

Safety and Efficacy of Flexible Ureterorenoscopy Surgery in Different Age Groups

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ABSTRACT

Objective: To comparatively investigate the efficacy, safety and complications of flexible ureterorenoscopy (f-URS) in the treatment of patients of different age groups (<60, 60-74 and ≥75 years) with proximal ureteral and kidney stones.

Study Design: Descriptive study.

Place and Duration of Study: Department of Urology, HSU Izmir Bozyaka Training and Research Hospital, HSU Ankara Diskapi Training, Research Hospital, and Mustafa Kemal University Faculty of Medicine, between March 2014 and June 2020.

Methodology: Nine hundred and fifty-six patients, who underwent f-URS due to proximal ureteral and kidney stones, were divided into three age groups as <60 years (Group 1), 60-74 years (Group 2) and ≥75 year (Group 3). The patients' American Society of Anesthesiologists (ASA) score, Charlson Comorbidity Index (CCI), anticoagulant use, stone-free rates and surgical and medical complication rates were examined for each group.

Results: There were 688 patients in Group 1, 230 in Group 2, and 38 in Group 3. A significant difference was observed between the age groups in terms of CCI and anticoagulant use ($p < 0.001$ for both). The highest rate of medical complications was observed in Group 3 at 42.1%, followed by Group 2 at 17.8%, while the lowest rate was observed in Group 1 at 2.3% ($p < 0.001$). As a result of the multivariate analysis, receiving anticoagulant treatment ($p = 0.002$) and having a high CCI ($p = 0.005$) were independent predictors of medical complication development.

Conclusion: It was clearly demonstrated that f-URS could be used as a safe and effective alternative for the treatment of moderate-size kidney stones in all age groups.

Key Words: Elderly, Geriatric patients, RIRS, Holmium laser lithotripsy, Urolithiasis, Safety, Efficacy.

How to cite this article: Koras O, Bozkurt IH, Karakoyunlu AN, Polat S, Yarimoglu S, Degirmenci T. Safety and Efficacy of Flexible Ureterorenoscopy Surgery in Different Age Groups. *J Coll Physicians Surg Pak* 2021; **31(06)**:679-685.

INTRODUCTION

Various studies have shown that the prevalence of kidney stones is increasing, and its incidence also rises with advancing age.¹ The World Health Organization (WHO) defines individuals aged 65 years and older as the elderly.² It is estimated that the population over the age of 60 years will exceed 2 billion over the next three decades, and stone disease will be more common in elderly patients, secondary to the increase in the incidence of kidney stones with the prolongation of life expectancy.³

There is still no standardisation for the surgical approach in elderly patients due to increasing comorbidities and surgical complications. Although aging itself is not a disease, it is feared that the decrease in functional organ reserve with aging may trigger complications in the perioperative and postoperative period. Therefore, it is very important to determine the surgical procedure to be performed in elderly patients.

Flexible ureterorenoscopy (f-URS), first performed in the 1990s,⁴ has become the first option in the treatment of upper urinary tract stones smaller than 2 cm, with the advances in flexible endoscopes, light and image quality, and stone breaking technologies.⁵ f-URS is a minimally invasive surgical procedure with a higher success rate than extracorporeal sound wave lithotripsy (ESWL) and less morbidity than percutaneous nephrolithotomy (PCNL) and open stone surgery.⁶ The treatment of upper urinary tract stones has changed in recent years due to low morbidity and high success rates.

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Received: March 08, 2021; Revised: April 28, 2021;

Accepted: May 18, 2021

DOI: <https://doi.org/10.29271/jcpsp.2021.06.679>

Table I: Patient and stone characteristics.

Variables	Group 1 (<60 years) (n = 688)	Group 2 (60-74 years) (n = 230)	Group 3 (≥75 years) (n = 38)	p-value
Age, years, median (IQR)	42 (34-49) ^a	62 (62-66) ^b	84 (79-87.25) ^c	<0.001
Gender, n (%)				
Female	212 (30.8) ^a	117 (50.9) ^b	15 (39.5) ^{a,b}	<0.001*
Male	476 (69.2) ^a	113 (49.1) ^b	23 (60.5) ^{a,b}	
BMI, kg/m ²	26.4 (24.0-29.1) ^a	28.5 (26.0-32.4) ^b	27.0 (23.0-29.4) ^a	<0.001
Previous history of ESWL, n (%)	109 (15.8)	39 (17.0)	8 (21.1)	0.686
Metabolic syndrome, n (%)	55 (8.0) ^a	64 (27.8) ^b	27 (71.1) ^c	<0.001
ASA category, n(%)				<0.001 [^]
ASA I	374 (54.4) ^a	31 (13.5) ^b	0 ^c	
ASA II	281 (40.8) ^a	137 (59.6) ^b	17 (44.7) ^{a,b}	
ASA III	33 (4.8) ^a	57 (24.8) ^b	15 (39.5) ^b	
ASA IV	0 ^a	5 (2.2) ^b	6 (15.8) ^c	
CCI, score	0 (0-1)	3 (2-4)	5 (5-6)	<0.001
Anticoagulant therapy, n (%)	69 (10.0)	33 (14.3)	12 (31.6)	<0.001
Abnormal renal anatomy, n (%)	42 (6.1)	22 (9.6)	5 (13.2)	0.075
Side, n (%)				0.205
Right	343 (49.9)	99 (43.0)	15 (39.5)	
Left	325 (47.2)	124 (53.9)	23 (60.5)	
Bilateral	20 (2.9)	7 (3.0)	0 (0.0)	
Stone location, n (%)				0.228
Lower calyx	126 (18.3)	58 (25.2)	8 (21.1)	
Middle calyx	52 (7.6)	22 (9.6)	3 (7.9)	
Upper calyx	41 (6.0)	6 (2.6)	1 (2.6)	
Pelvis	164 (23.8)	44 (19.1)	13 (34.2)	
Proximal ureteral	136 (19.8)	39 (17.0)	3 (7.9)	
Multicaliceal	94 (13.7)	34 (14.8)	4 (10.5)	
Kidney + ureteral	49 (7.1)	17 (7.4)	4 (10.5)	
Pelvis + single calyx	26 (3.8)	10 (4.3)	2 (5.3)	
Preoperative Hydronephrosis, n(%)				0.501
Grade 0	308 (44.8)	107 (46.5)	16 (42.1)	
Grade 1	310 (45.1)	92 (40.0)	15 (39.5)	
Grade 2	53 (7.7)	25 (10.9)	5 (13.2)	
Grade 3	17 (2.5)	6 (2.6)	2 (5.3)	
Stone length, mm	13 (10-20)	14 (10-20)	15 (10-20.5)	0.104
Stone density, HU	1033.5 (864.2-1204)	1023 (858.5-1201)	1015 (854.2-1123.5)	0.143
Number of stones, n (%)				0.801
Single	470 (68.3)	157 (68.3)	24 (63.2)	
Multiple	218 (31.7)	73 (31.7)	14 (36.8)	
Preoperative stent, n (%)	111 (16.1)	52 (22.6)	5 (13.2)	0.063
Intraoperative characteristics				
Operation time, min, median (IQR)	45 (35-60)	49.5 (38.75-65)	50 (45-70)	0.068
Fluoroscopy time, sec, median (IQR)	19 (10-40)	19 (9-40)	21 (10-40.5)	0.918
Use of ureteral access sheath, n(%)	524 (76.2)	175 (76.1)	30 (78.9)	0.924
Postoperative double-J stent placement, n(%)	628 (91.3)	220 (95.7)	38 (100.0)	0.018

*Likelihood ratio; ^Exact test. The same superscripts show that there are no statistically significant differences between groups.

ESWL: Extracorporeal shock wave lithotripsy, ASA: American Society of Anesthesiologists, CCI: Charlson Comorbidity Index, HU: Hounsfield unit.

The aim of this study was to comparatively investigate the efficacy, safety and complications in patients of different age groups (<60 years, 60-74 years and ≥75 years) who underwent f-URS for the treatment of kidney stones.

METHODOLOGY

After obtaining the approval of the Ethics Committee (Decision No. 27, meeting No. 13, dated: 12/11/2020), the data of 956 patients, who underwent f-URS for the treatment of proximal ureteral and kidney stones between 2014 and 2020 at HSU Izmir Bozyaka Training and Research Hospital, HSU Ankara Diskapi Training and Research Hospital, and Mustafa

Kemal University Faculty of Medicine, Turkey, were retrospectively analysed in three age groups: <60 years (Group 1), 60-74 years (Group 2), and ≥75 years (Group 3). The number, size, location and density [Hounsfield unit (HU)] of the stones and hydronephrosis degree were recorded. The patients' demographic characteristics, American Society of Anesthesiologists (ASA) score, Charlson Comorbidity Index (CCI), use of anticoagulants, operative time (time from the insertion of the cystoscope into the urethra to the insertion of the double-J stent into the ureter), fluoroscopy duration, stone-free rates, and surgical and medical complication rates were recorded for each group.

Table II: Postoperative results.

Variables	Group 1 (<60 years) (n = 688)	Group 2 (60-75 years) (n = 230)	Group 3 (≥75 years) (n = 38)	p-value
Postoperative characteristics n (%)				
Stone-free rate	561 (81.5)	181 (78.7)	28 (73.7)	0.354
Complication rate	74 (10.8)	38 (16.5)	6 (15.8)	0.057
CIRF ^a rate	31 (4.5)	18 (7.8)	2 (5.3)	0.152
Finally Success rate	602 (87.5)	196 (85.7)	31 (81.6)	0.430
Hospitalization time, day, median (IQR)	1 (1-1) ^a	1 (1-1) ^a	1 (1-3) ^b	0.003
Re-procedure requirement				0.696*
Follow-up	84 (12.2)	30 (13.0)	8 (21.1)	
ESWL	7 (1.0)	4 (1.7)	1 (2.6)	
Second RIRS	49 (7.1)	22 (9.6)	2 (5.3)	
PCNL	3 (0.4)	1 (0.4)	0	
Complication grades				0.143 [^]
Grade 1	54 (7.8)	31 (13.5)	5 (13.2)	
Postoperative hematuria	16	12	2	
Fever requiring antipyretics	38	18	3	
Perforation managed by without intervention	-	1	-	
Grade 2	6 (0.9)	4 (1.7)	0	
Fever requiring antibiotic	1	2	-	
Perirenal hematoma	1	-	-	
Non-obstructive steinstrasse	4	2	-	
Grade 3a	6 (0.9)	2 (0.9)	0	
Perirenal abscess requiring percutaneous drainage	-	1		
Perforation managed by ureteric stenting	1	-	-	
Stent migration	5	1		
Grade 3b	6 (0.9)	1 (0.4)	0	
Obstructive steinstrasse	5	-		
Ureter structure	1	1		
Grade 4	1 (0.1)	0	0	
Urosepsis	1	-	-	
Grade 5	1 (0.1)	0	1 (2.6)	
Death due to urosepsis	1	-	1	
Medical Complications	16 (2.3) ^a	41 (17.8) ^b	16 (42.1) ^c	<0.001
Arrhythmia	4	14	4	
Angina pectoris	2	8	3	
Dyspepsia	4	7	2	
TIA	-	2	2	
COPD faring	5	7	3	
Delirium	1	3	2	

*Likelihood ratio; [^]Exact test. The same superscripts show that there are no statistically significant differences between groups.
CIRF: Clinically insignificant residual fragment, Extracorporeal shock wave lithotripsy, PCNL: Percutaneous nephrolithotomy, TIA: Transient ischemic attack, COPD: Chronic obstructive pulmonary disease.*

Non-contrast computed tomography was preoperatively performed in all patients to evaluate the location, size, surface area (mm²) and other properties of the stones. Urine culture was taken from each patient before surgery, and those with urinary tract infection were given appropriate antibiotic treatment and taken into operation once no

growth was observed in their urine culture. The three groups were compared in terms of operative time, fluoroscopy duration, length of hospital stay, stone-free rate, clinically insignificant residual fragment (CIRF) and second attempt rates, and perioperative and postoperative complications according to the Clavien-Dindo classification.⁷

Table III: Univariate and multivariate analyses of factors associated with medical complications.

	OR (95% CI)	p value	OR (95% CI)	p value
BMI	1.069 (1.021-1.120)	0.005	1.053 (0.998-1.111)	0.062
Age category				
Group 1	ref.	<0.001	ref.	
Group 2	9.111 (5.001-16.559)	<0.001	2.122 (0.848-5.311)	0.108
Group 3	30.545 (13.552-68.850)	<0.001	2.412 (0.522-11.154)	0.260
Metabolic syndrome	3.768 (2.256-6.294)	<0.001	0.681 (0.338-1.373)	0.283
Stone length	0.973 (0.942-1.005)	0.099		
Stone density	1.000 (0.999-1.001)	0.922		
Operative time	1.013 (1.003-1.022)	0.010	1.004 (0.992-1.016)	0.478

ASA category				
ASA I	ref.		ref.	
ASA II	3.494 (1.646-7.414)	0.001	1.005 (0.408-2.478)	0.991
ASA III	13.750 (6.185-30.567)	<0.001	1.181 (0.358-3.896)	0.785
ASA IV	77.000 (19.086-310.654)	<0.001	1.052 (0.130-8.481)	0.962
Anticoagulant therapy	4.316 (2.528-7.367)	<0.001	2.885 (1.490-5.583)	0.002
CCI	2.086 (1.798-2.420)	<0.001	1.754 (1.185-2.598)	0.005

CI: Confidence interval, BMI: Body mass index, ASA: American Society of Anesthesiologists, CCI: Charlson Comorbidity Index.

Perioperative complications were divided into surgical and medical groups. Surgical complications were defined as either direct procedure-related or perioperative consequences (pelvis or calyx perforation, ureteral injury, bleeding, etc.), while medical complications were accepted as those that resulted from deterioration in the current state of a patient secondary to perioperative stress, intubation, and anesthesia.

All procedures were performed with the patients in the standard lithotomy position under general anesthesia. Intravenous antibiotic prophylaxis was applied to all patients at the beginning of anesthesia according to the EAU guidelines. Operations were performed with rigid and flexible ureteroscopy. Stones were pulverised with the Holmium: YAG laser. Urethral access sheath (UAS) placement at the beginning and double-J stent placement at the end of the operation were also undertaken according to the surgeon's preference. Stone-free rate was defined as the absence of a detectable stone on ultrasonography and radiography at the first postoperative month or the absence of a stone fragment larger than 2 mm on computed tomography. If there were residual stones at the follow-up, a second session was planned for retrograde intrarenal surgery (RIRS) or ESWL.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 23 for Windows. Categorical data were presented as numbers and percentages. The compliance of continuous data to normal distribution was evaluated with the Kolmogorov-Smirnov test. Continuous data did not conform to normal distribution and were given as median (interquartile range) values. Chi-square, Likelihood ratio or Exact test was used in the comparison of categorical data. The Kruskal-Wallis test was used for the comparison of non-normally distributed data. For the variables that were found to be significant, a pairwise analysis was also undertaken. The Bonferroni correction was applied in pairwise comparisons. The univariate logistic regression analysis was performed to evaluate the factors associated with medical complications, and parameters that were found to be significant at this stage were further examined using the multivariate analysis. A value of $p < 0.05$ was considered statistically significant.

RESULTS

A total of 956 patients were included in the study. The characteristics of the patients and stones are given in Table I. Body mass index was significantly higher in Group 2 compared to

the remaining groups ($p < 0.001$). The frequency of metabolic syndrome was found to be 8%, 27.8%, and 71.1% in Groups 1, 2 and 3, respectively ($p < 0.001$). There was a significant difference between the groups in terms of the ASA scores. The number of patients with high ASA scores (III, IV) was significantly higher in Groups 2 and 3 compared to Group 1. A significant difference was also observed between the age groups in terms of CCI and anticoagulant use ($p < 0.001$ for both). The intraoperative findings of the patients are shown in Table I. Only postoperative DJ stent use was significantly differ between the groups ($p = 0.018$).

The postoperative results of the patients are given in Table II. The length of hospital stay was statistically significantly higher in Group 3 ($p = 0.003$). Surgical complication development was similar in Groups 1, 2 and 3 at the rates of 10.8%, 16.5%, and 15.8%, respectively ($p = 0.057$). The classification of complications according to the Clavien-Dindo system is also shown in Table II. A significant difference was observed between the groups in relation to the medical complications ($p < 0.001$). The highest rate of medical complications was observed in Group 3 at 42.1%, followed by Group 2 at 17.8%, and the lowest in Group 1 at 2.3% ($p < 0.001$).

Table III presents the results of the univariate and multivariate analyses of factors associated with medical complications. The multivariate analysis revealed that receiving anticoagulant treatment ($p = 0.002$) and having a high CCI ($p = 0.005$) were independent predictors of medical complication development.

DISCUSSION

It has been shown that the incidence of kidney stones has increased in the elderly population in developed countries.¹ In this population, it is estimated that the stone prevalence is 19.1% among men and 9.4% among women.⁸ In addition, if urolithiasis is not treated in this age group, there is a higher rate of morbidity and infection,⁹ which has been associated with the absence of classical renal colic symptoms in certain patients delaying the diagnosis or the presence of complicated stones.⁸ The complications and outcomes of an operation are affected by the presence of complicated stones, aging, and increased comorbidities. In this study, the success rates were similar between all three groups, but complications were higher in the elderly patients.

The success of f-URS is higher than ESWL, and it has been proven that it has less morbidity than PCNL and open stone surgery.⁶ f-URS can be considered as a minimally invasive

endourological approach and has become a preferred option in the treatment of kidney stones with high success and limited complication rates, especially in complicated cases such as pregnancy, obesity, coagulopathy, skeletal deformity, and kidney anomalies.¹⁰ Previous studies have emphasised that f-URS has a high stone-free and lower complication rate, but the most appropriate treatment for elderly patients with kidney stones has not yet been clearly defined.¹¹ In a meta-analysis comparing patients that underwent f-URS and ESWL due to stone disease, the stone-free rate was reported to be higher and the rate of retreatment was lower in the f-URS group.¹² Similarly, in a study evaluating patients aged over 80 years, who underwent f-URS, the stone-free rate was found to be 71.4%.⁹ In the same study, operative time was found to be statistically significantly higher among the elderly patients, which was attributed to surgeons being more cautious in this patient group due to their age and comorbidities. Desai *et al.* found a >90% success rate for f-URS among patients with 1-2 cm stones.¹³ In this study, the stone-free rate was found to be high, consistent with the literature, and there was no significant difference between the groups in terms of the stone-free rate or operative time. There are many factors affecting the stone-free rate after f-URS, such as the surgeon's experience, stone size, stone location, and infundibulopelvic angle; however, patient age should also be included in these factors since there is limited fluid intake, immobilization, decreased tissue elasticity, and reduced kidney function in this population compared to relatively younger patients.

Various conditions that may affect stone formation (*e.g.*, inactivity, dysphagia, and insufficient fluid intake) and comorbidities (*e.g.*, hypertension, diabetes mellitus, kidney failure, and urinary tract infection) are considered to be effective in the high incidence of stones in the elderly population.¹⁴ In addition, most elderly people take drugs and vitamin supplements that can change their metabolic profile and predispose them to urinary stone disease.¹⁵ Buldu *et al.* reported the presence of hypertension, diabetes mellitus, or chronic obstructive pulmonary disease at a rate of 88% over the age of 65.¹⁶ Metabolic syndrome is another condition that increases with age and an effective factor in the formation of kidney stones.¹⁷

In this series, metabolic syndrome was higher among the elderly patients. Due to the deterioration in cardiopulmonary and renal function, the tolerance of elderly patients to invasive surgery may also be impaired. It is feared that the decrease in functional organ reserve with aging may trigger complications in the perioperative and postoperative period. In addition, any surgical and/or anesthesia-related complication may have a worse course in elderly patients. When f-URS and PCNL are compared, f-URS is a more non-invasive method, and performing multiple sessions of f-URS in >2 cm stones can protect the patient from the complications of PCNL, but we consider that this may increase the possibility

of encountering medical complications due to anesthetic use or surgical stress. Akman *et al.* compared f-URS with PCNL in elderly patients and found that length of hospital stay, fluoroscopy duration, and hemoglobin decrease rate were higher in PCNL, but the operation took longer in the f-URS group.¹⁸ In the same study, the stone-free rate in a single session of medium-sized kidney stones was 82.1% and 92.8% for the f-URS and PCNL groups, respectively, and a second procedure was required in 17.8% of patients who underwent f-URS.¹⁸ In another study, the stone-free rate was determined as 88% in a single session of f-URS in the elderly group, and the requirement of a second procedure was observed in 13.2%.¹⁹

In the current study, the total reoperation rate was 9.3%, and although the elderly group of patients had a relatively higher reoperation rate, there was no statistically significant difference between the groups. The reason for the relatively low reoperation rates may have been the small stone size. Beradinelli *et al.* found that the stone-free rate, operative time, UAS use, length of hospital stay, and requirement of additional procedures were not affected by patient age.²⁰ Similar to that study, the authors found no significant difference between the groups in terms of the stone-free rate, operative time, UAS use, and additional procedures. In a previous study, lower stone-free rate and minor complications (Clavien grade I) were observed in the elderly group.²¹ In contrast, another study reported no difference in the stone-free and complication rates of the elderly and young groups that underwent RIRS.¹⁹

According to the literature, the overall complication rate for RIRS is 3.2% in younger patients and 11.6% in elderly patients.^{22,23} In a study evaluating patients over 80 years, the intraoperative complication rate was reported to be 6.4% and postoperative complications were observed in 7.7% of the cases.⁹ In another study, medical complications were found at a rate of 42.2% in patients over 65 years who underwent f-URS.²⁴ Complications that occur due to non-surgical reasons (*e.g.*, arrhythmia, angina pectoralis, dyspnea, ischemic attack, respiratory distress, and delirium) are defined as medical, and increasing age was found to be a reason for these conditions.²⁴ The authors aimed to demonstrate the reliability of the efficacy of RIRS in patients aged over 60 years, considering that comorbid diseases and anti-coagulant use are more common in this population. In light of these findings, there was no statistical difference between surgical complications in the elderly and younger patient groups, and most of the complications were classified as minor in all groups. However, medical complications were much more common in Groups 2 and 3 than in Group 1. The rate of medical complications in Group 3 was 42.1%. Medical complications; *i.e.*, those caused by anesthesia or comorbidities, were observed at a higher rate in the elderly patients. Multivariate analysis for medical complications found anticoagulant use and a high CCI as independent predictive

factors. It is opinioned hereby that as the frequency of surgical stress increases in elderly patients, the more likely it becomes for them to develop irreversible medical complications. Therefore, before an elderly patient is taken into operation, a complete geriatric evaluation, including comorbidity scores, should be performed.⁹ A second situation that is as risky as surgery for this patient group is repetitive anesthesia. The solution here is to determine which patient should undergo which procedure to achieve the best results in the shortest and easiest manner as possible.

Concerning PCNL, the CROES global study reported 70 years of age to be an independent risk factor for the development and severity of complications and long-term hospital stay.²⁵ No such age limit has yet been determined for RIRS; thus, further studies with larger case series are required.

The most important limitation of this study is its retrospective design. It is absolutely necessary to further verify this issue with larger case series and prospective and multicenter studies. The safety of surgery in elderly and young patients should also be evaluated with nomograms. This study was limited in terms of the short postoperative follow-up. Furthermore, there are no definitive criteria to differentiate between surgical and medical complications in the postoperative period. Lastly, since all of the patients underwent surgery under general anesthesia, the rate of medical complications may have been higher; therefore, further studies should also include patients receiving spinal anesthesia.

CONCLUSION

Due to the presence of a higher number of comorbidities and deterioration of organ functions in elderly patients, it is difficult to determine the most appropriate procedure to achieve successful results with minimal complications that they can tolerate. f-URS has been clearly demonstrated as a safe and effective alternative for the treatment of medium-sized kidney stones.

ETHICAL APPROVAL:

This study was conducted with the approval from the Ethics Committee of the Mustafa Kemal University.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

PATIENTS' CONSENT:

Informed consents were obtained from all patients.

AUTHORS' CONTRIBUTION:

OK: Interpretation, drafting and final approval.

IHB: Analysis, critical revision and final approval.

ANK, SP: Data acquisition, conception and design.

SY: Conception, design and critical revision.

TD: Final approval.

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