Original Article

Postoperative pain factors after ureterscopic removal of stones in kidney and ureter

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Keywords:
Pain, postoperative, ureterolithiasis, nephrolithiasis, ureterorenoscopy

Abstract

Objective: Postoperative wpain after ureteroscopic removal of ureter and kidney stones frequently leads to re-hospitalization, revisit and increased cost. However, risk factors and incidence for early postoperative pain are still unclear. The aim of this study is to investigate the associated risk factors and the incidence of acute postoperative pain after ureteroscopic stone removal in the ureter and kidney.

Materials and Methods: Retrospective data from 306 consecutive patients who underwent ureteroscopic treatment for ureteral and kidney stones from January 2016 to December 2020 were collected. The patients were divided into two groups: (i) Mild postoperative pain (n = 179), defined as a pain score lower than four on the visual analog pain scale during the first operative day, and (ii) Moderate to severe postoperative pain (n = 127) was defined as a pain score of greater than or equal to 4 during the first operative day. Potential risk factors were included in the univariable and multivariable regression analyses to identify risk factors for developing moderate to severe pain.

Results: 127 (41.5%) patients experienced moderate to severe postoperative pain on the first postoperative day. From multivariable analysis, positive pre-operative urine culture, operative time of more than 60 minutes, a stone procedure in the ureter, a postoperative stent, and ureter injury greater than grade I were related to moderate to severe pain with significance risk ratios (RR) of 2.99, 3.70, 4.87, 3.30, and 2.96, respectively ($p < 0.05$).

Conclusion: Pain is a frequent postoperative problem associated with ureterscopic removal of stones and should be pro-actively treated with care. Patients are at a higher risk of moderate to severe pain if they required the ureteral procedure, had prolonged operative time, ureter injury after the procedure, needed a stent postoperatively, or had a history of positive preoperative urine culture.

Insight Urol 2022;43(2):119-27. doi: 10.52786/isu.a.57

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Manuscript received: February 16, 2022

Revision received: July 21, 2022

Accepted after revision: October 14, 2022

Introduction

Urinary tract stone has been identified as a common public health problem with a steadily increasing incidence.[1] Minimally invasive surgery is the mainstay for treatment of urinary tract stones, procedures including extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), and ureteroscopic removal of stones (URS). According to the European Association of Urology (EAU),[2] URS is recommended as an alternative treatment option for ureter stones and renal stone removal. URS can be accessed in an antegrade and retrograde fashion and the development of endourologic instruments has led to greater efficacy, fewer complications, and the rapid recovery of the patients. With the reduction in adverse events, URS can serve as an out-patient procedure,[3] but if the patient registers as more than two on the American Society of Anesthesiologists score (ASA) there is a risk for hospitalization.[4] The incidence of the patient after URS visiting the emergency department (ED) for pain was 14.8%, the most common presentation.[5] Other common revisit presentations were pyrexia, urinary tract infection, and hematuria. Ahn et al. reported that patients who underwent URS for ureter calculi show that acute postoperative pain (a visual analog scale of greater than or equal to 4) was related to young age, psychiatric illness, history of urinary tract infection, use of stone basket, large stone size and prolonged operative time.[6] However, a study by Oğuz et al. found that the female gender, a one-millimeter increase in stone diameter, prolonged sheath time, and presence of residual fragments are associated with postoperative pain.[7] A study by Luo et al. revealed that with regional anesthesia, there is a significantly lower pain score than with general anesthesia.[8] This study analyzed the data pertaining to 5-year retrospective patients who had undergone URS for ureteral and renal calculi at Thammasat hospital in order to identify risk factors and incidence of postoperative pain. It is anticipated that the outcomes of this study will help clinicians to be able to select patients for ambulatory surgery and advise with regard to the risks of postoperative pain before the procedure.

Materials and Methods

This study was a retrospective cohort study designed to investigate acute postoperative pain. From January 2016 to December 2020, 307 patients underwent URS at the Urology Department of Thammasat Hospital. Ethical approval was granted by the Thammasat University Ethics Committee in Human Research (Reference MTU-EC-SU-1-103/64). The patients included in the study were at the stage of preoperative preparation in the outpatient department; perioperative and postoperative care was carried out in accordance with our URS routine protocols.

The maximum diameter of the stone was measured preoperatively in each case using simple abdominal radiography, intravenous pyelogram, excretory urography, or non-enhanced computed tomography (CT). On the first day postoperative, the presence of residual stone was determined by plain KUB for opaque stone and ultrasound or non-contrast helical CT for non-opaque stone at one month postoperatively.

Before the date of surgery a mid steam urine sample was collected and cultured, and if positive the patient was treated for uropathogenic bacteria, in accordance with EAU guidelines.[9] Patients were admitted one day before surgery and blood samples were taken and a second urine sample. Prophylactic and postoperative antibiotics were included in our protocol. An anesthesiologist selected appropriate anesthesia. Ureteral access sheath (UAS) was not routinely used, and the sheath size was not more than 14 Fr. Preoperative stents were inserted in patients who needed urine diversion. All procedures were performed using a rigid ureteroscope (Richard Wolf 6/7.5 Fr, Karl Storz 6 Fr) or flexible URS (Richard Wolf COBRA, Karl Storz Flex-X, Olympus URF type). Either Holmium: YAG laser or pneumatic lithoclast were used as stone fragment devices and were selected according to the preference of the surgeon. The stones were removed by spontaneous passing, forceps, or basket. Balloon dilation was used only in patients with a narrowing ureteral orifice. A ureteral JJ stent, 6 Fr, was inserted if the surgeon thought it necessary but was placed routinely in a patient who had a ureteral injury, impacted stone, or residual stone, required a bilateral procedure, or had a solitary kidney. The ureteral injury was assessed as described by Traxer and Thomas grading.[10]

In our protocol, recording of pain status starts in the recovery room and continues until the day of discharge. In this study the visual analog

pain scale (VAS) score (normal range 0 to 10) was used to record pain levels by nurses on the ward. In the first 24 hours, pain level was recorded every hour for four hours; then every 2 hours, four times more; and finally, every 4 hours. No continuous analgesic medication was given. If the pain score was ≥ 4, pain relief was given and the outcome was checked 30 minutes after intravenous analgesic medication (morphine 2 mg) and 1 hour after oral medication (paracetamol 500 mg or naproxen 250 mg). Using this procedure, the majority of patients were discharged the next day. Appointments were made for two weeks after the procedure for stent removal and for four weeks for follow-up imaging by ultrasound, or CT scan. Presence of a residual stone was noted if the stone size was ≥ 3 mm on the first postoperative day or at the four week check.

After reviewing 307 chart records of treated patients, the URS procedure was reviewed and only one patient was excluded because the TURP was also carried out simultaneously. Three hundred and six patients were divided into two groups according to mild or moderate to severe acute postoperative pain. Moderate to severe postoperative pain was defined as a VAS score greater than 36 (anytime during the first 24 hours). Patients with moderate to severe pain were analyzed according to age, body mass index (BMI), ASA classification, history of UTI (within three months), history of a stone procedure or ESWL, positive preoperative urine culture, preoperative stent, choice of anesthesia, operative time, stone burden, stone location, abnormal anatomy, residual stone, unilateral or bilateral procedure, choice of lithotripsy, ureteral dilatation, degree of ureteral injury, choice of stone retrieval device, use of ureteral access sheath and use of postoperative ureteral stent. These were all analyzed to identify potential risk factors for predicting moderate to severe postoperative pain.

Statistical analysis

Statistical analysis was performed using STATA software (version 15). We divided the patients into mild and moderate to severe pain groups. We then compared the two groups using Student T-tests for continuous data. Fisher's exact tests for categorical data were used for patient characteristics; univariable analysis using binary regression was calculated for risk ratio. For multivariable analysis, the factors which have tendency-related pain ($p < 0.3$) were selected for multivariable analysis differences were deemed as statistically significant when the p-value was less than 0.05 ($p < 0.05$).

Sample size was calculated by reviewing previous studies for estimating the risk factors for postoperative pain. For the multivariable analysis, we needed 10 outcome events per variable. From a review of relevant literature, we found 12 factors to be related to postoperative pain. Risk factors for postoperative pain included gender, a positive preoperative urine culture, stone size, stone location, ureteral access sheath and ureteral dilator usage, anesthetic technique, preoperative stent, postoperative stent, bilateral procedure, operative time, ureter injury grading, and residual stone. Thus, 120 patients who had developed these outcomes were needed. This investigation is of a retrospective cohort study design, and we collected data from 2016 until 2020. Of the 307 patients who underwent URS for remove stone in kidney and ureter in that period, there were 127 moderate to severe pain events.[11]

Results

Patient characteristics are summarized in Table 1 with the retrospective data of 306 patients (male 157 and female 149), divided into Group 1 (59%) and Group 2 (41%). The age range of the patients was 16-89 years, and the mean ages of the patients were 60 and 58 years in Group 1 and Group 2, respectively. ASA classification was mostly class 2. An anesthesiologist usually chose general anesthesia (67.95%) more frequently than regional anesthesia (32.05%). The mean BMI, previous history of UTI, pre-op alpha-blocker, pre-op stent, equipment diameter large than 10 Fr, and residual stone fragment were the same between the two groups.

Overall stone free rate (SFR) of our study was 91%, for ureteric stone was 99%, for kidney stone 85% and in the case of a combination of kidney and ureter stone was 85%.

From the univariable analysis, positive preoperative urine culture, an operative time of more than 60 minutes, a stone procedure in ureter or ureter and kidney (compared with kidney alone), cumulative stone diameter more than 10 mm, postoperative stent, bilateral procedures, and ureteric injury more than grade 1 were shown

Table 1. Patient characteristics

Characteristics	Mild post-operative paina (n = 179)	Moderate-severe post-operative pain b (n = 127)	P-value
Age, years, mean (SD)	60 (12)	58 (13)	0.15
Gender			0.082
Male, n (%)	84 (46.93)	73 (57.48)	
Female, n (%)	95 (53.07)	54 (42.52)	
ASA classification			0.430
I, n (%)	50 (27.93)	27 (21.26)	
II, n (%)	92 (51.40)	72 (56.69)	
III, n (%)	37 (20.67)	28 (22.05)	
Anesthetic technique			0.216
Regional anesthesia, n (%)	64 (35.75)	36 (28.35)	
General anesthesia, n (%)	115 (64.25)	91 (71.65)	
BMI, kg/m^2, mean (SD)	24.86 (3.43)	24.63(3.65)	0.572
Previous history of UTI			0.621
Yes, n (%)	24 (13.41)	20 (15.75)	
No, n (%)	155 (86.59)	107 (84.25)	
Pre-op alpha-blocker			0.523
Yes, n (%)	55 (30.73)	34 (26.77)	
No, n (%)	124 (69.27)	93 (73.23)	
Pre-op stent			0.245
Yes, n (%)	31 (17.32)	29 (22.83)	
No, n (%)	148 (82.68)	98 (77.17)	
Pre-op urine culture positive			0.007
Yes, n (%)	28 (15.64)	37 (29.13)	
No, n (%)	151 (84.36)	90 (70.87)	
Previous ipsilateral stone removal procedure			0.785
Yes, n (%)	41 (22.91)	31 (24.41)	
No, n (%)	138 (77.09)	96 (75.59)	
Operative time, min, mean (SD)	55.94 (18.65)	67.72 (22.58)	< 0.001
Stone location			0.007
kidney, n (%)	79 (44.13)	34 (26.77)	
ureter, n (%)	88 (49.16)	80 (62.99)	
kidney and ureter, n (%)	12 (6.70)	13 (10.24)	
Cumulative stone diameter, mm, mean (SD)	11.87 (6.79)	14.30 (6.07)	0.0014
Post-op stent			
Yes, n (%)	128 (71.91)	118 (92.91)	< 0.001
No, n (%)	50 (28.09)	9 (7.09)	
Bilateral procedures			0.033
Yes, n (%)	9 (5.03)	15 (11.81)	
No, n (%)	170 (94.97)	112 (88.19)	
Ureter injury grading[c]			0.006
0, n (%)	165 (92.18)	105 (82.68)	
1, n (%)	12 (6.70)	11 (8.66)	
2, n (%)	1 (0.56)	8 (6.30)	
3, n (%)	1 (0.56)	3 (2.36)	
Equipment diameter large than 10 Fr[d]			0.818
Yes, n (%)	87 (48.60)	67 (52.76)	
No, n (%)	92 (51.40)	60 (47.24)	
Residual stone fragment from day 1 plain film or US at 1 month			1.000
Yes, n (%)	16 (8.94)	11 (8.66)	
No, n (%)	163 (91.06)	116 (91.34)	

SD = standard deviation, n = number, min = minute, ASA = American Society of Anesthesiologists, BMI = body mass index = UTI = urinary tract infection, mm = millimetres, Post-op = postoperative

[a]Visual analog pain scale less than 4, [b]Visual analog pain scale equal or more than 4, [c]Ureter grading by endoscopic view (described by Traxer and Thomas grading, grade10), [d]Included use of semirigid, flexible ureteroscope, balloon dilatation, or ureteral access sheath, during the operation

to be potential risk factors ($p < 0.05$). However, sex, age, ASA classification, BMI, previous history of UTI, preoperative stent, preoperative alpha-blocker, choice of anesthesia, usage of equipment diameter larger than 10 Fr, and residual stone were not related to moderate to severe postoperative pain in our study, as shown in Table 2.

For the multivariable analysis, we decided to exclude cumulative stone diameter because of the co-linearity with the operative time (Figure 1). The multivariable analysis shows that a positive preoperative urine culture (RR: 2.99 [1.15–2.02]); $p = 0.003$), an operative time of more than 60 minutes (RR: 3.7 [1.28–2.25]); $p < 0.001$), stone procedure in the ureter (RR: 4.87 [1.66–3.30]); $p < 0.001$), postoperative stent (RR: 3.30 [1.51–5.08]); $p = 0.001$), and ureteric injury > grade 1 (RR: 2.96 [1.20–2.53]); $p = 0.003$) remained significantly associated with moderate to severe postoperative pain, as shown in Table 3.

Discussion

Ureteroscopic removal of stones (URS) was widely used in patients in whom ESWL was either not successful or was not suitable for the treatment of ureteral stone and renal stone. Our study was focused on both URSL and RIRS, which have been deemed as safe and having a higher success rate for removing the stones. Our data showed that stone free rate following ureterscopic removal of stone in the ureter was 99%, in kidney was 85% and in combined ureter and kidney was 85%. Similar studies also show a stone free rate of URS for ureteral of 80 to 100%6 and for renal calculi of 91%.[12]

Nowadays, endourology can be carried out in an ambulatory care setting. It can reduce the need for admissions and thus, cut health care costs. Although postoperative pain is not a common complication in URS, it is one of the most tabled complaints from patients who underwent URS when visiting ED. From the results, early

Table 2. Univariable analysis to indicate risk for post-operative moderate to severe pain

Factor	Crude risk ratio	P-value
Age < 50 yr	1.15 (0.85 - 1.55)	0.398
Male gender	1.28 (0.98 - 1.68)	0.082
ASA classification > 2	1.25 (1.19 - 4.53)	0.229
BMI < 25	1.00 (0.76 - 1.34)	1.000
History of UTI	1.11 (0.78 - 1.59)	0.621
Pre-op alpha-blocker	0.90 (0.66 - 1.21)	0.523
Pre-op stent	1.21 (0.90 - 1.64)	0.245
Pre-op urine culture positive	1.52 (1.17 - 1.99)	0.006
Previous ipsilateral stone removal procedure	1.05 (0.77 - 1.43)	0.785
General anesthesia	1.22 (0.91 - 1.66)	0.216
Operative time more than 60 min	1.75 (1.33 - 2.31)	< 0.001
Stone procedure (in comparison to kidney) Ureter Ureter and kidney	 1.58 (1.15 - 2.19) 1.73 (1.08 - 2.76)	 0.005 0.022
Cumulative stone diameter > 10 mm	1.61 (1.21 - 2.13)	< 0.001
Post-op stent	3.14 (1.70 - 5.82)	< 0.001
Bilateral procedure	1.57 (1.12 - 2.21)	0.033
Ureteric injury > grade 1	2.13 (1.63 - 2.80)	0.002
Equipment diameter large than 10 Fr	0.97 (0.74 - 1.26)	0.817
Residual stone fragment	0.98 (0.61 - 1.58)	1.000

yr = years, BMI = body mass index, UTI = urinary tract infection, min = minutes, ASA = American Society of Anesthesiologists, mm = millimetres, Pre-op = preoperative, Post-op = postoperative, Fr = French (from French catheter scale)

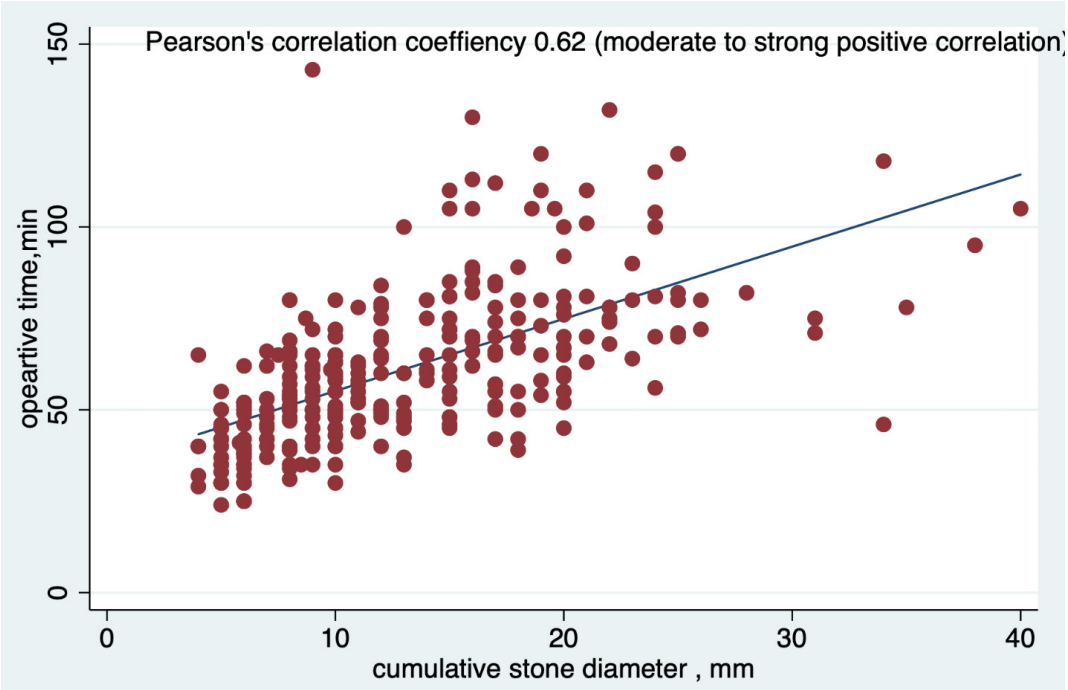

Figure 1. Correlation between operative time and stone size
min = minutes, mm = millimeters

Table 3. Multivariable analysis for post-operative moderate to severe pain (excluding cumulative stone size)

Factor	Adjusted risk ratio	P-value
Male gender	1.53 (0.94 - 1.55)	0.126
ASA classification > 2	1.00 (0.86 - 1.58)	0.316
Pre-op stent	-0.32 (0.72 - 1.25)	0.752
Pre-op urine culture positive	2.99 (1.15 – 2.02)	0.003
General anesthesia	1.90 (0.99 - 1.76)	0.058
Operative time more than 60 min	3.70 (1.28 - 2.25)	< 0.001
Stone procedure (compare to kidney)		
Ureter	4.87 (1.66 – 3.30)	< 0.001
Ureter and kidney	0.81 (0.76 – 1.93)	0.417
Post-op stent	3.30 (1.51 - 5.08)	0.001
Bilateral procedure	1.78 (0.97 – 1.78)	0.075
Ureteric injury > grade 1	2.96 (1.20 - 2.53)	0.003
Residual stone fragment	0.81 (0.75 – 1.97)	0.417

Yr = years, UTI = urinary tract infection, min = minutes, ASA = American Society of Anesthesiologists, Pre-op = preoperative, Post-op = postoperative, Fr = French
a Binary regression analysis

postoperative pain was a significant issue because experiencing postoperative pain was the most common concern expressed by patients.[13] It can interrupt sleep and limit the mobilization of the chest and skeletal muscles.[14] Moderate to severe pain scores also affected recovery time, length of hospital stay, readmissions, patient dissatisfaction and disturbance of quality of life, and increased costs.[15,16] The higher pain score was correlated with analgesic usage as patients whose immediate postoperative pain was poorly managed had a tendency to develop chronic pain after surgery.[17]

The mechanisms causing pain after URS were believed to be associated with many factors.

First, the operation can lead to hydroureter and hydronephrosis during use of URS irrigation solution. Furthermore, the acute distension of the renal capsule caused by the obstruction of urolithiasis and the consequent inflammation can result in pain. Pain receptors are located around the submucosa in the renal pelvis, calyces, renal capsule, and upper ureter.[18]

Pre-operative factors

Some factors, including age, gender, ASA classification, and BMI did not differ between the two groups, as was found in a similar study by Cakici et al.[19] Data pertaining to age, gender, BMI, and ASA classification showed no significant differences in complications after flexible URS. A preoperative stent was not related to moderate to severe postoperative pain, as was reported from the research conducted by Yuk et al. In that study they found that preoperative ureteral stenting did not affect perioperative complications or operative times, additional treatment rates, and stone-free rates. However, it increased the success rate of access sheath placement. Contrary to this result, Assimos et al.[20] reported that preoperative ureteral stenting decreased complications in patients with renal stones but not in those with ureteric stones. There was no relation between previous ipsilateral stone removal and moderate to severe postoperative pain. However, a previous report did describe an association with a lower rate of complaints by phone after the procedure.[21]

Positive urine culture is the single significant preoperative factor. The rationale behind this is that a positive urine culture increases the risk of infection and the resulting inflammation results in an increased incidence of pain and ED attendance.[5] There was no difference in pain between drug-resistant bacteria and non-drug-resistant bacteria.

However, intra-operative factors and general anesthesia techniques were not associated with moderate to severe postoperative pain to the same level as described in another study by Sahan et al.[22] There was no significant difference in GA and RA between postoperative pain among patients in our study who underwent URS, but Luo et al.[8] reported that the GA group had a significantly higher pain score than the RA group.

The location of stone also impacted on postoperative pain, especially stones located in the ureter and kidney. If the procedure was performed only in the ureter, it was more significantly related to postoperative pain than in stones in the kidney or stones in both the kidney and ureter. In our study, when we performed URS in both ureter and kidney simultaneously, we only selected patients who had a non-complex ureteral stone. This might explain a lower incidence of pain in patients who underwent URS in both the ureter and kidney at the same time.

The etiology of early postoperative pain after ureteroscopy is poorly understood and likely multifactorial but do include an increase intrapelvic pressure, extravasation of irrigation fluid, ureteral edema and ureteral injury.[23] In our study results, kidney stone removal had a significantly lower risk of postoperative pain. The majority of patient who had kidney stones underwent URS by flexible scope in combination with UAS and as a result intrarenal pelvis was lower than semi-rigid scope use. Fragmentation of ureteral stone was associated with a higher risk of ureteral injury.

An operative time of more than 60 minutes was another critical risk factor for predicting postoperative pain in our study. Operative time was related to hydronephrosis and hydroureter during operation, which cause ureteral edema and damage. Cheung et al.[24] also showed that surgery time greater than 60 minutes could increase the incidence of complications and postoperative pain. The factors which impacted the operative time were the cumulative stone size and bilateral procedure. In our study, stone size was associated with post-operative pain, but there was no significant relation with the bilateral procedure. This finding is similar to that described in a study by Ahn et al.[6] who discovered that moderate to severe postoperative pain was significantly associated with stone size but not significantly with operative time. A bilateral procedure had no impact a finding in common with other studies[25,26] which also reported no increased risk of complication in performing a bilateral URS.

Our study showed that ureteral injury was associated with postoperative pain ($p = 0.004$). To the contrary, a study from Oğuz et al.[7] had a different outcome. We suspected that the outcome was different because, their study[7] only included data pertinent to ureteral injury grade 1, while in our study patients with ureteral injury grade 1-3 were included.

Post-operative factor

Use of a postoperative stent is also related to postoperative pain. We found that cases that required a postoperative stent usually have a more significant ureteral injury, undergo dilation of the ureter wider than 10 Fr and had impact stone which made more significant ureteral mucosal injury and pain. Cheung et al.[24] also reported an association between the ureteral stents and pain. Nestler et al.[27] observed that discomfort and pain increased with the diameter of the indwelling ureter stent. In another study, el-Faqih et al.[28] showed that the patients who required ureteral stents developed dysuria and pain in 79% and 29% of cases, respectively. Du et al.[21] found that the most frequent complaint by the patients were symptoms associated with the stent. On the other hand, Segalen et al.[29] showed that there were no differences between patients with a postoperative stent and other patients with regard to pain and complications.

As is the case with all research, our study has some limitations. First, this study was retrospective in design; therefore, the information collected for analysis, e.g., stone removal technique, access sheath time, and reason for a postoperative stent may not be completely standardized. Secondly, multiple surgeons participated in the study, and the various surgical techniques, and the learning curve of the teams can have an impact on the result. Interestingly, Netsch et al.[30] showed that the learning curve has no impact on stone free rate and low grade complications. Thirdly, CT scans were not carried out on day one post operative on the patients in our study therefore there is the potential for us to have missed detection of some non-opaque stones.

Conclusions

Pain is a significant problem in postoperative URS. The risk factors associated with patients who had the procedure for ureteral stones were prolonged operative time, ureter injury and needed implantation of a stent after the procedure. These findings were similar to those in patients with a history of positive preoperative urine culture for bacteria. In conclusion, patients who have some or all of these factors need to be treated with caution, monitored for pain, and advised with regard to hospitalization after the procedure.

Conflict of Interest

The authors declare no conflict of interest.

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