Fluoroless-ureteroscopy for definitive management of distal ureteral calculi: randomized controlled trial

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Introduction: *To assess the conversion rate during fluoroless-ureteroscopy (URS) and evaluate the feasibility, safety, and efficacy of fluoroless-URS as a definitive management of distal ureteral calculi.*
Material and methods: *Between May 2013 and August 2015, patients with radio-opaque distal ureteral calculi of ≤ 1 cm in size were randomized to undergo fluoroless-URS or standard URS. Patients with previous ureteral surgery, ureteral kinking, ureteral stricture, single kidney, additional proximal ureteral or renal calculi, uncontrolled coagulopathy, and/or congenital anomalies of the urinary tract were excluded. Patients' demographics, stone characteristics, operative data, stone free status, and complications were compared between both groups.*
Results: *Seventy-four cases in the fluoroless-URS group were compared with 80 cases in the standard-URS group. There was no significant difference in the baseline characteristics between both groups in terms of the mean patient's age (28.8 ± 13.3 versus 29.5 ± 14.6 years; p = 0.76), body mass index (28.2 ± 33 versus 27.6 ± 2.3 kg/m^2; p = 0.19), and stone size (7.2 ± 1.5 versus 7.3 ± 1.7 mm; p = 0.70), respectively. Furthermore, there was no significant difference in the outcome parameters between both groups in terms of operative time (42.4 ± 8.3 versus 40.3 ± 6.5 min; p = 0.08), stone free rate (93.2% versus 95%; p = 0.06), and overall complications (12.2% versus 8.75%; p = 0.08), respectively. There was significant difference between both techniques in terms of fluoroscopy time (p < 0.001). However, 6 (7.5%) fluoroless-URS cases necessitated the use of fluoroscopy intraoperatively.*
Conclusion: *Ureteroscopic management of distal ureteral stones using fluoroless-URS technique could be feasible and safe, without radiation exposure for patients and medical personnel. However, fluoroscopy should always be available during fluoroless-URS.*

Key Words: ureteroscopy, fluoroscopy, management, ureteral calculi, outcomes

Introduction

Ureteral stones represent one-fifth of urinary stones and distal ureteral location was identified in about 70% of cases; the majority of these ureteral stones are symptomatic and require active intervention.[1,2] The introduction and the continuing progress in endoscopic instruments, especially ureteroscopes, revolutionized the management of ureteral stones.[3] However, ureteroscopy (URS) is classically performed under fluoroscopic guidance. Despite the fact that ionizing radiation exposure is minimal during ureteroscopy, there is a group of patients with recurrent urinary calculi, such as cystinuric patients, and are exposed to potentially higher doses of ionizing radiation during diagnosis, treatment, and follow up of their stone disease. These are vulnerable group and are at higher risk for the potential stochastic and deterministic hazards of ionizing radiation.[4,5] Fluoroless-URS has been shown to be safe under certain circumstances. However, it is not clear how often fluoroscopy will be needed during fluoroless-URS. Therefore, the aim of this randomized study was to assess the conversion

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rate from fluoroless-URS to standard-URS and compare the outcomes between both techniques in terms of the stone free rate and complications during management of distal ureteral calculi. Our hypothesis was that the conversion rate will not exceed 10% and fluoroless-URS could be performed with a safety profile and outcomes comparable with standard-URS.

Materials and methods

Study design

This prospective randomized study was conducted at our tertiary care center between May 2013 and August 2015. Local research ethics were followed and informed consents were obtained. One-hundred and sixty patients, presented and diagnosed with symptomatic radio-opaque distal ureteral stones of ≤ 1 cm in size, were recruited. All patients underwent KUB (kidney-ureter-bladder), ultrasound abdomen and pelvis, and intravenous urography (IVU) or non-contrast computed tomography (NCCT). Stone size was measured by the largest diameter on KUB or NCCT. Preoperative laboratory investigations included complete blood count, serum creatinine, blood urea nitrogen, bleeding profile, and urine culture. Patients with positive urine culture received the appropriate antibiotic prior to the intervention. Patients with previous ureteral surgery, ureteral tortuosity (kinking), ureteral stricture, single kidney, additional proximal ureteral or renal calculi, uncontrolled coaggulopathy, and/or congenital anomalies of the urinary tract were excluded.

Patients who fulfilled the inclusion and exclusion criteria and accepted to participate in the study were randomized into two groups using closed envelopes. One group included 80 patients who were treated by standard-URS, and the other group included 80 patients who were treated by fluoroless-URS, Figure 1.

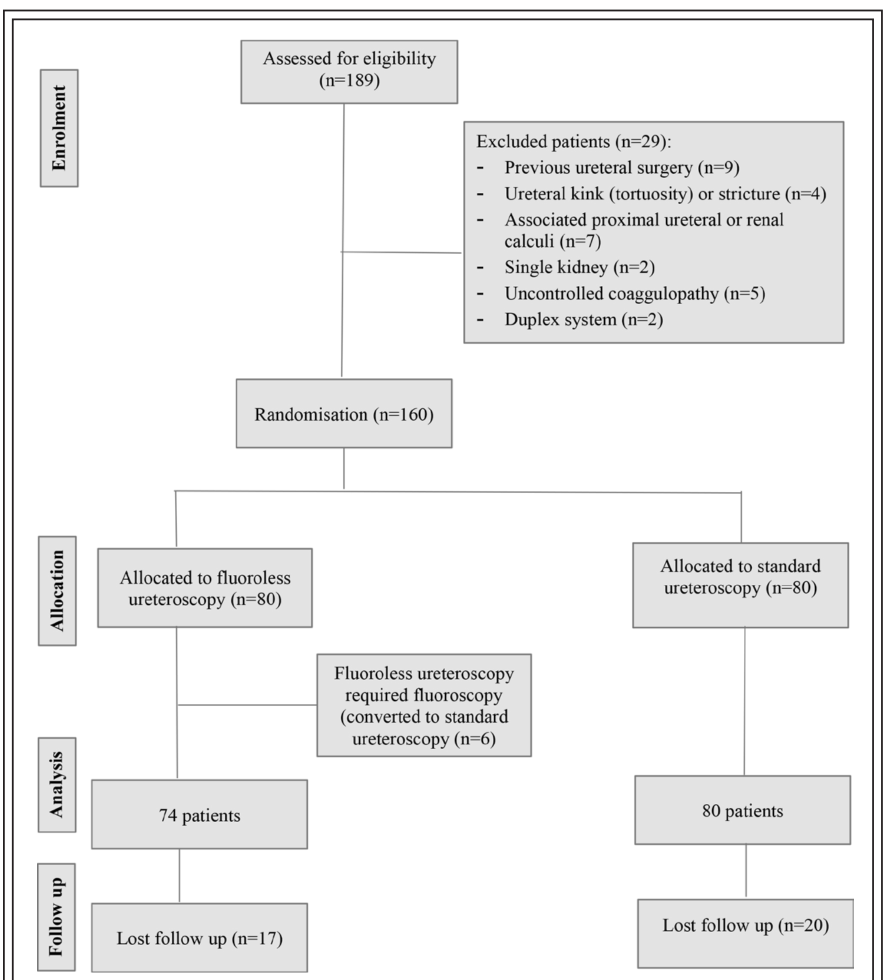

Figure 1. Flow chart.

Operative technique

Under spinal anesthesia, cystourethroscopy was performed in lithotomy position in both groups to exclude any pathology in the urethra and bladder and identify the ureteral offices.

In the fluoroless-URS group, 0.035-inch sensor guidewire with hydrophilic tip (Boston Scientific), was introduced through the targeted ureteral orifice. The guidewire was smoothly manipulated up until reaching the stone and was then advanced up in the kidney using both tactile and visual cues. Whenever, a resistance was met at the level of the stone, fine down and up movements were performed to manipulate the wire beyond the stone until facing the resistance from contacting the kidney. The length of the guidewire was used as an indicator for reaching the kidney. An open-tip 6F ureteral catheter was then advanced over the guidewire up the kidney and the guidewire was removed. Observation of warm urine coming out from the ureteral catheter was a good sign of correct placing of the guidewire. A 0.038 inch PTFE (Polytetrafluoroethylene) guidewire was then inserted through the ureteral catheter and the catheter was removed. The 9.5F semi-rigid ureteroscope (Karl Storz), was used to check the distal part of the ureter, assure the correct placement of the guidewire, and see the stone. Whenever needed, 6F to 10F polytetrafluoroethylene (Teflon) dilators were used to dilate the ureteral orifice to facilitate ureteroscope entrance and stone extraction. The stones were removed either in-toto or after disintegration by the pneumatic Swiss lithoclast. The stones were removed using a dormia basket and/or forceps. The whole ureter was then inspected by the semi-rigid ureteroscope up to the renal pelvis to exclude the presence of residual fragments and/or false passage in the upper ureter and make sure that the guidewire resides in the kidney. The semirigid ureteroscope was then removed and an open-tip ureteral catheter was advanced over the guidewire and fixed to an indwelling 16F Foley catheter for 24 hours.

In the standard-URS group, the procedure was similar. Yet, the guidewire and the ureteral catheter were inserted under fluoroscopic guidance.

Urinary ultrasonography and KUB were performed 6 hour postoperatively to detect residual stones and confirm the position of the ureteral catheter. Cases without obvious residual stones in both KUB and US were considered stone free. All patients were asked to show up after 4-6 weeks to undergo follow up KUB. The primary outcome of this study is the conversion rate from fluoroless-URS to standard-URS. The secondary outcomes were the stone free rate and the early complications.

Statistical analysis

Calculation of the sample size for this randomized controlled trial was carried out using the G* Power 3.1.9.2 for Windows, which was freely downloaded from the website: http://www.gpower.hhu.de/ that was accessed on January 11th 2013. The sample size was calculated based on an arbitrarily expected conversion rate of 10% with a power ((1-β err probability) of 0.85, and two-tailed α err probability of 0.05 and effect size (d) of 0.5, with allocation ratio N2/N1 = 1 required 73 patients for each group. Data were collected, tabulated, and analyzed using the IBM SPSS Statistics for Windows (IBM Corporation, Armonk, NY, USA) version 22. Descriptive data were presented as numbers and percentages or means ± standard deviations. The Fisher exact test or Chi-Square test were used to compare categorical variables while the Student (t) test or Mann Whitney-U test were used for comparing continuous variables. Two tailed p values of < 0.05 were considered statistically significant

Results

Seventy- four cases in the fluoroless-URS group were compared with 80 cases in the standard-URS group, Figure 1. There was no statistically significant difference between both groups in patients' characteristics in terms of the age (28.8 ± 13.3 versus 29.5 ± 14.6 years), female gender (44.6% versus 39.8%), and BMI (28.2 ± 3.3 versus 27.6 ± 2.3 kg/m^2) in the fluoroless-URS group compared with the standard-URS group, respectively (p values > 0.05), Table 1. Similarly, there was no statistically significant difference between both groups in the stone characteristics in terms of the mean size (7.2 ± 1.5 versus 7.3 ± 1.7) and right sided stones (44.6% versus 56.3%) in the fluoroless-URS group compared with the standard-URS group, respectively (p values > 0.05), Table 1. Male predominance was observed in both groups, (41/74) in the fluoroless-URS group and (49/80) in the standard-URS group.

Regarding the operative and outcome parameters, there was no significant difference between the fluoroless-URS and the standard-URS group in terms of the mean operative time (42.4 ± 8.3 versus 40.3 ± 6.5 minutes) and stone free rate (SFR) (93.2% versus 95%). There was significant difference between both techniques in terms of fluoroscopy time ($p < 0.001$), Table 1.

Furthermore, the overall complication rates were comparable between the fluoroless-URS and the standard-URS (12.2% versus 8.75 %), respectively. In the fluoroless-URS group, there were four cases (5.4%) of stone migration; one was extracted from the middle ureter by the semi-rigid ureteroscope during the procedure while the other three cases were managed by auxiliary shock wave lithotripsy (SWL) 1 week after the procedure. In the standard-URS group, there were two cases (2.5%) with stone migration, in one of them the stone was extracted by ureteroscopy from the middle ureter, and in the second case the stone migrated up to the kidney and managed later on by auxiliary SWL. Furthermore, two cases of fever (> 37.5ºC) and hematuria (> 24 hour) were identified in each group. The fever in all cases persisted less than 48 hours and managed by the same scheduled antibiotic and antipyretic. Hematuria was moderate and managed by continuation of the intravenous fluid for 24-48 hours. Both the ureteral catheter and the urethral catheter were removed 24 hours postoperatively in all patients, except for two patients in each group with hematuria persisted > 24 hour where these were removed after 48 hours. In terms of the follow up, 57 (77%) patients showed up in fluoroless-URS group

TABLE 1. **Baseline characteristics and outcomes**

Parameter	Fluoroless-URS (n = 74)	Standard-URS (n = 80)	p value
Mean age (years)	28.8 ± 13.3	29.5 ± 14.6	0.76
Gender			0.46
Male: No (%)	41 (55.4%)	49 (29.5%)	
Female: No (%)	33 (44.6%)	31 (39.8%)	
Mean stone size (mL)	7.2 ± 1.5	7.3 ± 1.7	0.70
Stone side			0.15
Right	33 (44.6%)	45 (56.3%)	
Left	41 (55.4%)	35 (43.7%)	
Mean body mass index	28.2 ± 3.3	27.6 ± 2.3	0.19
Mean operative time (minutes)	42.4 ± 8.3	40.3 ± 6.5	0.08
Fluoroscopy time (minutes)	0.0 ± 0.0	1.2 ± 0.6	< 0.001
Complications			0.42
Overall	9 (12.2%)	7 (8.75%)	
Stone migration (Clavien Grade IIIa/Grade IIIb)	4 (5.4%)	2 (2.5%)	
Fever (Clavien Grade I)	2 (2.7%)	2 (2.5%)	
Hematuria (Clavien Grade I)	3 (4.1%)	3 (3.8%)	
Stone free status			0.21
Stone free	69 (93.2%)	76 (95%)	
Residual stone	5 (6.8%)	4 (5%)	0.21

and 60 (75%) showed up in standard-URS group and the stone free rate was 100% in both groups, Figure 1.

Six (7.5%) fluoroless-URS cases necessitated the use of fluoroscopy intraoperatively due to failure to advance the guidewire up in the kidney due to impacted stone in four cases and due to occurrence of false passage in two cases, Figure 1. All six cases were completed successfully and the standard technique of inserting 6F open-tip ureteral catheter tied to a 16F indwelling urethral catheter was followed except in the two cases with false passage where 6/28 JJ stent was inserted and left for 2 weeks. The mean fluoroscopy time for these cases was 0.8 ± 0.3 minute.

Discussion

Despite the high percentage of spontaneous passage of small ureteral calculi,[6] larger stones may need active intervention. Ureteroscopy is the ideal modality for removing distal ureteral stones.[6] Endoscopic procedures are safer when performed under fluoroscopic guidance.[7] However, the use of ionizing radiation may be harmful to patients and medical team leading to eye diseases,[8] neoplastic changes[5] and orthopedic problems from wearing heavy protective aprons.[9]

Several attempts were made to decrease ionizing radiation exposure during URS. Controlling the foot pedal by the urologist and using the "last image hold" decreased radiation exposure by 40 times (from 100 mSv to 2.5 mSv).[10] Furthermore, the use of physical markers and laser guidance resulted in 82% reduction in fluoroscopy time (FT) (from 86.1 to 15.5 seconds; $p < 0.001$), without affecting operative time or procedural outcomes.[11] In addition, using pulsed fluoroscopy at 4 frames/second resulted in 62.4% reduction in FT (from 109.1 to 44.1 seconds), when compared with the standard fluoroscopy at 30 frames/sec during ureteroscopy.[12] Moreover, when Lipkin et al and His and Harper used fluoroscopy reduction techniques, the median effective dose was brought down to 1.13 mSv and 0.05 mSv during ureteroscopy, respectively.[13,14]

Prior publications demonstrated variable techniques to obtain radiation-free ureteroscopic procedure.[15-17] The aim of the current study was to assess the rate of conversion from fluoroless-URS to standard-URS and evaluate the outcomes of fluoroless-URS compared with the outcomes of the standard-URS for management of distal ureteral calculi.

The mean operative time of fluoroless-URS ranged from 34.51 to 53 min in previous studies.[14,15] In the present study, the mean operative time was slightly longer in the fluoroless-URS group compared with the standard-URS group (42.4 ± 8.3 min versus 40.3 ± 6.5 min). However, this difference was statistically insignificant.

In terms of the complications, these were insignificantly higher in the fluoroless-URS group compared with the standard-URS group. The complications in the fluoroless-URS group in the current study, including stone migration, fever, and hematuria were comparable with the complications in Tepeler et al study.[16]

In this study, a SFR of 93.2% was achieved in fluoroless-URS cohort, which was comparable with the SFR in the standard-URS group (95%). These results were congruent with the results of Mandhani et al and Tepler et al where the SFR in the fluoroless-URS was 94.2% and 96.77%, respectively.[15,16]

However, fluoroless insertion of JJ stent has been reported,[18] there was no need for JJ stent insertion in the current except in the two cases where fluoroless-URS was converted to standard-URS due to false passage. In our department, we follow a standardized technique of inserting a 6F open-tip ureteral catheter and tie it to an indwelling 16F urethral catheter, leave both overnight, remove them the next morning and discharge our patients. This avoids another invasive cystoscopy to remove JJ stents.

It is worth noting that despite the strict selection criteria, fluoroscopy was needed in 6 (7.5%) of fluoroless-URS cases. Therefore, we strongly recommend that C-arm should be available during fluoroless-URS and the urologist should not hesitate to use it, when needed.

This randomized prospective study has some limitations which could be addressed in the rigorous selection criteria, and inclusion of distal ureteral stones only. Another limitation could be the relatively small mean stone size. However, our intention was to restrict the selection criteria hoping to achieve complete ureteroscopy without the use of ionizing radiation. Also, we only included the distal ureteral calculi because we do not have the set up for flexible ureteroscopy and laser lithotripsy. Another limitation is the lack of assessing long term outcomes such as ureteral stricture disease. Nonetheless, to our knowledge this the first level 1 evidence study to address the feasibility and safety of fluoroless-URS, under certain circumstances, keeping in mind that the conversion rate is around 7.5%. Therefore, fluoroscopy should be available in the standby state for the safety of the patient and better outcome of the procedure. Future multicenter studies are needed to include proximal ureteral calculi and adjust the selection criteria for complete fluoroless-URS.

Conclusion

Ureteroscopic management of distal ureteral stones using fluoroless-URS technique could be feasible and safe, with comparable outcomes with the standard-URS and zero radiation exposure for patients and medical personnel. However, fluoroscopy should always be available during fluoroless-URS because it will be needed in almost 7.5% of cases. □

References

1. Bensalah K, Pearle M, Lotan Y. Cost-effectiveness of medical expulsive therapy using alpha-blockers for the treatment of distal ureteral stones. *Eur Urol* 2008;53(2):411-418.
2. Ketabchi AA, Aziziolahi GA. Prevalence of symptomatic urinary calculi in Kerman, Iran. *Urol J* 2008;5(3):156-160.
3. Türk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M, Knoll T. EAU Guidelines on Interventional Treatment for Urolithiasis. *Eur Urol* 2016;69(3):475-482.
4. Nascimento R, Coleman J, Solomon S. Current and future imaging for urologic interventions. *Curr Opin Urol* 2008;18(1):116-121.
5. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. *N Engl J Med* 2007;357(22):2277-2284.
6. Preminger GM, Tiselius HG, Assimos DG et al. 2007 Guideline for the management of ureteral calculi. *Eur Urol* 2007;52(6):1610-1631.
7. Geavlete P, Multescu R, Geavlete B. Health policy: reducing radiation exposure time for ureteroscopic procedures. *Nat Rev Urol* 2011;8(9):478-479.
8. Kleiman N. Radiation cataract. New insights on risk and basic safety standards. Brussels: European Commission. 2007;81-95.
9. Ross AM, Segal J, Borenstein D, Jenkins E, Cho S. Prevalence of spinal disc disease among interventional cardiologists. *Am J Cardiol* 1997;79(1):68-70.
10. Bagley DH, Cubler-Goodman A. Radiation exposure during ureteroscopy. *J Urol* 1990;144(6):1356-1358.
11. Greene DJ, Tenggadjaja CF, Bowman RJ et al. Comparison of a reduced radiation fluoroscopy protocol to conventional fluoroscopy during uncomplicated ureteroscopy. *Urology* 2011;78(2):286-290.
12. Elkoushy MA, Shahrour W, Andonian S. Pulsed fluoroscopy in ureteroscopy and percutaneous nephrolithotomy. *Urology* 2012;79(6):1230-1235.
13. Lipkin ME, Wang AJ, Toncheva G et al. Determination of patient radiation dose during ureteroscopic treatment of urolithiasis using a validated model. *J Urol* 2012;187(3):920-924.
14. Hsi RS, Harper JD. Fluoroless ureteroscopy: zero-dose fluoroscopy during ureteroscopic treatment of urinary tract calculi. *J Endourol* 2013;27(4):432-437.
15. Mandhani A, Chaudhury H, Gupta N, Singh HK, Kapoor R, Kumar A. Is fluoroscopy essential for retrieval of lower ureteral stones? *Urol Int* 2007;78(1):70-72.
16. Tepeler A, Armagan A, Akman T et al. Is fluoroscopic imaging mandatory for endoscopic treatment of ureteral stones? *Urology* 2012;80(5):1002-1006.
17. Olgin G, Smith D, Alsyouf M, Arenas JL et al. Ureteroscopy without fluoroscopy: a feasibility study and comparison with conventional ureteroscopy. *J Endourol* 2015;29(6):625-629.
18. Brisbane W, Smith D, Schlaifer A, Anderson K, Baldwin DD. Fluoro-less ureteral stent placement following uncomplicated ureteroscopic stone removal: a feasibility study. *Urology* 2012;80(4):766-770.