Ureteroscopy under conscious sedation: A proof-of-concept study

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Abstract

Introduction: Ureteroscopies (URSs) are commonly performed under general anesthesia (GA) to maximize patient tolerability and minimize surgical complications. However, given the improvements in endoscopic technology and risks associated with GA, alternate forms of anesthesia have been postulated. We aimed to evaluate the outcomes of URS under conscious sedation.
Methods: We completed a retrospective cohort study from November 2019 to June 2020 at a tertiary-level hospital. All URSs that were performed under urologist-directed conscious sedation were included. Our primary outcome was the ability to complete URSs, defined as success rate. Secondary outcomes included: stone-free rate, intraoperative complication rate, hospital admission rate, and sedation requirement. Univariate- and multivariate-adjusted logistic regression analyses were employed.
Results: Ninety-nine URSs were included. Most (73/99, 73.7%) were performed for urolithiasis. The overall success rate was 83.8% (83/99), with 81.0% (34/42) intra-renal and 70.0% (16/23) proximal ureter success rates. The stone-free rate was 80.8% (59/73). No intraoperative

Key Messages

We demonstrated the ability to effectively perform diagnostic and therapeutic ureteroscopy under urologist-directed conscious sedation, especially in the proximal ureter and renal pelvis. This approach may expedite patient care without compromising on safety. This study is of extra importance during the restraints on our healthcare system during the COVID-19 pandemic.

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complications nor hospital admissions were reported. The mean amount of sedation required was three (interquartile range [IQR] 2–4] mg of midazolam and 100 (100–150) µg of fentanyl. On multivariate analysis, midazolam was significantly associated with increased success (odds ratio 2.496, 95% confidence interval 1.057–5.892, p=0.037).
Conclusions: We have shown that proximal and intra-renal URS under conscious sedation is safe and effective. We were limited by our lack of followup, small sample size, selection bias to chose healthy patients, and lack of patient tolerability data. Patients and healthcare systems may benefit from implementing this innovation more broadly.

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Introduction

Since the first rigid ureteroscopy (URS) in 1912[1] and the first flexible URS in 1964,[2] URS has evolved over the years to become a fixture in the modern-day urologist's skillset when managing upper urinary tract pathology. Typically, this endoscopic procedure has been performed in the operating room with general anesthesia (GA) due to perceived reduced patient tolerability and risks of sudden patient movement, resulting in ureteric injury.[3] However, recent studies that have described the outcomes and complications of URS provide evidence to suggest that GA has minimal impact on patient tolerability and rates of ureteric injury are independent of GA.[4-7] We must then ask if GA is necessary, especially considering that there are risks associated with GA and substantial resources required for it.[8]

Modern outpatient clinics and hospitals are equipped with procedure suites where minor procedures may be performed under local anesthesia and/or intravenous conscious sedation, the combination of which is known as loco-sedative anesthesia. This approach offers an excellent opportunity for performing URSs in an increasing number of patients who are unwilling or unfit for GA. Since 1993, our centre has affirmed the feasibility and safety of distal URS under loco-sedative anesthesia.[9-11] Notably, the largest analysis of distal URS under loco-sedative anesthesia was conducted at our centre from 2004 to 2014.[11] The authors revealed a successful stone-free rate of 97% with minimal (3.2%) complications. Since this study was reported, endoscopic technology has vastly improved, and we have been routinely performing URS under loco-sedative anesthesia in the proximal ureter and renal pelvis.

While others have studied URS under loco-sedative anesthesia and local anesthesia,[9-19] none have described using loco-sedative anesthesia to evaluate the entire upper urinary tract. Therefore, the objective of this study was to retrospectively evaluate the outcomes of URS, especially as it concerns stone manipulation and management of upper tract urothelial carcinoma under loco-sedative anesthesia for the entire upper tract. Our primary outcome was whether the procedure accomplished its intention, deemed as successful. Secondary outcomes included stone-free rate, intra-operative complications, admission rate, and mean sedation requirement.

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Methods
This retrospective cohort study was conducted at a tertiary-level hospital in Winnipeg, Manitoba, Canada. All patients who were consented for a URS from one of two experienced, academic staff urologists without formal endourology fellowship training from November 2019 and April 2020 were included in the study. Resident trainees participated in the URSs under direct supervision from urologists, the extent of which corresponded to their training level with urologists taking over when indicated. Approval from the institutional research ethics board was obtained.

After the urologist performed a tailored history and physical, reviewed relevant imaging, and obtained informed consent, the patient was brought to a urology-dedicated procedure suite. This suite has built-in fluoroscopy, continuous vitals (blood pressure, heart rate, oxygen saturation) monitoring, and dedicated nursing staff who have been trained in administering conscious sedation. Supplemental oxygen was provided via nasal prongs, with saturations maintained above 90%. Most patients received a starting intravenous dose of 100 µg of fentanyl and 2 mg of midazolam, as directed by the urologist and administered by the nurse. Starting doses were decreased by 50% for elderly patients and those with impaired cardiac or pulmonary function.[20] Doses were titrated up for those who required better pain control, in increments of 25–50 µg of fentanyl and 1 mg of midazolam.

The procedure began by placing the patient in the dorsal lithotomy position, where their perineum and genitalia were prepped and draped. Xylocaine-containing lubricating gel (10 mL lubricating gel with 2% xylocaine) was instilled per urethra in males and placed on the scopes for females. A 17-French flexible cystoscope was then inserted through the urethra and into the bladder to complete a cystoscopy. The ureteric orifice of interest was identified, cannulated with 5-French ureteric catheter, and a retrograde pyelogram was performed. A safety wire was then passed into the renal pelvis through the ureteric catheter under fluoroscopic guidance. In the case of a pre-URS stent (which had been left in on average for 3 weeks), the stent was grasped and cannulated with a safety wire. The patient was de-instrumented, and a 6-French ureteroscope (flexible, semi-rigid, or rigid, the type of which was determined by the urologist) was inserted per urethra and into the ureter of interest. The need for an access sheath, holmium:YAG laser fibre, four-wire helical stone basket, 15- or 18-French balloon dilator, biopsy forceps, and / or JJ-ureteric stent was individualized. Post-URS stents were used in patients who required balloon dilation, an access sheath, or extensive manipulation, as determined by the urologist. The patient was subsequently de-instrumented. Stone specimens were sent for analysis and biopsies were sent for pathologic evaluation. The patient was monitored in a recovery room for at least one hour following URS. The patient was subsequently discharged home or admitted to the hospital.

Pre-operative data were obtained through an electronic chart review (and review of imaging). These data included age, sex, diagnosis, largest stone diameter and number of stones on side of interest (in urolithiasis patients). Intra-operative data were obtained through a review of surgeons' dictations, nursing's medication administration record, and fluoroscopy reports.

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These data included laterality of procedure (unilateral or bilateral), location of object of interest (native kidney, transplanted kidney, proximal ureter, mid-ureter, or distal ureter), previous ureteric stent, instruments used, amount of conscious sedation administered, success of procedure, reasons for failure, and intra-operative complications. Post-operative data were obtained through an electronic chart review (and review of imaging). These data included stone-free rate (success of procedures performed for urolithiasis, as demonstrated intraoperatively by complete stone removal or fragments dusted to the size of the laser fibre diameter and one-month post-operative with kidney, ureter, and bladder radiograph and ultrasonography of the renal tract without evidence of any further stone burden) and admission rate.

Categorical data was reported as absolute values with frequencies and analyzed using Chi-squared or Fisher's exact test. After determining data distribution with normality testing, continuous data was reported as means with standard deviation or medians with interquartile ranges [IQR: 25-75] and analyzed with Student T or Mann-Whitney U tests. Multivariate-adjusted logistic regression analysis was subsequently performed to calculated variables associated with success with odds ratios (ORs) and 95% confidence intervals (95% CI) reported. A p-value <0.05 was considered statistically significant. SPSS Version 24.0 (SPSS Inc, IBM, Armonk, NY) was used for data analysis.

Results

Ninety-nine URSs were performed: seventy-three (73.7%) for urolithiasis, twenty-four (24.2%) for upper tract urothelial carcinoma (UTUC), and two (2.0%) for evaluation of ureteric obstruction. The mean age of our population was 61.2 ± 13.7 years, with fifty-five (55.6%) males and forty-four (44.4%) females. Twenty-eight (28.3%) URSs were performed in the distal ureter, six (6.1%) in the mid-ureter, twenty-three (23.2%) in the proximal ureter, and forty-two (42.4%) in the renal pelvis and/or calyces. Within the UTUC cohort, seven (29.2%) were diagnostic (used biopsy or basket with satisfactory tissue sample) and five (20.8%) were therapeutic (used laser to fulgurate lesions). The urolithiasis cohort, as compared to the UTUC or obstruction cohort, were younger ($p < 0.001$), female at a greater proportion ($p = 0.036$), received a post-operative ureteric stent at a greater proportion ($p = 0.006$), and had a higher total dose of midazolam ($p = 0.017$, Table 1).

The mean amount of sedation required was 3 [interquartile range (IQR): 2–4] mg of midazolam and 100 [IQR: 100–150] µg of fentanyl. Other important operative factors include: twenty-three (23.2%) pre-operative ureteric stents, eighty-one (81.8%) post-operative ureteric stent insertions, a largest median stone diameter of 6 [4 – 7] millimetres, a median number of stones on the side of interest of 2 [1 – 3], and a median fluoroscopy time of 56.5 [30.8 - 96.3] seconds (Table 1).

We achieved an overall success rate of 83.8% (83/99), with a 96.9% (26/27) success rate for distal and mid ureteric URSs and a 78.9% (55/69) success rate for proximal and intra-renal URSs. Our overall stone-free rate was 80.8% (59/73) (Table 1). Patients with a successful URS had more distal URSs ($p = 0.043$), shorter fluoroscopy time ($p = 0.039$), and a lower rate of post-

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URS ureteric stent insertion (p = 0.038). Notably, the amount of conscious sedation was similar between cohorts (p = 0.150 and 0.916, Table 2).

On multivariable-adjusted analysis, urolithiasis was associated with reduced success (OR = 0.157, 95% CI: 0.025-0.973; p=0.047) and greater use of midazolam was associated with increased success (OR= 2.496, 95% CI: 1.057–5.892; p=0.037). An exploratory multivariable-adjusted analysis in patients with urolithiasis demonstrated a positive association between midazolam use and success (OR = 3.419, 95% CI: 1.081 - 10.820; p = 0.036; Table 3).

No intra-operative complications, intra-operative conversions to GA, and post-operative hospital admissions were reported. However, reasons for failure included high stone burden or impaction (4/16, 25%), poor visualization (6/16, 37.5%), a tortuous or tight ureter (5/16, 31.3%), and inability to tolerate sedation (1/16, 6.3%). The chief reason for failure in the urolithiasis cohort was poor visualization (6/14, 42.9%), and the chief reason for failure in the UTUC or obstruction cohort was a tortuous or tight ureter (2/2, 100%; Table 4). Nine (56.3%) of these failures underwent successful repeat URS under loco-sedative anesthesia and seven (43.7%) proceeded to extracorporeal shockwave lithotripsy or the operating room.

Discussion

To our knowledge, this is the first study to evaluate URS under urologist-directed loco-sedative anesthesia for the entire upper urinary tract, especially within the proximal ureter and renal pelvis. Herein, we have shown that our approach is safe and effective in managing upper tract pathology for appropriately selected patients—with greater success in those receiving higher doses of midazolam and those who are being assessed for UTUC or obstruction. Furthermore, our success rate and complication rates were similar to those reported with GA,[4-5] and local or loco-sedative anesthesa[9-19] (with success rates ranging between 78-100% and complication rates ranging between 1-11%). This comparison provides external validity to our findings and indicates that in carefully selected patients, URS under loco-sedative anesthesia is likely non-inferior to that with GA.

Surprisingly, URS for urolithiasis was less successful than URS for UTUC or obstruction. Differences in baseline characteristics between the two cohorts may have contributed to this finding. Additionally, our anecdotal experience is that URSs for urolithiasis are more involved as compared to that for UTUC or obstruction. Objectively, this explanation is supported by the increased use of adjuncts such as lasers, baskets, and dilators, the higher doses of midazolam required, and the higher rate of post-URS stent insertion. Therefore, we suspect that less intensive URSs would be associated with greater success. This explanation is supported by our univariate analysis findings of significantly greater success with more distal procedures, less fluoroscopy use, and less post-URS stenting. Despite the concern that more challenging URSs may be less successful and therefore less amenable to loco-sedative anesthesia, we have also shown that intra-renal and proximal ureteric regions can be evaluated effectively with our technique without compromising on safety.

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Another unexpected finding was the lack of association between pre-URS stent and success. In our study, 83.3% of cases without a pre-URS stent were successful whereas 78.3% with a pre-URS stent were successful. This difference, albeit small, may be explained by the reason pre-URS stents were used: stents were inserted for patients deemed difficult to access, with the goal of achieving passive dilation. Despite this initial difficulty, the addition of a pre-URS stent seemed to have conferred a benefit. Furthermore, nine of these failures that underwent successful repeat URS under loco-sedative anesthesia all received a post-URS stent after the first attempt, supporting the role of a pre-URS stent in achieving success.

Our results also demonstrate that higher doses of midazolam were associated with greater procedural success. Among its many properties, midazolam is an effective anxiolytic and amnestic. Midazolam allows for relaxed patients that potentially results in less perceived patient harm, improved surgical vision, and consequently, less operator stress. Interestingly, fentanyl was not associated with success, perhaps indicating that analgesia may not be as important of a factor as anxiolysis in optimizing tolerability for URS.

Recently, some authors have suggested avoiding conscious sedation entirely and performing URS with only local anesthetic. One study used only intraurethral lidocaine to treat upper urinary tract calculi with a median size of 8 mm.[17] Their overall stone-free rate was 84%, with a 91.5% stone-free rate in the mid and distal ureter. A second study used total intra-ureteric topical anesthesia for treatment of a single ureteric calculus less than 1 cm (excluding intra-renal calculi).[18] Their success rate was 91.3%, with 61% of patients not requiring further analgesia; however, 6% had complications and 17% felt that the pain was significant enough to not consent for a repeat procedure. Finally, a third study used intraurethral lidocaine and intra-ureteric marcaine with or without conscious sedation.[19] Only 22% of patients did not require conscious sedation, with a further 49% requiring conscious sedation. Together, these studies indicate that in most patients, URS was better tolerated and more likely to be successful under loco-sedative anesthesia; however, local anesthetic alone may be an option for patients who are unable to tolerate conscious sedation.

URS with spinal anesthesia (SA) is another alternative analgesic regimen. A retrospective study comparing SA to GA in patients undergoing semirigid URSs showed similar success and complication rates.[21] Several studies have also shown patients reporting less postoperative pain with SA than GA according to visual pain scores.[21-22] However, there may still be a higher risk of complications when using SA compared to GA for URSs.[23] Additionally, the induction and recovery times are long when using SA.[3] There is scarce evidence comparing SA to loco-sedative anesthesia. Future studies are therefore required to determine whether loco-sedative anesthesia is non-inferior to SA.

To minimize the risk of failure of URS under loco-sedative anesthesia, early identification of high stone burden or impaction on imaging, patients with prior high anesthetic needs, a tortuous or tight ureter on retrograde pyelogram, or poor visualization during the procedure may be helpful in either not offering this regimen or abandoning it early and arranging

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alternative means of managing the patients' condition. Additionally, anecdotally, some patients displayed discomfort when inserting an access sheath or attempting balloon dilation. While increased analgesia may mitigate this discomfort and allow for a successful procedure, this finding may also indicate poor patient tolerance and considering early abandonment of the procedure is warranted.

While this innovation was implemented prior to and during the coronavirus disease 2019 (COVID-19) pandemic, we offer proof of concept for a solution to the reduction of urology operating room slates during the COVID-19 pandemic and thereafter. The COVID-19 pandemic has become an unprecedented challenge for our healthcare systems. From March 2020 to June 2021, cancellations and delays have resulted in approximately 560,000 fewer surgeries than pre-pandemic levels in Canada.[24] Since that time, this number has likely increased, given new waves as well as the shortage of personal protective equipment, ventilators, drugs, and staff. Optimistically, during the pandemic, loco-sedative anesthesia has demonstrated success in other areas of medicine.[25-27] We suggest that URS under loco-sedative anesthesia may be one of the "out-of-the-box solutions" in urology toward eliminating the surgical backlog and minimizing additional financial pressures on our already thinned financial reserve.[27]

It is essential to recognize the limitations inherent in our study. Given the retrospective nature of our study, we were unable to accurately collect data on pre-existing health conditions, ureteroscopes used per procedure, operating time, and long-term post-operative outcomes. Additionally, while no post-operative admissions were recorded, we were unable to capture patients presenting to the emergency department following their URS. This information may have allowed for us to better explain differences that were seen. Importantly, while operative time was not directly captured, it can be inferred from fluoroscopy time and amount of sedation required. Nevertheless, in our experience, the time needed to perform a URS under loco-sedative anesthesia itself was not vastly different from that in the operating room. In fact, the ability to control one's own fluoroscopy, avoid pre-operative GA or SA and post-operative waking periods, and recover patients in a urology dedicated area has allowed us to fit more cases into a day by reducing overall care time per patient.

A second limitation was our small sample size, which may explain results that just approached significance or did not approach significance. Despite the small sample size, it is encouraging to note the lack of intra-operative complications, intra-operative conversions to GA, and post-operative hospital admissions using this technique.

A third limitation was an inherent selection bias to offer URSs under loco-sedative anesthesia to cases perceived as less risky—those with lower stone burden or pre-URS stent. While these factors may have artificially inflated our success rate; we have shown that, with increased experience, cases that were previously thought to be best suited for GA are now being done under loco-sedative anesthesia.

Finally, we did not validate patient tolerability. During situations of perceived patient intolerability, a stent is often placed, and the patient is brought to the operating room for their

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procedure to be performed with GA. While objective data are useful, understanding the clinical value, through the lens of the patient, would be invaluable.

To address some of these issues, we have recently completed a prospective cohort database on patient-reported outcomes of URS under loco-sedative anesthesia, which we hope to report on soon.

Conclusions

Herein, we have demonstrated the safety and efficacy of URS under loco-sedative anesthesia for upper tract pathology in carefully selected patients. With improved technology, the ability to perform these procedures outside of the operating room has the potential to increase resource availability without reducing patient safety or procedural efficacy.

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Figures and Tables

Table 1. Comparation of clinical characteristics between patients that underwent URS due to urolithiasis vs. UTUC or obstruction

	Overall n=99 (100.0%)	**Urolithiasis** n=73 (73.7%)	**UTUC or obstruction** n=26 (26.3%)	**p**
Age (y)	61.2±13.7	57.6±12.8	71.4±10.8	**<0.001**
Sex				
Male	55 (55.6%)	36 (49.3%)	19 (73.1%)	
Female	44 (44.4%)	37 (50.7%)	7 (26.9%)	**0.036**
Fluoro time (s)	56.5 (30.8–96.3)	56 (31–89.8)	62 (25.8–111.8)	0.666
Side				

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Unilateral	93 (93.9%)	71 (97.3%)	22 (84.6%)	
Bilateral	6 (6.1%)	2 (2.7%)	4 (15.4%)	**0.040**
Transplanted kidney				
Yes	3 (3.0%)	2 (2.7%)	1 (3.8%)	
No	96 (97.0%)	71 (97.3%)	25 (96.2%)	0.999
Location of interest				
Distal ureter	28 (28.3%)	23 (31.5%)	5 (19.2%)	
Mid ureter	6 (6.1%)	4 (5.5%)	2 (7.7%)	
Proximal ureter	23 (23.2%)	18 (24.7%)	5 (19.2%)	
Intra-renal	42 (42.4%)	28 (38.4%)	14 (53.8%)	0.475
Largest stone diameter (mm)*	–	6 (4–7)	–	
Number of stones on the side of interest*	–	2 (1–3)	–	
Previous ureteric stent				
Yes	23 (23.2%)	18 (24.7%)	5 (19.2%)	
No	76 (76.8%)	55 (75.3%)	21 (80.8%)	0.574
Access sheath used				
Yes	33 (33.3%)	26 (35.6%)	7 (26.9%)	
No	66 (66.7%)	47 (64.4%)	19 (73.1%)	0.419
Laser used				
Yes	43 (43.4%)	38 (52.1%)	5 (19.2%)	
No	56 (56.6%)	35 (47.9%)	21 (80.8%)	**0.004**
Basket used				
Yes	62 (62.6%)	61 (83.6%)	1 (3.8%)	
No	37 (37.4%)	12 (16.4%)	25 (96.2%)	< **0.001**
Dilation				
Yes	21 (21.2%)	19 (26%)	2 (0.7%)	
No	78 (78.8%)	54 (74%)	24 (92.3%)	**0.050**
Biopsy taken				
Yes	7 (7.1%)	1 (1.4%)	6 (23.1%)	
No	92 (92.9%)	72 (98.6%)	20 (76.9%)	< **0.001**
Post-URS stent insertion				
Yes	81 (81.8%)	65 (89.0%)	16 (61.5%)	
No	18 (18.2%)	8 (11.0%)	10 (38.5%)	**0.006**
Fentanyl (μg)	100 (100–150)	100 (100–150)	100 (100–100)	0.084
Midazolam (mg)	3 (2–4)	3 (3–4)	2 (2–3.75)	**0.017**
Successful procedure				
Yes	83 (83.8%)	59 (80.8%)	24 (92.3%)	0.225
No	16 (16.2%)	14 (19.2%)	2 (7.7%)	

*Only stone-related procedures. URS: ureteroscopies; UTUC: upper tract urothelial carcinoma.

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Table 2. Comparation of clinical characteristics between patients that underwent URS that had a successful vs. unsuccessful outcome			
	Successful n=83 (83.8%)	**Unsuccessful** n=16 (16.2%)	**p**
Cohort			
Urolithiasis	59 (71.1%)	14 (87.5%)	
UTUC or other	24 (28.9%)	2 (12.5%)	0.225
Age (y)	61.4±14.1	60.2±11.8	0.741
Sex			
Male	46 (55.4%)	9 (56.3%)	
Female	37 (44.6%)	7 (43.8%)	0.999
Fluoro time (s)	53.5 (25.8–86.8)	87.5 (53–156)	**0.039**
Side			
Unilateral	77 (92.8%)	16 (100.0%)	
Bilateral	6 (7.2%)	0 (0.0%)	0.585
Transplanted kidney			
Yes	1 (1.2%)	2 (12.5%)	
No	82 (98.8%)	14 (87.5%)	0.067
Location of interest			
Distal ureter	27 (32.5%)	1 (6.3%)	
Mid ureter	6 (7.2%)	0 (0.0%)	
Proximal ureter	16 (19.3%)	7 (43.8%)	
Intra-renal	34 (41.0%)	8 (50.0%)	**0.043**
Largest stone diameter (mm)*	6 (4–7)	5.5 (4.8–7.5)	0.600
Number of stones on the side of interest*	2 (1– 3)	2.5 (1– 4)	0.609
Previous ureteric stent			
Yes	18 (21.7%)	5 (31.3%)	
No	65 (78.3%)	11 (68.8%)	0.518
Access sheath used			
Yes	28 (33.7%)	5 (31.3%)	
No	55 (66.3%)	11 (68.8%)	0.847
Laser used			
Yes	39 (47.0%)	4 (25.0%)	
No	44 (53.0%)	12 (75.0%)	0.104
Basket used			
Yes	55 (66.3%)	7 (43.8%)	
No	28 (33.7%)	9 (56.3%)	0.088
Dilation			
Yes	18 (21.7%)	3 (18.8%)	
No	65 (78.3%)	13 (81.3%)	0.792
Biopsy taken			

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Yes	7 (8.4%)	0 (0.0%)	
No	76 (91.6%)	16 (100.0%)	0.594
Post-URS stent insertion			
Yes	65 (78.3%)	16 (100.0%)	
No	18 (21.7%)	0 (0.0%)	**0.038**
Fentanyl (µg)	100 (100–150)	100 (100–150)	0.916
Midazolam (mg)	3 (2–4)	3 (2–3)	0.150

*Only stone-related procedures. URS: ureteroscopies; UTUC: upper tract urothelial carcinoma.

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Table 3. Multivariable adjusted analysis showing the association between clinical characteristics and successful outcome after URS, with an exploratory analysis in patients with urolithiasis			
	OR	**95% CI**	**p**
Cohort			
UTUC or obstruction	1		
Urolithiasis	0.157	0.025–0.973	**0.047**
Age (per year)	1.005	0.947–1.066	0.880
Sex			
Male	1		
Female	1.048	0.276–3.971	0.945
Location of interest			
Distal ureter	1		
Mid and proximal ureter	0.135	0.013–1.381	0.091
Intra-renal	0.138	0.014–1.332	0.087
Fluoro time (per second)	0.994	0.987–1.002	0.132
Fentanyl (per µg)	0.998	0.981–1.016	0.837
Midazolam (per mg)	2.496	1.057–5.892	**0.037**
Urolithiasis cohort			
Age (per year)	1.001	0.936–1.071	0.970
Sex			
Male	1		
Female	1.151	0.258–5.127	0.854
Location of interest			
Distal ureter	1		
Mid and proximal ureter	0.195	0.017–2.231	0.189
Intra-renal	0.163	0.014–1.917	0.149
Largest stone diameter (per mm)	0.982	0.732–1.319	0.906
Number of stones on the side of interest (per stone)	0.880	0.620–1.250	0.476
Fluoro time (per second)	0.994	0.982–1.007	0.361
Fentanyl (per µg)	0.993	0.974–1.011	0.439
Midazolam (per mg)	3.419	1.081–10.820	**0.036**

CI: confidence interval; OR: odds ratio; URS: ureteroscopies; UTUC: upper tract urothelial carcinoma.

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Table 4. Subset descriptive explanations for unsuccessful URS by urolithiasis vs. UTUC or obstruction			
	Overall n=16 (16.2%)	**Urolithiasis** N=14 (19.2%)	**UTUC or obstruction** n=2 (7.7%)
Reason for failure			
High stone burden or impaction*	4 (25.0%)	4 (28.6%)	–
Poor visualization	6 (37.5%)	6 (42.9%)	0
Tortuous or tight ureter	5 (31.3%)	3 (21.4%)	2 (100.0%)
Unable to tolerate sedation	1 (6.3%)	1 (7.1%)	0

*Only stone-related procedures. URS: ureteroscopies; UTUC: upper tract urothelial carcinoma.

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