtaining an additional opiate prescription within 30 days or 60 days after surgery. A multivariable logistic regression model was fit to include all potential predictors, such as demographic, surgical, and opiate prescription variables. The opiate prescription variables were separately modeled as they were highly correlated. All analyses were carried out using Stata version 14 (StataCorp, LLC). All statistical tests were based on two-sided probability and $p < 0.05$ was considered statistically significant.

Results

A total of 310 patients underwent ureteroscopy during the study period. Excluded patients included 33 undergoing ureteroscopy for diagnosis other than ureteral or renal stone disease, 36 undergoing staged procedures, and 33 who were not primary residents of Tennessee. A total of 208 patients were included in the final analysis.

The patient population was predominantly male ($n = 116$, 56%) and white ($n = 191$, 92%). Most individuals were middle-aged (mean ± SD age 52.4 ± 15.1 years), with ASA scores of two ($n = 85$, 41%) or three ($n = 110$, 53%), and without concurrent psychiatric diagnoses ($n = 172$, 83%). There were 80 patients (38.5%) who had prior stone-related surgical procedures.

Preoperatively, a minority of patients were chronic opiate users ($n = 21$, 10%, Table 1). Within 30 days before surgery, 61% ($n = 127$) had received at least one opiate prescription, whereas 6% ($n = 12$) had received at least three prescriptions. Nonopiate prescriptions were prescribed preoperatively ~20–25% of the time.

Most ureteroscopic procedures performed were unilateral ($n = 173$, 83%), and the majority of patients did not have preoperative indwelling ureteral stents ($n = 139$, 67%). Ureteral access sheaths were used commonly ($n = 129$, 55%), and the majority of patients had stents placed intraoperatively ($n = 200$, 96%). Patients most commonly had stents removed 4–7 days postoperatively ($n = 124$, 60%).

Postoperatively, the majority of patients received opiate prescriptions ($n = 196$, 93.3%) with an average MED of 105.2 (mean ± SD, 105.2 ± 91.2). Patients most commonly received 4–7 days of opiate medications ($N = 104$, 50%). In addition, patients received nonopiate medications ~75% of the time (Table 1).

Overall, 12% ($n = 25$) of patients dispensed an additional opiate prescription within 30 days after ureteroscopy (Table 2). On univariate analysis, associated factors included younger age, greater number of preoperative prescriptions, greater number of providers prescribing opiates preoperatively, and higher MED use preoperatively (Table 3). Having a concurrent psychiatric diagnosis and chronic opiate use history trended toward but did not achieve significance ($p = 0.14$ and 0.09, respectively). Age and opiate-related associations remained significant upon multivariate analysis when modeling opiate variables separately (Supplementary Tables S1–S3). In this group, 10 patients (40%) had no reported complications, 12 patients (48%) made phone calls to the clinic for pain-related concerns, four patients (16%) had unanticipated clinic visits, two patients (8%) were seen in the emergency department, and there was one hospital readmission (4%, data not shown).

Approximately 1 in 15 patients ($n = 14$, 6.7%) received an additional opiate prescription after 60 days postoperatively (Table 2). The majority of opiate prescriptions ($n = 13$, data not shown) provided to these patients were provided by providers not affiliated with the urology department. Within this cohort, there was one unanticipated clinic visit, one emergency room visit, and two documented phone calls related to pain (data not shown). On univariate analysis, associated factors included a greater number of preoperative prescriptions, greater number of providers prescribing opiates preoperatively, and higher preoperative MED use (Table 3). On multivariate analysis, greater opiate exposure preoperatively, lower BMI, and greater ASA were significant predictors (Table 4 and Supplementary Tables S1–S3). No patient who filled an additional opiate prescription beyond 60

Table 1. Patient Characteristics

Demographics	
Age, years (mean ± SD)	52.4 ± 15.1
BMI (mean ± SD)	30.5 ± 8.1
Sex (%)	
Male	116 (55.8)
Female	92 (44.2)
Race (%)	
Caucasian	191 (91.8)
Other	18 (8.2)
ASA score (%)	
1	9 (4.3)
2	85 (40.9)
3	110 (52.9)
4	3 (1.9)
Prior psychiatric diagnosis (%)	
Yes	36 (17.3)
No	172 (82.7)
Prior stone procedure (%)	
Yes	80 (38.5)
No	128 (61.5)
Medication history	
Chronic opiate use (%)	
Yes	21 (10.1)
No	187 (89.9)
Preoperative opiate prescriptions <30 day, number (%)	
0	81 (38.9)
1	64 (30.8)
2	42 (20.2)
3+	21 (10.1)
Preoperative providers prescribing opiates <30 day, number (%)	
0	81 (38.9)
1	74 (35.6)
2	41 (19.7)
3+	12 (5.8)
Preoperative MED prescribed, tertiles (mean ± SD)	
Group 1 ($N = 49$)	107.8 ± 39.9
Group 2 ($N = 37$)	240.6 ± 45.5
Group 3 ($N = 41$)	3203.7 ± 7157.4
Preoperative oxybutynin prescription (%)	
Yes	47 (22.6)
No	161 (77.4)
Preoperative tamsulosin prescription (%)	
Yes	56 (26.9)
No	152 (73.1)
Preoperative phenazopyridine (%)	
Yes	45 (21.6)
No	163 (78.4)
Postoperative opiate prescription, days (%)	
0	14 (6.7)
1–3	79 (38.0)
4–7	104 (50.0)
7+	13 (6.3)
Postoperative MED prescribed (mean ± SD)	105.2 ± 91.2
Postoperative oxybutynin prescription (%)	
Yes	156 (75.0)
No	52 (25.0)
Postoperative tamsulosin prescription (%)	
Yes	153 (73.6)
No	55 (26.4)
Postoperative phenazopyridine prescription (%)	
Yes	156 (75.0)
No	52 (25.0)
Surgical factors	
Laterality (%)	
Right	74 (35.6)
Left	99 (47.6)
Bilateral	35 (16.8)
Preoperative ureteral stent (%)	
Yes	69 (33.2)
No	139 (66.8)
Stone size, diameter (mean ± SD)	8.48 ± 4.82
Operative time, minutes (mean ± SD)	55.7 ± 28.4
Use of ureteral access sheath intraoperatively (%)	
Yes	124 (59.6)
No	84 (40.4)
Postoperative stent duration, days (%)[a]	
0	8 (3.9)
1–3	34 (16.4)
4–7	124 (59.6)
7+	40 (19.2)

[a]Stent duration information missing on electronic medical record for two patients.

ASA = American Society of Anesthesiologists; MED = morphine equivalent dose.

days postoperatively was a chronic opiate user in the preoperative period.

Discussion

Managing pain after surgery is important for decreasing pain-related complications but must be balanced with minimizing opiate misuse, dependence, and overdose.[4,6–8] Studies have shown there is a large MED range of opiate medications provided to patients after common surgeries,[9] and that a majority of patients report unused leftover opioid medication after procedures.[7,8,10] Specifically, unanticipated visits after ureteroscopy for stone disease has been reported to be 6.6%, and the majority of these visits are made due to pain.[5,11] An important finding of our study is that most patients before stone surgery have had opiate exposure within the previous 30 days, and a significant proportion have had multiple prescriptions. This highlights a fundamental challenge of addressing how and when opiates are prescribed to kidney stone patients as they often encounter multiple providers across different settings.

Table 2. Additional Opiate Prescriptions After Ureteroscopy

Within 30 days postoperatively (%)	
Yes	25 (12.0)
No	183 (88.0)
After 60 days postoperatively (%)	
Yes	14 (6.7)
No	194 (93.3)

Table 3. Factors Associated with Obtaining an Additional Opiate Prescription Within 30 Days or More Than 60 Days After Ureteroscopy

	Within 30 days		*After 60 days*	
Variable	*OR (95% CI)*	*p*-value	*OR (95% CI)*	*p*-value
Age	0.97 (0.93–0.99)	0.009	1.01 (0.98–1.06)	0.32
BMI	1.01 (0.96–1.07)	0.61	0.95 (0.87–1.03)	0.23
Female	0.55 (0.23–1.35)	0.19	0.68 (0.22–2.11)	0.51
Caucasian	0.97 (0.21–4.54)	0.97	1.99 (0.41–9.72)	0.40
ASA score	0.88 (0.38–2.03)	0.76	0.54 (1.18–24.82)	0.03
ASA 2	0.47 (0.085–2.57)	0.38	UTC	UTC
ASA 3	0.43 (0.080–2.30)	0.32	UTC	UTC
ASA 4	1.17 (0.074–18.35)	0.91	UTC	UTC
Prior psychiatric diagnosis	2.07 (0.79–5.39)	0.14	1.33 (0.35–5.03)	0.67
Prior stone procedure	1.08 (0.46–2.53)	0.87	0.62 (0.19–2.05)	0.44
Chronic opiate use	2.61 (0.86–7.89)	0.09	UTC	UTC
Preoperative opiate prescriptions, number	1.58 (1.6–2.37)	0.026	1.57 (1.14–2.16)	0.005
Preoperative opiate prescription, days	1.6 (1.11–2.32)	0.012	1.02 (1.00–1.03)	0.032
Preoperative providers prescribing opiates	1.68 (1.08–2.62)	0.022	1.55 (1.00–2.39)	0.048
Preoperative MED prescribed				
Group 1 (lower tertile)	0.39 (0.08–1.91)	0.24	2.58 (0.42–16.0)	0.31
Group 2 (middle tertile)	1.11 (0.31–3.93)	0.88	4.79 (0.84–27.42)	0.08
Group 3 (upper tertile)	3.35 (1.22–9.14)	0.02	5.49 (1.02–29.63)	0.048
Preoperative oxybutynin prescription	1.09 (0.41–2.92)	0.86	UTC	UTC
Preoperative tamsulosin prescription	0.48 (0.16–1.47)	0.20	0.19 (0.02–1.52)	0.12
Preoperative phenazopyridine	0.89 (0.32–2.53)	0.83	0.59 (0.13–2.72)	0.49
Postoperative opiate prescriptions, days	1.0 (0.86–1.16)	0.98	0.9 (0.70–1.15)	0.38
Postoperative MED prescribed	1.0 (1.00–1.00)	0.99	1.00 (0.99–1.01)	0.79
Postoperative oxybutynin	1.38 (0.49–3.89)	0.54	1.24 (0.33–4.62)	0.75
Postoperative tamsulosin	1.5 (0.54–4.22)	0.44	2.26 (0.49–10.4)	0.30
Postoperative phenazopyridine	1.38 (0.49–3.89)	0.54	4.64 (0.59–36.3)	0.14
Stone size, diameter	0.96 (0.87–1.06)	0.40	0.99 (0.88–1.11)	0.83
Operative time, minutes	1.0 (0.99–1.02)	0.81	1.00 (0.98–1.02)	0.87
Ureteral access sheath use	0.84 (0.36–1.96)	0.70	1.24 (0.40–3.83)	0.71
Laterality				
Left	1.47 (0.39–5.55)	0.57	1.45 (0.29–7.18)	0.65
Right	1.67 (0.43–6.48)	0.46	0.94 (0.16–5.41)	0.95
Preoperative ureteral stent	0.76 (0.30–1.91)	0.56	0.53 (0.14–1.96)	0.34
Postoperative ureteral stent duration, days				
1–3	0.4 (0.06–2.70)	0.35	UTC	UTC
4–7	0.38 (0.07–2.08)	0.27	UTC	UTC
7+	0.43 (00.07–2.74)	0.37	UTC	UTC

Due to small sample size of patients who required opiate prescriptions 60 days after ureteroscopy, several data points had frequency of zero and OR was unable to be calculated.

OR = odds ratio; UTC = unable to calculate.

Table 4. Multivariable Logistic Regression Model–Days of Preoperative Opiate Prescriptions

	Within 30 days		*After 60 days*	
Variable	*OR (95% CI)*	*p*-value	*OR (95% CI)*	*p*-value
Age	0.82 (0.69–0.98)	0.027	0.97 (0.79–1.20)	0.81
Sex	0.61 (0.22–1.70)	0.35	0.52 (0.15–1.84)	0.32
Race	1.21 (0.22–6.56)	0.82	3.8 (0.61–24.18)	0.15
BMI	0.98 (0.93–1.04)	0.58	0.89 (0.80–0.98)	0.022
ASA score	1.31 (0.74–2.31)	0.36	3.08 (1.25–7.61)	0.014
Laterality (left)	1.38 (0.32–5.90)	0.66	2.62 (0.46–14.97)	0.279
Laterality (right)	1.31 (0.29–5.81)	0.72	1.14 (0.17–7.64)	0.089
Preoperative opiate prescription, days	1.73 (1.14–2.61)	0.009	1.97 (1.16–3.36)	0.013

Multivariable logistic regression models were performed for number of preoperative opiate prescriptions, days of preoperative opiate prescriptions, and number of providers prescribing opiate prescriptions preoperatively. These variables were modeled separately, and additional models are provided in Supplementary Tables S1–S3.

In our study, 12% of patients required an additional opioid prescription within a 30-day period after ureteroscopy. Risk factors identified included younger age and higher preoperative opiate use, which have been shown in prior studies to be associated with higher postoperative opiate use.[12–14] A recent nationwide survey reported one in seven youths have prior inappropriate use of opiates, which may lead to increased tolerance to opiates and perception of pain in this patient cohort.[15–17] Some patients in our study obtained more than three opiate prescriptions preoperatively and obtained opiate prescriptions from more than a single provider (Table 2). These findings mirror those in a study by Kappa and colleagues, who found that both younger age and higher preoperative opiate use were predictors of obtaining opiate pain medications from multiple providers after ureteroscopy.[18] Interestingly, although preoperative opiate use was a predictor of increased postoperative opiate requirements, chronic opiate use–which we defined as having more than two opiate prescriptions >60 days preoperatively–only trended toward significance likely due to small sample size.

We found that ~7% of patients continued to fill opiate prescriptions over 60 days after ureteroscopy, suggesting that a small but significant proportion of patients are at high risk for opioid dependence postoperatively. Only 1 of these 14 patients had this prescription obtained from our department. A study from the Centers for Disease Control found that increases in chronic opioid use were observed if patients received more than one opioid prescription, had longer duration of opioid use, or had higher quantities (MED) of opioid prescribed.[19] Another study demonstrated ~6% of patients with new persistent opiate use after surgical procedures.[6] In our study, risk factors for persistent opiate use included higher preoperative use, lower BMI, and greater ASA score.[6] Notably, none of the patients with persistent opiate use in our study had a history of chronic opiate use. The rate of persistent opiate use in our study was notably higher than previously reported by Shah and colleagues, which estimated opioid dependence to be present in 0.09% of patients after urologic procedures based on diagnostic codes.[4] For stone procedures, including percutaneous and endoscopic surgery, 0.10% and 0.15% of patients had hospital visits for opioid dependence or overdose within 90 and 365 days, respectively.[4] The differences between our studies likely lies in the methods used to identify patients with persistent opiate use after ureteroscopy. Patients with higher ASA scores have a higher risk of developing postoperative complications,[20] and new or preexisting comorbidities may be unmasked or exacerbated by surgery, which may result in higher opioid consumption postoperatively. It is possible that patients with higher ASA scores continued to require opiate medications for management of other comorbidities and not postureteroscopy pain, but these data were not reviewable in the TN CSMD.

While this study was not designed to determine the optimal postoperative pain regimen for patients undergoing ureteroscopy, it is apparent that the analgesic needs for each patient are different. Preoperative counseling regarding expectations after surgery, and proper use of opiate medications postoperatively have been demonstrated to decrease postoperative opiate consumption while maintaining adequate pain control.[21,22] Opiate-free protocols after ureteroscopy have been shown to be feasible.[23] Intraoperative use of nonopiate medications, such as intravenous toradol and belladonna opium suppositories have been shown to help with postoperative pain control after ureteroscopy.[11,24] Notably in this study, no surgical factors were identified as risk factors for persistent opiate use, including stent duration or sheath use. After surgery, providing a standardized MED per postoperative opiate prescription may help minimize the quantity of opiates prescribed and/or unused by patients.[10] It is important to note that patients who have had prior exposure to opiate medications seem to be at greater risk for continued opiate use, and these at-risk patients may benefit most from targeted counseling regarding the risks and alternatives to opiate medications. Furthermore, providing prescriptions for nonopiate medications including nonsteroidal anti-inflammatory drugs, alpha-blockers, oxybutynin, and phenazopyridine may result in decreased opiate requirement.[25–27]

Our findings should be interpreted within the context of the limitations of the retrospective design. The relatively low number of patients identified with persistent opiate use after ureteroscopy reduced the power to detect associations. The precise MED amount consumed by each patient is unknown. While we restricted this study to residents of the state, it is possible that prescriptions were given to patients outside of the state that would not be captured in the CSMD. Prescription data from TN CSMD does not list the indication for opioid prescription or specialty of the provider prescribing opiates, and additional prescriptions may have been prescribed for conditions related to stone disease or other diagnoses not related to kidney stone disease.

Conclusion

The majority of kidney stone patients receive opiate medications before surgery and often from multiple providers. Higher preoperative use of opiates was associated with receiving an additional opiate prescription within 30 days and persistent opiate use beyond 60 days after surgery. Younger age, lower BMI, and higher ASA score were also associated with persistent opiate after ureteroscopy.

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Author Disclosure Statement

The authors have no disclosures to declare.

Supplementary Material

Supplementary Table S1
Supplementary Table S2
Supplementary Table S3

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Abbreviations Used

ASA = American Society of Anesthesiologists
BMI = body mass index
MED = morphine equivalent dose
TN CSMD = Tennessee Controlled Substance Monitoring Database
UTC = unable to calculate