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ORIGINAL ARTICLE

Impact of gender on success and complication rates after ureteroscopy

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Abstract
Purpose To investigate the impact of gender differences on treatment success, intraoperative and postoperative complications in patients undergoing ureteroscopy (URS).
Materials and methods A prospectively maintained database of 927 consecutively performed ureteroscopies on solitary ureteral stones in four different centers was retrospectively analyzed. Stones were detected with preoperative computed tomography scans or intravenous urography imaging. Patients received intravenous antibiotics as perioperative prophylaxis. Patients with symptomatic urinary tract infections (UTI) prior to surgery were excluded. Follow-up was up to 2 weeks after URS or stent removal.
Results Two hundred and eighty-six women and 641 men were included in this study. Mean stone size was 9 mm (range 2–35 mm). A double-J stent was placed in 240 (83 %) women and 527 (82 %) men at the end of surgery ($p = 0.075$). There was no significant gender difference in terms of stent dislocation ($p = 0.239$). Two hundred and fifty-one women (87 %) and 564 men (87 %) were stone-free after the first procedure ($p = 0.917$). Intraoperative complications were observed in 14 (4.8 %) women and 37 (5.9 %) men ($p = 0.313$). Severe UTI presenting with fever (>38 °C) and requiring prolonged hospitalization with parenteral antibiotics were observed in 11 (3 %) women and 8 (1 %) men postoperatively. This difference was statistically significant ($p = 0.025$).
Conclusion No significant differences between female and male patients harboring ureteral stones with respect to intraoperative complications were detected. Although stone characteristics were comparable between groups, a small number of women had significantly more severe UTI's postoperatively. Our current therapy regimen for URS seems to be efficient and safe both for females and males.

Keywords Gender · Urolithiasis · Ureteroscopy · Complications · Urinary tract infections

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Introduction

Gender differences research increasingly gains attention in all areas of medicine today. With better understanding of gender differences for specific illnesses, tailored therapies can be achieved. Even though the incidence of urolithiasis is increasing globally, reports on gender-specific differences in urolithiasis treatment are scarce [1].

Ureteroscopy (URS) has dramatically changed the management of ureteral calculi. This minimal invasive technique has demonstrated high overall success rates up to 95 % and lower overall complication rates of 9–25 % in all stones throughout the ureter [2–6].

Many factors like stone size, stone location, stone composition and surgical skills have been widely investigated in terms of their correlation with complications during or after the procedure [7–9].

With this study, we aim to investigate the impact of gender differences on treatment success, intraoperative and postoperative complications.

Materials and methods

A prospectively maintained database of 927 consecutively performed semirigid ureteroscopies on solitary ureteral stones in four different centers was retrospectively analyzed. Patient distribution consisted of the following urological departments:

- Five hundred and fifty-nine patients from the Medical University of Vienna-Austria,
- One hundred and seventy-five patients from the VKF American Hospital, Istanbul-Turkey,
- Sixty-seven patients from the Dr. Lutfi KIRDAR Kartal Research and Training Hospital, Istanbul-Turkey,
- One hundred and twenty-seven patients from the KBC Split-Croatia.

In 816 patients, stones were detected with preoperative computed tomography (CT) scans and in 111 patients with intravenous urography imaging (IVU). Largest cross-sectional dimension was taken as stone size. Iliac vessel crossing was taken as a reference point in CT scans, and border of pelvic brim was taken as a reference point in IVU's for stone location with stones being categorized as proximal or distal. Patients received single-shot intravenous (i.v.) antibiotics with the induction of anesthesia as perioperative prophylaxis. In general, i.v. cephalosporins were used, and patients with positive urine cultures prior to operation received targeted i.v. antibiotic regimens and were operated after eradication of their urinary tract infections (UTI). Patients with symptomatic UTI prior to surgery and patients who had prior double-J (DJ) stenting were excluded. Stone-free rates were determined either with intraoperative endoscopic visualization after basket removal of a solitary stone, postoperative CT scans or kidney–ureter–bladder X-rays in radiopaque stones supported with ultrasound examinations. Intraoperative and postoperative complications were registered immediately. The modified Clavien classification system, which has also been evaluated previously for ureteroscopy, was used to grade complications [10].

The indication for stent placement was decided by each surgeon intraoperatively depending on his/her judgment of an increased risk of complications such as residual fragments, bleeding, perforation or prolonged manipulation of ureteral wall.

Follow-up was up to 2 weeks after URS or stent removal.

The following semirigid ureteroscopes were used in all of the 4 centers.

- Wolf 9.8/8 F, Wolf 8.5/6.5 F, Richard Wolf GmbH, Knittlingen, Germany.
- Olympus, 8.6/9.8 F Olympus, Germany.
- Storz 8F, Karl Storz GmbH, Tuttlingen, Germany.

In one center, an electro-pneumatic generator, Lithoclast 2290 Luxury Cart (Swiss Lithoclast, Nyon, Switzerland), was used for stone disintegration. In the other centers, following holmium laser lithotripters were utilized.

- Sphinx 30W, LISA laser products OHG
- Versa Pulse PowerSuite 100w, Lumenis

The data were collected separately in all four centers and then merged into a single database. IBM SPSS software (version 21, SPSS Inc., Chicago, IL) was used for statistical analysis. Chi-squared test was used for qualitative variables, and unpaired t test was employed for quantitative variables. A two-sided p value ($p < 0.05$) was considered to be statistically significant.

Results

Two hundred and eighty-six women and 641 men were included in this study. Median patient age was 47 years (range 18–88). There was no gender difference in terms of age ($p = 0.113$) or operation times (OT) with mean OT for females 40.5 versus 41.85 min for males ($p = 0.791$). Three hundred and sixty-three stones were observed to be proximal and 564 stones to be distal. There was no correlation between stone localization and patient's gender ($p = 0.663$).

Median stone size was 9 mm (range 2–35 mm). Stone size did not significantly differ with respect to patient's gender ($p = 0.111$).

Two hundred and fifty-one women (87 %) and 564 men (87 %) were stone-free after the first procedure. The gender difference was not statistically significant ($p = 0.917$). In 90 cases, a re-intervention due to residual fragments was necessary.

No significant correlation between patient's gender and the necessity for re-intervention was observed ($p = 0.330$).

Intraoperative complications were observed in 14 women (4.8 %) and 37 men (5.9 %) without any statistical significance ($p = 0.313$).

Table 1 Intraoperative complications

Intraoperative complications	Female		Male		Total		*p* value	Clavien classification
	N	(%)	*N*	(%)	*N*	(%)		
Ureteral injury/bleeding	5	1.7	14	2.2	19	2.0	0.665	I
Injury to ureteral orifice	1	0.3	1	0.2	2	0.2	0.555	I
Urethral via falsa	0	0.0	2	0.3	2	0.2	0.344	Id
Kidney hematoma	1	0.3	2	0.3	3	0.3	0.923	II
Extravasation (kidney)	5	1.7	10	1.6	15	1.6	0.829	IIIa
Extravasation (ureter)	2	0.7	6	0.9	8	0.5	0.722	IIIa
Necrosis of the ureter	0	0.0	2	0.3	2	0.2	0.345	IIIb

Table 2 Postoperative complications

Postoperative complications	Female		Male		Total		*p* value	Clavien classification
	N	(%)	*N*	(%)	*N*	(%)		
Colicky pain without residual stone	11	3.8	9	1.4	20	2.2	0.042	I
Hydronephrosis without residual stone	2	0.7	2	0.3	4	0.4	0.500	I
Impaired kidney function	0	0.0	2	0.3	2	0.2	0.454	I
Hematoma	0	0.0	2	0.3	2	0.2	0.454	I
Complicated UTI/sepsis	11	3.8	8	1.2	19	2.0	0.025	II (18 cases)/IV (1 case)
Gross hematuria/bladder tamponade	1	0.3	2	0.3	3	0.3	0.705	IIIa
Ureteral stenosis	0	0.0	3	0.5	3	0.3	0.363	IIIb
DJ-stent dislocation	4	1.4	16	2.5	20	2.2	0.239	IIIb
Colicky pain with residual stone	3	1.0	12	1.9	15	1.6	0.468	IIIb
Hydronephrosis with residual stone	7	2.4	13	2.0	20	2.2	0.650	IIIb

None of the intraoperative complications correlated with patient's gender (Table 1). All of the intraoperative complications were classified as Clavien grade I–III.

Patients with ureteral extravasation were managed with DJ-stenting for up to 2 weeks. Only in one patient, a percutaneous nephrolithotomy was performed in the same session.

A DJ-stent was placed in 240 (83 %) women and 527 (82 %) men at the end of surgery. The indication for stent placement was decided by each surgeon intraoperatively depending on her/his judgment of an increased risk of complications such as residual fragments, bleeding, perforation or prolonged manipulation.

Patient's gender did not affect the indication for DJ-stent placement ($p = 0.075$). Furthermore, there was no significant difference between gender groups with respect to stent dislocation with four women and 16 men presenting with stent dislocation after surgery ($p = 0.239$).

Postoperative complications were observed in 35 women and 63 men accounting for 12 and 10 %, respectively. This was not statistically significant ($p = 0.378$). A total number of 102 postoperative complications were observed (Table 2). With the exception of one case, all postoperative complications were categorized as Clavien grade I–III.

In one out of three patients presenting with ureteral stricture, a ureteroneocystostomy was performed. The remaining two had no evidence of a persistent ureteral stricture following DJ-stent removal after 4 weeks with regular IVU examinations.

Severe UTI were observed in 19 patients, 11 women and eight men postoperatively. This difference was statistically significant ($p = 0.025$). Three female and three male patients with UTI harbored residual fragments. Out of 19 patients with UTI, only one female patient had an infection stone (magnesium–ammonium–phosphate). Preoperative urine cultures showed significant bacteriuria only in three of female patients, who were all treated with targeted antibiotics before the operation. Five patients had prolonged hospitalization due to UTI. Three patients were readmitted to hospital after being discharged due to symptomatic UTI and parenteral antibiotics were administered. None of the patients with UTI had hydronephrosis. One male patient received a percutaneous nephrostomy catheter in order to prevent sepsis. One female patient developed a *Escherichia coli* sepsis. Age was not a prognostic factor for the development of postoperative UTI among women (Fig. 1).

Patients with residual fragments had more UTI's than patients without residual fragments within the whole patient cohort and this was statistically significant ($p = 0.020$).

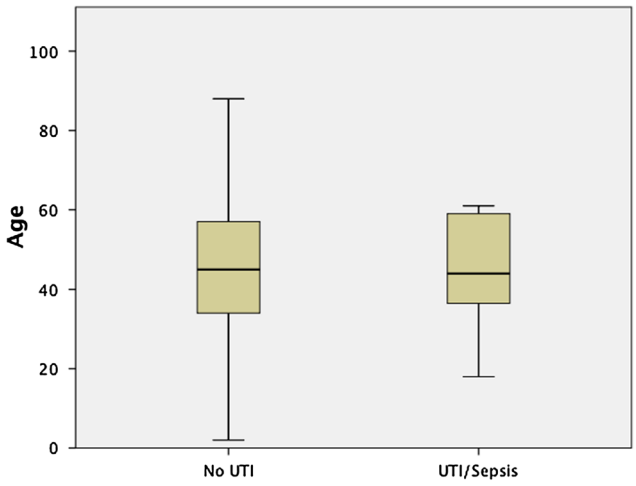

Fig. 1 Age distribution of UTI among women

Moreover, the ratio of residual fragments was higher in the group of patients with severe UTI or sepsis when compared to whole patient cohort (31 vs. 12 %), but 19 patients with UTI/sepsis represent only 2 % of 927 patients. Therefore, results are statistically of limited significance.

Characteristics of patients with severe UTI/Sepsis are presented in Table 3.

Discussion

Ureteroscopy is a standard urologic procedure. Although being more invasive, URS has proved to achieve higher success rates and faster stone delivery rates compared with SWL [11–13].

Kurahashi et al. [14] retrospectively analyzed 2,129 consecutive patients with ureteral stones who underwent URS at their institution. Their multivariate analysis showed no statistical association between gender and therapeutic outcome following a single URS ($p = 0.09$). Similarly in our study, stone-free rates after the first procedure did not show any statistical difference with respect to gender ($p = 0.91$).

Kurahashi et al. found residual fragments in 569 patients of which 454 (21 %) required a subsequent SWL. Furthermore, in 14 patients, a successive ureterolithotomy or percutaneous nephrolithotripsy was performed. Unlike Kurahashi's patients, in our study, only 90 patients (9 %) required a re-intervention. Twenty-five patients with residual fragments were treated with URS, 58 patients with SWL and seven patients with PNL without any statistical difference with respect to gender.

Furthermore, in Kurahashi's series, intraoperative ureteral perforation occurred in 14 patients, 12 of those were managed with drainage by an internal double-J stent. In two patients, nephrectomy had to be performed. In addition, postoperative complications were observed in 13 patients, including UTI in six, ureteral stricture in four and sepsis in three patients.

Mandal et al. [10] prospectively collected the data of 120 consecutive patients (71 men and 49 women) to analyze perioperative complications of URS. They recorded a total of 79 perioperative complications in 36 patients (21 male, 15 female) without any statistical difference in terms of gender ($p = 0.903$).

El-Nahas et al. [9] retrospectively studied the factors predicting unfavorable results of URS. Their study consisted of 841 patients including 567 males and 274 females. The overall complication rate was reported in 61 procedures (6.7 %). Intraoperative complications included mucosal injury in 26 (2.9 %), extravasation in 14 (1.5 %) and ureteral perforation in 12 (1.3 %) procedures. These findings were similar to ours. Of the intraoperative complications identified, 49 (94 %) could be managed by DJ-stenting. Univariate analysis revealed unfavorable results in 107 (17.1 %) male and 50 (17.7) female patients without any statistical difference between the two ($p = 0.840$).

On the contrary, Fuganti et al. [15] defined gender as a risk factor for intraoperative complications in semirigid ureteroscopy. They analyzed 1,235 ballistic ureterolithotripsies of which 802 (64.9 %) patients were men. A total of 55 (4.4 %) intraoperative complications occurred in 1,235 procedures.

The multivariate logistic regression analysis revealed gender (male) to be a significant predictor for intraoperative complications with an odds ratio of 2,69 ($p = 0.12$). According to their study, large prostates may pull the base of the endoscope up while opposing its tip to ureteral wall and hence predisposing to injury. In our study, we detected no significant difference between two genders in terms of

Table 3 Characteristics of patients with severe UTI or Sepsis

Patients with UTI/sepsis	Mean stone size (mm)	Stone-free rate	Diabetes mellitus	Preoperative significant bacteriuria
Male $n = 8$	15	5 (63 %)	1 (12 %)	1 (12 %)
Female $n = 11$	10	8 (72 %)	1 (9 %)	3 (27 %)
Total $n = 19$	16	13 (68 %)	2 (10 %)	4 (21 %)

ureteral injury. Urethral via falsa was the only male-specific complication recorded in our series.

In our study, 19 patients (2 %) presented with severe UTIs. These findings were similar to Elashry's. In his study, UTIs were observed after 121 out of 5,133 procedures [5]. On the contrary, Kurahashi and his colleagues [14] reported UTIs in six cases and urosepsis in three cases with a total of only nine (0.4 %) out of 2,129 patients. In our study, preoperative urine cultures of patients with severe UTI's were mostly sterile. Bacteria enclosed within the stones that were set free during stone impaction were presumably responsible for these UTI's.

Sugihara et al. [16] analyzed 12,372 URS patients between 2007 and 2008. A total of 4,454 female and 7,918 male patients were included in their study. They developed a nomogram to predict severe adverse events after URS. Their results revealed 3.01 % of female patients to show severe AEs. On the other hand, this ratio was only 2.05 % among male patients. This difference was statistically significant ($p = 0{,}001$). According to their nomogram, female sex was a risk factor for developing AEs after URS. They believe women's higher vulnerability to UTIs to be the underlying reason. Similarly, in our study, women had significantly more UTIs than men.

The necessity for antibiotic prophylaxis for URS is an ongoing discussion. To answer this question, Clinical Research Office of the Endourological Society (CROES) investigated postoperative infection rates in patients with a negative baseline urine culture undergoing ureteroscopic stone removal [17]. The authors matched 1,141 patients with ureteral stones or 184 patients with kidney stones who did not receive antibiotic prophylaxis with those who were predefined by risk factors, including gender, American Society of Anesthesiologists (ASA) score and ureteral stent placement. Preoperative antibiotic prophylaxis did not reduce the rates of postoperative UTI and fever; however, female gender, Crohn's and cardiovascular disease and a high ASA score were specific risk factors for postoperative infection in this patient group. Their overall prevalence of fever or UTI was comparable to our postoperative UTI rates (2.2 vs. 2 %). Similar to our findings, in their study, women presented with significantly more UTI and fever after URS procedures. In contrary to the findings of CROES, in our patient cohort, eight male and three female patients who had Crohn's disease did not have postoperative UTI or sepsis.

A comparison of these studies is shown on Table 4.

Our study was not designed to answer the question of necessity for antibiotic prophylaxis during URS. Although female patients presented with UTI/sepsis more frequently compared to men (3.8 %), advocating prolonged antibiotic regimes for all women undergoing URS cannot be concluded.

Limitations of our study

Even though our study database was maintained in a prospective nature, our data analysis was performed in a retrospective manner. Moreover, inter-operator variability and lack of stone cultures are the limitations of our study.

Table 4 Comparison of different studies on gender research for the treatment of urolithiasis

Study comparison	Total *N*	Female		Male		Chi-square
		N/Total *N* of females	%	*N*/Total *N* of males	%	
El-Nahas et al. [9] unfavorable results[a]	841	50/283	17.7	107/625	17.1	0.840
Mandal et al. [10] overall complications	120	15/49	30.6	21/71	29.5	0.903
Kurahashi et al. [14] residual fragments	2,129	159/566	28.3	410/1,563	26.2	0.039
Sugihara et al. [16] adverse events[b]	12,372	134/4,454	3.01	162/7,918	2.05	0.001
Martov et al. [17] UTI or fever after URS				UTI	Fever	
Odds ratio for females (95 % CI) full				2.73 (1.51, 4.92)	2.21 (1.42, 3.43)	
Özsoy et al. (present study)	Total *N*	Female		Male		Chi square
		N/Total *N* of females	%	*N*/Total *N* of males	%	
Intraoperative complications	927	14/286	4.8	32/641	4.9	0.313
Postoperative complications	927	35/286	12	63/641	10	0.378
Residual stones	927	35/286	12	77/641	13	0.917

[a] Unfavorable results: residual fragments, complications or need for re-intervention

[b] Adverse events: (I) in-hospital mortality, (II) postoperative medication including catecholamine, g globulin, protease inhibitors, medications for disseminated intravascular coagulation and transfusion, (III) postoperative interventions such as percutaneous nephrostomy, central vein catheterization, intensive care unit, dialysis and mechanical cardiopulmonary support

Conclusion

No significant differences between female and male patients harboring ureteral stones with respect to intraoperative complications were detected. Although stone characteristics were comparable between groups, a small number of women had significantly more severe UTI's postoperatively. Our current therapy regimen for URS seems to be efficient and safe both for females and males.

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