

# Exploring the Impact of Gender-Specific Approaches in Retrograde Intrarenal Surgery: Effects on Operative Efficiency and Patient Recovery

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**Objective:** Very limited data are available exploring the potential influence of gender on Retrograde Intrarenal Surgery outcomes. This study investigates the gender-specific influence of ShuoTongureteroscopy (ST-urs) and Flexible Ureteroscopy (F-urs) surgeries on operation efficacy and patient recovery in a sample of the Somali population.

**Materials and Methods:** We enrolled 390 participants. Participants were stratified into four gender-specific subgroups based on ureteroscopy operation type: 27.7% males in S-urs (group1), 44.4% females in S-urs (group2), 18.7% males in F-urs (group3), and 9.2% females in F-urs (group4). Primary outcomes included operation time, postoperative hospital stay duration, and VAS Pain Score. Multivariate logistic regression was used to assess associations.

**Results:** The mean age was  $29.53 \pm 7.61$  years, 72.1% male and 27.9% female, with 46.4% of the patients undergoing ST-urs and 53.6% undergoing F-urs. Women had higher odds of prolonged hospital stays (OR = 2.62, 95% CI: 1.43–4.82,  $p < 0.001$ ) and post-operation pain (OR = 5.06, 95% CI: 2.95–8.68,  $p = 0.002$ ). Among men who underwent F-urs procedure, there was a significantly higher odds ratio (OR) of 6.14 (95% CI: 2.86–13.19,  $p < 0.001$ ) for experiencing a long operation time. Conversely, for females, those who underwent S-urs surgery had a notably lower OR of 0.32 (95% CI: 0.13–0.79,  $p = 0.013$ ) for long operation time, whereas those who underwent F-urs surgery exhibited a substantially elevated OR of 5.36 (95% CI: 1.85–15.53,  $p < 0.001$ ). Both females undergoing F-urs surgery (OR: 5.16, 95% CI: 2.61–10.21,  $p < 0.001$ ) and those undergoing F-urs surgery (OR: 5.25, 95% CI: 2.17–12.73,  $p < 0.001$ ) experienced significantly higher post-operative pain.

**Conclusion:** Our research reveals gender disparities in retrograde intrarenal surgery outcomes. Women experience longer hospital stays and higher postoperative pain levels compared to men. F-urs procedures are associated with longer operation times and hospital stays, particularly affecting women. Contrarily, ST-urs offers shorter operation times for women but leads to prolonged hospital stays and heightened postoperative pain.

**Keywords:** ureteroscopy, gender-specific, Flexible ureteroscopy, ShuoTong

## Introduction

Nephrolithiasis ranks among the most prevalent urologic ailments globally,<sup>1–3</sup> with recurrence rates over ten years reaching 80%. Recent studies indicate a steady rise in incidence, notably higher in males than females. Variations in urolithiasis prevalence across populations can be attributed significantly to climate, gender, dietary, fluid consumption, and socioeconomic status.<sup>2</sup>

Technological advances have revolutionized the treatment of upper urinary tract stones measuring less than 2 cm with retrograde intrarenal surgery (RIRS), as the AUA and EAU recommended.<sup>4,5</sup> Flexible ureteroscopy (F-urs), in particular, has gained traction due to reported advantages such as minimal trauma, quick recovery, and high stone clearance rates, often recommended as the primary treatment.<sup>6</sup> Introducing a novel approach, ShuoTongureteroscopy (ST-urs) combines negative pressure to facilitate stone removal while reducing residual fragments and the risk of postoperative complications.<sup>7–9</sup> ST-urs also maintains lower renal pelvic pressure, reducing infection and bleeding risks associated

with lengthy surgeries and hospital stays.<sup>8</sup> Both F-urs and ST-urs have become widely embraced techniques for treating urolithiasis.<sup>7</sup>

However, gender-specific differences in incidence, risk factors, and kidney stone compositions between males and females may impact the efficacy of these procedures.<sup>10,11</sup> Despite their prominence, the relationship between gender and the efficiency of F-urs and ST-urs in treating lower volume renal stones remains largely unexplored, especially within the Somali population. It remains uncertain whether gender-specific factors significantly forecast the efficacy of these procedures and patient recovery outcomes. Thus, this study aims to investigate the gender-specific influence of F-urs and ST-urs surgeries on operation efficacy, defined by factors such as operation time, hospital stay duration, postoperative pain levels, and stone-free rates.

## Materials and Methods

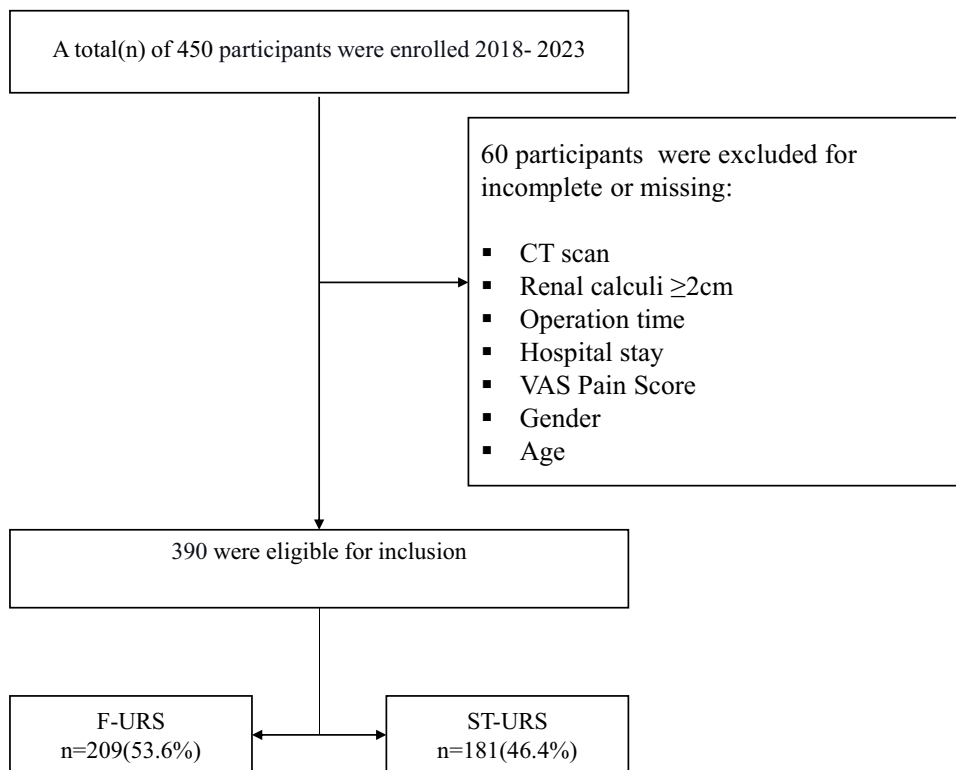
### Study Design and Population

A retrospective analysis was conducted on clinical data extracted from the hospital information system for patients who underwent F-urs and ST-urs surgery at the Mogadishu Urology Centre between January 2018 and December 2023. Initially, 450 patients were randomly recruited, but those with renal calculi  $\geq 2$  cm in size, and incomplete or missing CT scans, blood test results, operation time, hospital stay, and pain score data were excluded. The final sample size available for analysis was 390 patients (Figure 1).

### Description of Operative Efficiency and Patient Recovery

#### Operative Efficiency

Operative efficiency is characterized by the effectiveness and productivity of surgical procedures, which are measured by operation time.<sup>12</sup> It signifies the proficiency of a surgical team in achieving the desired outcome while minimizing risks and making efficient use of resources during the procedure.<sup>12</sup> The operative time defined as the duration or length of time



**Figure 1** Flow diagram of eligible participants.

**Abbreviations:** F-urs, Flexible ureteroscopy; ST-urs, ShuoTongureteroscopy.

that a surgical procedure takes from the start to the finish, including preparation and completion phases. Shorter operation times (<40 minutes) often indicate a more streamlined and proficient surgical process, while longer times ( $\geq 40$  minutes) may suggest inefficiencies or complications.<sup>8</sup>

### Patient Recovery

Patient recovery is defined as the process through which a patient recuperates and returns to their normal state of health, typically marked by hospital discharge following surgery.<sup>8,12</sup> In this investigation, patient recovery was assessed using postoperative pain levels and the duration of hospital stay.

## Baseline Assessment of Potential Confounders and Effect Modifiers

We obtained information on characteristics that might confound our outcome from hospital system records. These records included data on age, sex (self-reported), stone size and location, type of operation, stone hardness (Hounsfield units), number of stones, presence of hydronephrosis (estimated via non contrast CT scan), stone-free rate, and post-surgical VAS Pain Score.

The approval form was received from the ethical research board committee of Mogadishu Urology Center (REF). MUC-9016). In addition, informed consent was obtained from all patients. This study was carried out following the Helsinki Declaration contents.

## Statistical Analysis

Statistical computations were conducted using SPSS 25.0 (IBM, Armonk, New York). We employed multivariate logistic regression models to explore the association between operation time, hospital stay, and post-operation pain, considering gender, operation type, and gender-specific operation type. Clinical continuous variables were presented as mean  $\pm$  standard deviation, while categorical variables were expressed as absolute values (percentages). To control for confounding variables and assess the independent association between operation time, hospital stay, and post-operation pain across gender, operation type, and gender-specific operation type subgroups, we constructed a model. The model was fully adjusted for age, gender (excluded in gender comparison), stone size, stone hardness, operation type (excluded in operation comparison), and stone location. All p-values were two-sided; values less than 0.05 and 95% confidence intervals were considered statistically significant.

## Results

### Characteristics of the Study Population

A total of 390 participants were enrolled in the study, with a mean age of  $29.53 \pm 7.61$  years. Among them, 72% were men, 64.6% presented with renal pelvic kidney stones, and 88.7% had single kidney stone. Surgical intervention, ST-urs, was performed in 46.4% of the participants, while F-urs was utilized in 53.6% of cases. The average operative time was  $38.68 \pm 11.41$  minutes, and the post operation hospital stay lasted  $3.08 \pm 0.77$  days (Table 1).

### Operating Time: Comparison Between Male Vs Female and ST-Urs Vs F-Urs

In general, there was no significant difference in long operating times between men and women (OR = 0.73, 95% CI: 0.35–1.54,  $p = 0.409$ ). However, women had higher odds of prolonged hospital stays (OR = 2.62, 95% CI: 1.43–4.82,  $p < 0.001$ ), and post-operation pain (OR = 5.06, 95% CI: 2.95–8.68,  $p = 0.002$ ). Additionally, in comparison between ST-urs Vs F-urs, F-urs had higher odds than ST-urs for long operating time (OR = 8.43, 95% CI: 4.39–16.17,  $p < 0.001$ ), prolonged hospital stays (OR = 8.43, 95% CI: 4.63–15.36,  $p < 0.001$ ), and no significant association with post operation pain. Furthermore, a significant interaction ( $p < 0.001$ ) between gender-operation type interaction (Tables 2 and 3 and Figure 1).

### Gender-Specific Operation Type, Longed Operation Time, and Patient Recovery

When participants were stratified by gender and operation type, men who underwent S-urs surgery served as the control group. Among men who underwent F-urs surgery, there was a significantly higher odds ratio (OR) of 6.14 (95% CI: 2.86–13.19,  $p < 0.001$ ) for experiencing a long operation time. Conversely, for females, those who underwent S-urs

**Table 1** Baseline Clinical and Demographic Characteristics of Participants Stratified by Gender for RIRS (ST-Urs and F-Urs) Surgery

Variables	Overall n=390	Group1 n=108 (27.7)	Group2 n=173 (44.4)	Group3 n=73 (18.7)	Group4 n=36 (9.2)	P value
Age, yrs	29.53±7.61	27.83±8.05	29.44±7.54	30.89±6.56	32.25±7.50	<b>0.006</b>
Gender, n(%)						<b>&lt;0.001</b>
Male	281(72.1)	108(38.4)	173(61.6)	0(0.0)	0(0.0)	
Female	109(27.9)	0(0.0)	0(0.0)	73(67.0)	36(33.0)	
Stone Location, n(%)						<b>&lt;0.001</b>
Middle pole	47(12.0)	12(11.1)	32(18.5)	1(1.4)	2(5.6)	
Renal pelvic	252(64.6)	50(46.3)	102(59.0)	68(93.2)	32(88.9)	
Upper pole	56(14.4)	38(35.2)	15(8.7)	3(4.1)	0(0.0)	
Renal pelvic and Lower pole	1(0.3)	1(0.9)	0(0.0)	0(0.0)	0(0.0)	
Renal pelvic and Middle pole	29(7.4)	6(5.6)	20(11.6)	1(1.4)	2(5.6)	
Upper and middle poles	5(1.3)	1(0.9)	4(2.3)	0(0.0)	0(0.0)	
Operation Type, n(%)	38.68±11.41	33.16±9.76	43.95±11.47	33.58±8.24	40.28±8.94	<b>&lt;0.001</b>
S-urs	181(46.4)	108(59.7)	0(0.0)	73(40.3)	0(0.0)	
F-urs	209(53.6)	0(0.0)	173(82.8)	0(0.0)	36(17.2)	
Operating Time, mins	38.68±11.41	27.90±3.91	45.34±9.20			<b>&lt;0.001</b>
Stone Free Rate, n(%)	389(99.7)	107(27.5)	173(44.5)	73(18.8)	36(9.3)	0.454
Hospital Stay, days	3.08±0.77	2.60±0.70	3.31±0.66	3.03±0.85	3.47±0.77	<b>&lt;0.001</b>
Stone Size, cm	1.85±0.42	1.76±0.54	1.91±0.30	1.87±0.50	1.74±0.24	<b>0.016</b>
Stone Hardness, HU	992.67±312.78	1015.00±231.78	947.63±196.55	1067.53±196.55	990.67±312.78	<b>0.039</b>
Number of Stone, n(%)						<b>&lt;0.001</b>
Single	346(88.7)	99(28.6)	140(40.5)	73(21.1)	34(9.8)	
Multiple	44(11.3)	9(20.5)	33(75.0)	0(0.0)	2(4.5)	
Hydronephrosis, n(%)						<b>&lt;0.001</b>
0	243(62.3)	70(64.8)	127(73.4)	33(45.2)	13(36.1)	
I	22(5.6)	5(4.6)	16(9.2)	1(1.4)	0(0.0)	
II	48(12.3)	20(18.5)	16(9.2)	10(13.7)	2(5.6)	
III	77(19.7)	13(12.0)	14(8.1)	29(39.7)	21(58.3)	
Pain Grades, n(%)						<b>&lt;0.001</b>
No pain	22(5.6)	0(0.0)	19(11.0)	3(4.1)	0(0.0)	
Mild	167(42.8)	69(63.9)	66(38.2)	22(30.1)	10(27.8)	
Moderate	123(31.5)	29(26.9)	50(28.9)	36(49.3)	8(22.2)	
Severe	78(20.0)	10(9.3)	38(22.0)	12(16.4)	18(50.0)	

**Notes:** Variables are presented as number (%) and Mean±SD. Group 1 comprises males who underwent S-urs, Group 2 comprises females who underwent F-urs, Group 3 comprises males who underwent F-urs, and Group 4 comprises females who underwent F-urs. Bold indicates statistically significant.

**Abbreviations:** HU, Hounsfield units; MEU, Morphine equivalent units; S-urs, Shoutongureteroscopy; F-urs, Flexible ureterorenoscopy; Mins, Minutes; VAS, Visual Analog Scale.

**Table 2** General Comparison of Long Operating Time Male Vs Female Patients, and ST-Urs Vs F-Urs

Exposure	Unadjusted		*Fully Adjusted Model	
	OR (95% CI)	P value	OR (95% CI)	p value
Men Vs Women	0.47(0.30–0.74)	0.001	0.73(0.35–1.54)	0.409
S-urs Vs F-urs	7.14(4.50–11.32)	<0.001	8.43(4.39–16.17)	<b>&lt;0.001</b>

**Notes:** Interaction between Gender and Type of operation(SOTN and FURS): P <0.001. Partially adjusted model for age and gender; \*Fully adjusted model for age, gender, BMI, T2DM (excluded in T2DM comparison), TC, LDL-C (excluded in LDL-C comparison), Cr, HTN and CHD. Bold indicates statistically significant.

**Abbreviations:** OR, Odds ratio; CI, Confidence interval; RIRS, Retrograde Intrarenal Surgery. Other abbreviation as in Table 1.

**Table 3** General Comparison of Patient Long Operative Time Between Male and Female Patients, and RIRS

Exposure	Unadjusted		*Fully Adjusted Model	
	OR (95% CI)	P value	OR (95% CI)	p value
Men Vs Women	Hospital stays			
	1.22(1.73–2.06)	<b>0.043</b>	2.62(1.43–4.82)	<b>0.002</b>
	Post Surgical pain			
	2.56(1.61–4.08)	<b>&lt;0.001</b>	5.06(2.95–8.68)	<b>&lt;0.001</b>
ST-urs Vs F-urs	Hospital stays			
	8.10(4.65–14.11)	<b>&lt;0.001</b>	8.43(4.63–15.36)	<b>&lt;0.001</b>
	Post Surgical pain			
	1.30(0.87–1.93)	0.202	1.05(0.64–1.73)	0.835

**Notes:** P for interaction <0.001. \*Fully adjusted for age, gender(excluded in gender comparison), Stone size, stone hardness, operation type(excluded in operation comparison), and stone location. Bold indicates statistically significant. Other abbreviation as in Tables 1 and 2.

surgery had a notably lower OR of 0.32 (95% CI: 0.13–0.79,  $p = 0.013$ ) for long operation time, whereas those who underwent F-urs surgery exhibited a substantially elevated OR of 5.36 (95% CI: 1.85–15.53,  $p < 0.001$ ) (Table 4, Figure 2).

In terms of prolonged hospital stays, male patients undergoing ST-urs surgery were the reference group. F-urs surgery was associated with a significantly higher OR of 6.99 (95% CI: 3.72–13.14,  $p < 0.001$ ). Among females undergoing ST-urs surgery, there was an OR of 2.18 (95% CI: 1.14–4.15,  $p = 0.018$ ), whereas no significant association was found for those undergoing FURS surgery (Table 5).

Regarding post-operative pain, males undergoing ST-urs surgery were the reference group, with no significant association observed for F-urs surgery in males (OR: 1.07, 95% CI: 0.91–1.94,  $p = 0.822$ ). However, both females undergoing F-urs surgery (OR: 5.16, 95% CI: 2.61–10.21,  $p < 0.001$ ) and those undergoing F-urs surgery (OR: 5.25, 95% CI: 2.17–12.73,  $p < 0.001$ ) experienced significantly higher post-operative pain (Table 5, Figure 2).

**Table 4** Long Operative Time in Women and Men Undergoing RIRS (S-Urs and F-Urs) Techniques

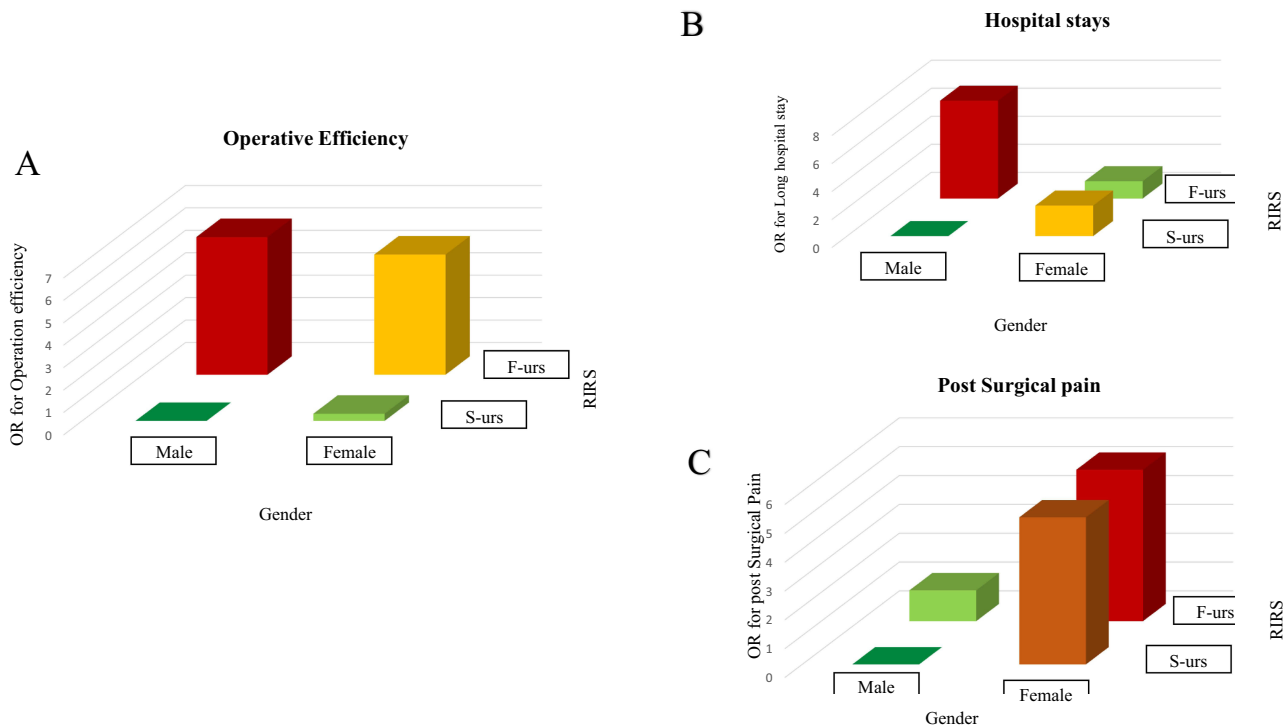
Exposure Gender	RIRS	Unadjusted		*Fully Adjusted Model	
		OR (95% CI)	p value	OR (95% CI)	p value
Male	ST-urs	Ref=1			
	F-urs	7.22(4.15–12.56)	<0.001	6.14(2.86–13.19)	<0.001
Female	ST-urs	0.81(0.44–1.49)	0.488	0.32(0.13–0.79)	<b>0.013</b>
	F-urs	4.36(1.87–10.17)	0.001	5.36(1.85–15.53)	<b>0.002</b>

**Notes:** \*Fully adjusted for age, Stone size, stone hardness, number, and stone location. Bold indicates statistically significant.

**Abbreviations:** OR, Odds ratio; CI, Confidence interval; RIRS, Retrograde intrarenal surgery Other abbreviation as in Tables 1 and 2.

### Discussion

Urinary stone disease (nephrolithiasis) affects approximately 12% of the global population,<sup>2</sup> with guidelines recommending ST-urs and F-urs as primary treatments in low volume renal stones.<sup>13,14</sup> Despite this, the potential influence of gender on surgical outcomes has not been previously explored. This study addresses this gap by presenting data on operational efficiency and postsurgical recovery within the Somali population. The study assesses operation time, hospital stay, and postoperative pain across genders. Our findings reveal no significant difference in operating times between men and women. However, women had a higher likelihood of experiencing longer hospital stays and postoperative pain. In ST-urs versus F-urs, F-urs was associated with longer operation times and hospital stays compared to ST-urs, with no significant correlation with postoperative pain. Furthermore, there was a significant interaction between ureteroscope operation type and gender, implying that gender plays a significant role in influencing surgical efficacy and patient recovery.



**Figure 2** Odds ratio for longer operation time, hospital stay, and post-operational pain associated with gender. (A): OR for Operation efficiency, (B):OR for Prolonged hospital stay, (C): OR for Post Surgical Pain. **Abbreviations:** OR, Odds Ratio; F-urs, Flexible ureteroscopy; ST-urs, ShuoTongureteroscopy; RIRS, Retrograde Intra-Renal Surgery.

**Table 5** Patient Patients' Recovery in Women and Men Undergoing RIRSTechniques

Exposure Gender	RIRS	Unadjusted		*Fully Adjusted Model	
		OR (95% CI)	p value	OR (95% CI)	p value
		<i>Hospital stays</i>			
Male	S-urs	Ref=1			
	F-urs	8.73(4.75–16.03)	<0.001	6.99(3.72–13.14)	<0.001
Female	S-urs	2.07(1.12–3.82)	0.02	2.18(1.14–4.15)	0.018
	F-urs	2.13(0.15–6.13)	0.100	1.24(0.24–6.13)	0.199
		<i>Post Surgical pain</i>			
Male	S-urs	Ref=1			
	F-urs	1.83(1.12–3.00)	<0.001	1.07(0.91–1.94)	0.822
Female	S-urs	3.40(1.82–6.33)	<0.001	5.16(2.61–10.21)	<0.001
	F-urs	4.60(2.01–10.53)	<0.001	5.25(2.17–12.73)	<0.001

**Notes:** \*Fully adjusted for age, Stone size, stone hardness, number, and stone location. Other abbreviation as in Tables 1 and 2.

We further analyzed the interaction between gender and ureteroscopy operation type (F-urs and S-urs). Using men undergoing ST-urs as the control group, we found that F-urs was associated with long operation times in both men and women. Additionally, it led to prolonged hospital stays in men but not in women, and it was linked to post-surgical pain in women but not in men. Contrariwise, ST-urs was associated with shorter operation times, prolonged hospital stays, and post-operative pain in women.

F-urs and ST-urs are widely embraced and favored for treating renal stone measuring less than 2 cm in size with the techniques gaining traction in the field.<sup>8,15</sup> Managing elevated intrarenal pressure during F-urs poses a significant clinical challenge, often resulting in prolonged operation times.<sup>7,16</sup> This dilemma is exacerbated by the heightened risk of liquid, bacterial, and endotoxin absorption into the bloodstream, potentially leading to complications such as systemic inflammatory response syndrome, sepsis, and long-term renal dysfunction.<sup>16,17</sup>

A novel lithotripsy technique, known as ST-urs and pioneered in China,<sup>9</sup> effectively addresses the challenges associated with traditional methods.<sup>18</sup> ST-urs utilizes an innovative irrigation and vacuum suction platform controlled through a specialized ureteral access sheath.<sup>8,18</sup> Surgeons can modulate negative pressure during the procedure, thereby mitigating renal pelvic pressure and facilitating simultaneous stone suction and crushing. This approach reduces the risk of infection and bleeding while enhancing overall surgical outcomes.<sup>8</sup> ST-urs offers enhanced safety compared to traditional ureteroscopy methods by providing clear and direct visualization during ureteral access sheath placement, thereby minimizing the risk of ureteral injury.<sup>8</sup> Additionally, it helps to minimize hospital stay and post-operation pain, as evidenced by our study. A key advantage of ST-urs lies in its ability to manage renal pelvic pressure effectively.<sup>7,8</sup> By allowing surgeons to adjust negative pressure levels, the technique ensures optimal conditions for stone suction and crushing while reducing the risk of complications, such as infection and bleeding.<sup>8</sup> Furthermore, the precise control provided by ST-urs during ureteral access sheath placement minimizes the risk of inadvertent injury to the ureter.<sup>8</sup> This aspect of the technique is particularly crucial in ensuring patient safety and optimizing surgical outcomes. In our study, we observed that patients undergoing ST-urs experienced shorter hospital stays and reduced post-operative pain compared to those treated with traditional methods. This finding underscores the clinical benefits of the technique and highlights its potential to improve patient comfort and recovery.

A four-year retrospective analysis regarding gender influence on RIRS outcomes included 6669 patients who underwent RIRS for renal stones recruited from the Flexible Ureteroscopy Outcomes Registry (FLEXOR) conducted by Emiliano et al reported that female patients had significantly longer hospital stays (3.8 vs 3.5 days;  $P < 0.001$ ), postoperative fever rates (6.9% vs 5.7%), and lower stone-free rate after the procedure (76.97.03% vs 79.03 ( $P = 0.032$ )). The authors concluded that female patients have slightly significantly higher overall complications and slightly increased residual fragment rate (4). In

line with these findings, our investigation reveals that women are more frequently associated with longer operation times, postoperative pain, and longer hospital stays. In contrast, we did not find significant differences in regard to stone-free rates among gender groups.

Previous studies have highlighted the correlation between differences in stone composition among males and females,<sup>19,20</sup> which significantly impact the clinical outcomes of ureteroscopy surgery.<sup>20</sup> This can be attributed to men's higher propensity for developing calcium oxalate monohydrate stones, excreting elevated levels of calcium and oxalate,<sup>21</sup> displaying lower urine pH levels, and experiencing urine supersaturation of uric acid compared to women.<sup>10,11</sup> Data from previous investigation have also identified various mechanisms through which estrogen influences the expression and activity of uric acid transporters, elucidating gender-based disparities in pathology and their influence on the type of ureteroscopy.<sup>22,23</sup> Specifically, estrogen appears to play a role in modulating the transport of uric acid, which may contribute to the differences observed between men and women in stone composition and urinary physiology.<sup>23</sup>

Our study demonstrates several strengths that bolster its credibility and reliability. Firstly, we have implemented strict adjustment protocols to account for potential confounders, ensuring accurate analysis of variables. By meticulously controlling for extraneous factors, we strengthen internal validity and mitigate spurious associations. Additionally, our research design incorporates rigorous methodologies and analytical techniques, upholding the high scientific standards.

Our investigation is not without limitations. Limitations include a small number of gender-specific operation-type subgroups and data from a single center, limiting generalizability. Second, stone-type data was not included, which significantly impacts the clinical outcomes of ureteroscopy surgery due to the unavailability of stone analysis throughout the country. Future studies should aim for multicenter designs, randomization, and longer follow-up periods to address these limitations and strengthen findings.

## Conclusion

Our findings reveal gender disparities in RIRS surgery outcomes. Women tend to experience prolonged hospital stays and higher postoperative pain levels compared to men. F-urs procedures correlate with long operation times and hospital stays, particularly affecting women. Conversely, ST-urs offers women shorter operation times but leads to prolonged hospital stays and heightened postoperative pain. Surgeons should recognize these complexities to tailor care for different patient groups, optimizing preoperative and postoperative management to mitigate complications effectively.

## Data Sharing Statement

All study data and materials can be obtained from the corresponding author.

## Ethics Approval

The approval form was received from the ethical research board committee of Mogadishu UrologyCenter (REF. MUC-9016). This study was carried out following the Helsinki Declaration contents.

## Informed Consent

Informed consent was obtained from all patients.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no competing interest.

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