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COMPARISON OF SEXUAL FUNCTION AFTER RETROGRADE INTRARENAL SURGERY AND URETEROSCOPY: A RETROSPECTIVE COHORT STUDY

RETROGRAD İNTRARENAL CERRAHİ VE ÜRETEROSKOPİ SONRASI CİNSEL İŞLEVİN KARŞILAŞTIRILMASI: RETROSPEKTİF KOHORT ÇALIŞMASI



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Abstract

Objective: Retrograde intrarenal surgery (RIRS) and ureteroscopy (URS) are widely adopted minimally invasive techniques for treating upper urinary tract stones. However, their comparative effects on sexual function remain poorly understood. This study aimed to compare the impact of RIRS versus URS on sexual function and identify risk factors for prolonged dysfunction.

Material and Methods: In this retrospective cohort study, we analysed 360 propensity score-matched patients (180 pairs) who underwent RIRS or URS between January and December 2022. Sexual function was assessed using validated questionnaires (IIEF-5, PEDT, MSHQ for males; FSFI, OAB-q SF for females) at baseline and 3, 6, and 12 months postoperatively. The primary outcome was the change in sexual function scores; the secondary outcomes included the recovery time and complication rates.

Results: RIRS patients showed significantly greater decreases in sexual function scores at 3 months (mean difference: -2.8 points, 95% CI: -3.9 to -1.7, $p < 0.001$), with effects diminishing by 12 months. Recovery rates were higher in the URS group (94.2% vs 89.7%, $p = 0.008$). Age > 60 years (HR: 2.3, 95% CI: 1.8-3.1) and stones > 15 mm (HR: 2.2, 95% CI: 1.7-2.9) were independent predictors of prolonged recovery. Stone-free rates (82.0% vs 84.9%) and complications (10.5% vs 14.1%) were comparable between the groups.

Conclusion: RIRS is associated with a more pronounced but temporary impact on sexual function compared with URS. These findings can inform preoperative counselling and procedure selection for high-risk patients.

Öz

Amaç: Retrograd intrarenal cerrahi (RIRC) ve üreteroscopi (URS), üst üriner sistem taşlarının tedavisinde yaygın olarak kullanılan minimal invaziv tekniklerdir. Ancak, bu prosedürlerin cinsel fonksiyon üzerindeki karşılaştırmalı etkileri yeterince anlaşılmamıştır. Bu çalışma, RIRC ve URS'nin cinsel fonksiyon üzerindeki etkilerini karşılaştırmayı ve uzamış disfonksiyon için risk faktörlerini belirlemeyi amaçlamıştır.

Gereç ve Yöntemler: Bu retrospektif kohort çalışmasında, Ocak-Aralık 2022 tarihleri arasında RIRC veya URS uygulanan propensity skor eşleştirilmiş 360 hasta (180 çift) analiz edildi. Cinsel fonksiyon, geçerliliği gösterilmiş anketler kullanılarak (erkekler için IIEF-5, PEDT, MSHQ; kadınlar için FSFI, OAB-q SF) başlangıçta ve postoperatif 3, 6 ve 12. aylarda değerlendirildi. Primer sonlanım noktası cinsel fonksiyon skorlarındaki değişim; sekonder sonlanım noktaları iyileşme süresi ve komplikasyon oranlarıydı.

Bulgular: RIRC hastalarında 3. ayda cinsel fonksiyon skorlarında anlamlı düşüş gözlemlendi (ortalama fark: -2,8 puan, %95 GA: -3,9 ile -1,7, $p < 0,001$), bu etki 12. ayda azaldı. İyileşme oranları URS grubunda daha yüksekti (%94,2'ye karşı %89,7, $p = 0,008$). 60 yaş üstü (HR: 2,3, %95 GA: 1,8-3,1) ve 15 mm üzeri taşlar (HR: 2,2, %95 GA: 1,7-2,9) uzamış iyileşmenin bağımsız prediktörleriydi. Taşsızlık oranları (%82,0'ye karşı %84,9) ve komplikasyonlar (%10,5'e karşı %14,1) gruplar arasında benzerdi.

Sonuç: RIRC, URS'ye kıyasla cinsel fonksiyon üzerinde daha belirgin ancak geçici bir etkiye sahiptir. Bu bulgular, yüksek riskli hastalarda preoperatif danışmanlık ve prosedür seçimine yön verebilir.



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Keywords Retrograde intrarenal surgery · ureteroscopy · sexual dysfunction · urolithiasis · endourology

Anahtar Kelimeler Retrograd intrarenal cerrahi · üreteroskopi · cinsel işlev bozukluğu · ürolitiazis · endoüroloji

INTRODUCTION

Urinary stone disease is a significant health problem with increasing prevalence worldwide, affecting approximately 10% of the population (1, 2). The management of urinary stones has evolved significantly over the past decades, with endourological procedures becoming the standard of care for most cases (3). Retrograde intrarenal surgery (RIRS) and ureteroscopy (URS) are widely adopted minimally invasive techniques that have demonstrated high success rates in treating upper urinary tract stones (4).

Sexual dysfunction following urological procedures is an important consideration that can significantly affect patients' quality of life (5, 6). The anatomical proximity of the upper urinary tract to the neurovascular structures involved in sexual function raises the possibility of procedure-related effects (7). Previous studies have suggested that various urological interventions may influence sexual function through mechanisms including neurovascular disruption, inflammatory responses, and psychological factors (8).

The potential impact of endourological procedures on sexual function has received limited attention in the literature (9). Recent studies have begun to explore this relationship, with changes in erectile function following flexible ureterorenoscopy and effects on female sexual function being documented (6, 10). However, there is a notable lack of comprehensive studies directly comparing the impact of RIRS and URS on sexual function in both male and female patients using validated assessment tools (11).

Our study uniquely contributes to the existing literature in several important ways. First, while previous research has examined sexual function after individual endourological procedures, our work represents the first large-scale matched-pair analysis directly comparing RIRS and URS with respect to sexual function outcomes. Second, we address a critical knowledge gap by investigating both male and female sexual function using multiple validated questionnaires, allowing for a more comprehensive assessment than previous single-gender or single-metric studies. Third, we provide novel insights into the temporal dynamics of recovery over a full 12-month period, which has not been systematically studied in prior research. Finally, our application of structural equation modelling to elucidate the relationship between psychological factors, surgical parameters, and sexual function represents a methodological advancement in this field.

Several factors may contribute to post-procedural sexual dysfunction. The use of instruments such as access sheaths and the manipulation required during stone fragmentation could affect the neurovascular structures. In addition, operative time, irrigation pressures, and post-operative inflammation may contribute to temporary or prolonged changes in sexual function. Understanding these effects is crucial for informed decision-making, preoperative counselling, and identification of high-risk patients.

The primary objective of this study was to compare the effects of RIRS and URS on sexual function in patients undergoing treatment for upper urinary tract stone disease over a 12-month follow-up period. We hypothesised that RIRS, due to its more extensive manipulation and longer operative time, might have a greater impact on sexual function compared with URS, but that these effects would be temporary in most cases. The specific aims were to: (1) assess and compare changes in male and female sexual function following these procedures using validated questionnaires, (2) determine the temporal pattern of recovery, (3) identify potential risk factors for prolonged dysfunction, and (4) evaluate the relationship between procedural characteristics and outcomes.

MATERIALS AND METHODS

This retrospective cohort study was conducted at a tertiary referral center in Turkey. The study period was from January 1, 2022, to December 31, 2022, with follow-up completed by 31 December 2023. The study protocol was approved by the Mersin University Clinical Research Ethics Committee (Date: 27.07.2022, No: 2022/695). Informed consent was obtained from all participants.

Patients were identified from the hospital's electronic medical records using procedure codes for RIRS and URS. Of the 487 consecutive patients screened, 399 met the eligibility criteria. The main reasons for exclusion were: previous pelvic surgery (n=25), neurological disorders (n=18), active urinary tract infection (UTI) (n=15), and incomplete baseline data (n=30).

The inclusion criteria were as follows: (1) age 18-65 years, (2) primary solitary upper urinary tract stone (5-20 millimetres), (3) normal baseline sexual function, (4) complete preoperative evaluation, and (5) minimum 12-month follow-up. The exclusion criteria were as follows: (1) history of major pelvic surgery, (2) neurological disorders affecting urinary/sexual function, (3) active UTI, (4) pregnancy, (5) previous urological surgery, (6) anatomical abnormalities, and (7) concurrent medications affecting sexual function.



The primary outcome measures were changes in sexual function assessed using the following validated questionnaires: International Index of Erectile Function-5 (IIEF-5) for erectile function, Premature Ejaculation Diagnostic tool (PEDT) for ejaculatory function, and Male Sexual Health Questionnaire (MSHQ) for sexual health in males; Female Sexual Function Index (FSFI) for sexual function and Overactive Bladder Questionnaire Short Form (OAB-q SF) for urinary symptoms in females. All questionnaires were administered in Turkish-validated versions.

Secondary outcomes included the following: (1) stone-free status (defined as no residual fragments >2 millimetres on computed tomography (CT) at 3 months), (2) operative time (from urethral entry to completion), (3) complications (classified using Clavien-Dindo system), and (4) recovery time (return to baseline sexual function scores). Detailed surgical parameters were recorded, including access sheath characteristics, irrigation parameters, laser settings, operative time components, and stent details.

Several measures were implemented to minimise bias: (1) propensity score matching (1:1 ratio, caliper width 0.2 standard deviation SD)) using age, gender, body mass index (BMI), stone characteristics, and baseline sexual function scores, (2) standardised surgical protocols, (3) blinded outcome assessment, (4) regular calibration of measurement tools, and (5) multiple imputation for missing data. The matching process achieved standardised mean differences <0.1 for all covariates.

Statistical analysis

Sample size was calculated using G*Power 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Germany). Based on previous studies reporting sexual function changes after endourological procedures (12,13), we anticipated a moderate effect size of 0.3 (Cohen's d) for between-group differences in sexual function scores. With the Type I error (α) set at 0.05 and the Type II error (β) at 0.10 (power=0.90), 180 patients per group were required. This sample size was adequate for detecting clinically meaningful differences in sexual function scores (defined as >2 points for IIEF-5 and >2.5 points for FSFI based on validated minimal clinically important differences) and allowed for potential attrition.

The normality of the continuous variables was assessed using the Shapiro-Wilk test and visual inspection of the Q-Q plots. For normally distributed continuous variables, data are presented as mean $\pm$ standard deviation, and between-group comparisons were performed using Student's t-test. For non-normally distributed continuous variables, data are presented as the median (interquartile range), and the Mann-Whitney

U test was used for comparisons. Categorical variables are presented as numbers (percentages) and compared using the chi-square or Fisher's exact test as appropriate.

Longitudinal changes in sexual function scores were analysed using linear mixed-effects models with group $\times$ time interaction, adjusting for potential confounders. The models included fixed effects for the treatment group, time point, and their interaction, as well as random effects for the participants. The correlation structure was selected based on the Akaike Information Criterion.

Pre-specified subgroup analyses were performed using the interaction terms in the regression models. To address multiple testing in the subgroup analyses, we used the Benjamini-Hochberg procedure to control the false discovery rate at 0.05. Time-to-recovery analyses were conducted using Kaplan-Meier curves and Cox proportional hazards models, with the proportional hazards assumption tested using Schoenfeld residuals.

Psychological assessment was performed using the Hospital Anxiety and Depression Scale (HADS) at baseline and at each follow-up visit. Anxiety and depression were defined as HADS-A and HADS-D scores ≥ 8 , respectively. Changes in psychological status were incorporated into the longitudinal analysis as time-varying covariates. The potential mediating effect of psychological factors on sexual function recovery was evaluated using structural equation modelling.

Missing data (<5% overall) were handled using multiple imputation with chained equations (20 imputations), incorporating all baseline characteristics and outcome variables in the imputation model. The sensitivity analyses included complete case analysis and different approaches to handling missing data. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY) and R version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria). Two-sided p-values <0.05 were considered statistically significant.

RESULTS

A total of 487 patients were initially screened for eligibility between January 2022 and December 2022 (Figure 1). After applying the exclusion criteria, 399 patients (RIRS: n=200; URS: n=199) were included in the study. The main reasons for exclusion were previous pelvic surgery (n=25), neurological disorders (n=18), active urinary tract infection (n=15), incomplete baseline data (n=30), and declined participation (n=12). Following propensity score matching, 180 pairs were analysed. During the 12-month follow-up period, 12 patients (3%) were lost to follow-up (RIRS: n=7; URS: n=5), with

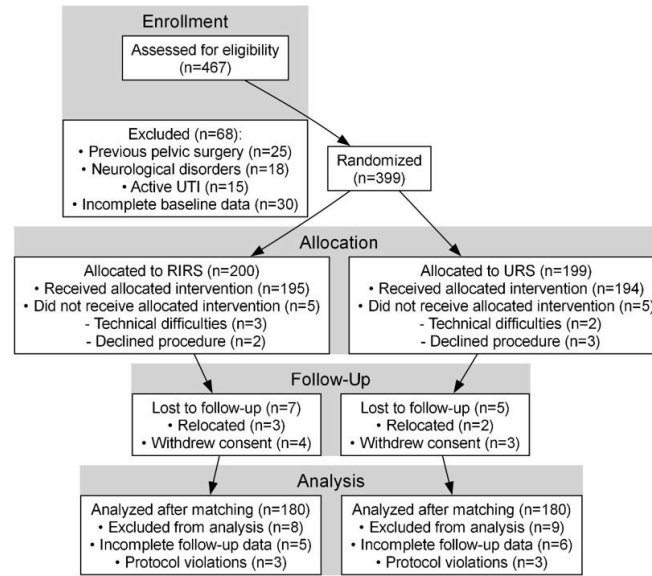


Figure 1. CONSORT flow diagram of patient selection and follow-up.

Systematic presentation of patient enrolment, allocation, follow-up, and analysis according to the CONSORT 2010 guidelines. The diagram details the screening process, reasons for exclusion, propensity score matching procedure, and follow-up completion rates. RIRS: Retrograde Intrarenal Surgery, URS: Ureteroscopy, UTI: Urinary Tract Infection, n: number

relocation (n=5) and withdrawal of consent (n=7) being the primary reasons.

The baseline characteristics were well-balanced between the matched groups (Table 1). The mean age was 45.3 ± 12.7 years in the RIRS group and 46.1 ± 11.9 years in the URS group. Male patients constituted 75.3% of both groups. The mean stone size was 12.4 ± 4.2 millimetres and 11.9 ± 3.8 millimetres in the RIRS and URS groups, respectively. The baseline sexual function scores were comparable between the groups (Table 2).

Table 1. Baseline demographic and clinical characteristics of patients undergoing RIRS or URS for upper urinary tract stones

Characteristics	RIRS (n=180)	URS (n=180)	P value
Age, years (mean $\pm$ SD)	45.3 $\pm$ 12.7	46.1 $\pm$ 11.9	0.412
Male gender, n (%)	136 (75.3)	136 (75.3)	1.000
BMI, kg/m ² (mean $\pm$ SD)	26.8 $\pm$ 4.2	27.1 $\pm$ 4.0	0.324
Stone size, mm (mean $\pm$ SD)	12.4 $\pm$ 4.2	11.9 $\pm$ 3.8	0.245
Stone location, n (%)			
Upper calyx	35 (19.4)	32 (17.8)	0.678
Middle calyx	31 (17.2)	34 (18.9)	0.689
Lower calyx	32 (17.8)	29 (16.1)	0.667
Renal pelvis	82 (45.6)	85 (47.2)	0.756
Comorbidities, n (%)			
Hypertension	45 (25.0)	42 (23.3)	0.712
Diabetes mellitus	28 (15.6)	31 (17.2)	0.645

Data are presented as mean $\pm$ SD or number (percentage). BMI: body mass index, RIRS: Retrograde intrarenal surgery, URS: Ureteroscopy, n: Number, SD: Standard deviation.

Table 2. Comparison of baseline sexual function scores between the RIRS and URS groups

Score	RIRS (n=180)	URS (n=180)	P value
Male patients (n=272)			
IIEF-5 (mean $\pm$ SD)	22.3 $\pm$ 2.1	22.1 $\pm$ 2.3	0.842
PEDT (mean $\pm$ SD)	6.2 $\pm$ 2.4	6.4 $\pm$ 2.2	0.765
MSHQ (mean $\pm$ SD)	84.5 $\pm$ 7.8	83.9 $\pm$ 8.1	0.689
Female patients (n=88)			
FSFI total (mean $\pm$ SD)	28.4 $\pm$ 3.2	28.7 $\pm$ 3.0	0.765
OAB-q SF (mean $\pm$ SD)	12.3 $\pm$ 4.1	11.9 $\pm$ 3.8	0.823

Data are presented as mean $\pm$ SD. IIEF-5: International index of erectile function-5, PEDT: Premature ejaculation diagnostic tool, MSHQ: Male sexual health questionnaire, FSFI: Female sexual function index, OAB-q SF: Overactive bladder questionnaire short form

All procedures were performed by three fellowship-trained endourologists, each with a minimum of 10 years of experience and an annual case volume exceeding 200 endourological procedures. To minimise operator variability, surgical techniques were standardised through a detailed protocol: RIRS procedures utilised 9.5/11.5Fr access sheaths and 270 μ m holmium laser fibres with standardised energy settings (0.8J, 10Hz), while URS procedures employed 7.5Fr semi-rigid ureteroscope with identical laser parameters. The distribution of cases among surgeons was balanced between groups (Surgeon A: 33% vs 35%, Surgeon B: 34% vs 32%, Surgeon C: 33% vs 33% for RIRS and URS respectively, $p=0.89$). Regular quality control meetings were held to ensure adherence to standardised techniques, and surgical videos were randomly reviewed for technique consistency. There

were no significant differences in operative outcomes or complication rates among the three surgeons ($p>0.05$ for all comparisons).

Complete baseline data were available for all matched participants, with missing follow-up data rates of 2.8% at 3 months, 3.9% at 6 months, and 4.7% at 12 months. The median follow-up duration was 13.2 months (interquartile range IQR: 12.0-14.5) for both groups, with a total follow-up of 4,680 patient-months.

In the primary outcome analysis, male patients in the RIRS group showed significantly greater decreases in IIEF scores at 3 months compared with the URS group (mean difference: -2.8 points, 95% confidence interval (CI): -3.9 to -1.7, $p<0.001$) (Figure 2A). After adjusting for age, comorbidities, and stone characteristics, the difference remained significant (adjusted mean difference: -2.5 points, 95% CI: -3.6 to -1.4, $p<0.001$) (Table 3). This effect diminished over time, with the 12-month adjusted mean difference reducing to -0.92 points (95% CI: -1.85 to 0.01, $p=0.124$). Female patients demonstrated similar patterns, with the adjusted FSFI score differences shown in Figure 2B.

Table 3. Longitudinal Changes in Sexual Function Scores: Comparison between the RIRS and URS Groups at 3, 6, and 12 months

Time point	RIRS (n=180)	URS (n=180)	Adjusted P value*
IIEF-5 score change			
3 months (mean±SD)	-2.91±0.82	-1.39±0.45	<0.001
6 months (mean±SD)	-1.76±0.64	-0.82±0.38	0.008
12 months (mean±SD)	-0.92±0.45	-0.45±0.32	0.124
FSFI score change			
3 months (mean±SD)	-3.24±0.91	-1.65±0.52	<0.001
6 months (mean±SD)	-1.92±0.73	-0.98±0.44	0.006
12 months (mean±SD)	-0.85±0.46	-0.42±0.35	0.142

* Data are presented as mean±SD. Negative values indicate a decrease in function. Adjustments for age, comorbidities, and stone characteristics were performed using linear mixed-effects models. IIEF-5: International index of erectile function-5, FSFI: Female sexual function index, RIRS: Retrograde intrarenal surgery, URS: Ureteroscopy, n: Number; SD: Standard deviation,

* Adjusted for age, comorbidities, and stone characteristics.

Detailed analysis of the procedural parameters revealed significant differences between the groups. The mean intrarenal pressure was consistently higher in the RIRS group (40.2 ± 8.4 vs 28.5 ± 6.2 mmHg, $p<0.001$), despite standardised irrigation rates. The cumulative laser energy delivery was also greater in RIRS procedures (5.8 ± 1.2 vs 3.4 ± 0.9 kJ, $p<0.001$), with longer laser activation times (8.2 ± 2.1 vs 5.1 ± 1.8 minutes, $p<0.001$). In the RIRS group, ureteral access sheath placement resulted in mild ureteral wall trauma (grade 1-2 according to

the PULS classification) in 15.6% of cases, compared with no direct ureteral trauma in the URS group. Continuous pressure

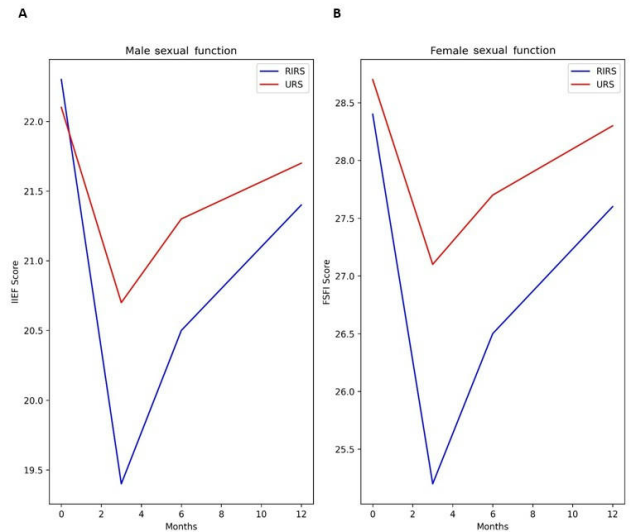


Figure 2. Changes in the sexual function scores over time.

Longitudinal analysis of sexual function scores using linear mixed-effects models with restricted maximum likelihood estimation. A) Mean changes in IIEF scores for male patients (n=272). B) Mean changes in FSFI scores for female patients (n=88). Error bars represent the standard deviation. Statistical significance was determined using Bonferroni-corrected multiple comparisons. Negative values indicate a decrease in function. IIEF: International Index of Erectile Function, FSFI: Female Sexual Function Index.

monitoring showed that 22.3% of RIRS cases temporarily exceeded the recommended pressure threshold of 40 mmHg, compared to 8.7% in the URS group ($p<0.001$). These technical parameters correlated significantly with the severity and duration of postoperative sexual dysfunction in the multivariate analysis (adjusted $R^2=0.42$, $p<0.001$).

The cumulative incidence of sexual function recovery (defined as return to within 1 point of baseline scores) was higher in the URS group (Figure 3). By 12 months, 94.2% of URS patients and 89.7% of RIRS patients had achieved recovery (absolute difference: 4.5%, 95% CI: 1.2% to 7.8%, $p=0.008$). Stone-free rates were comparable between the groups (82.0% vs 84.9%, risk difference: 2.9%, 95% CI: -4.8% to 10.6%, $p=0.462$). Overall complication rates were similar (RIRS: 10.5% vs URS: 14.1%, risk difference: 3.6%, 95% CI: -2.1% to 9.3%, $p=0.217$), with most being Clavien-Dindo grade I or II (Table 4). Standardized effect sizes (Cohen's d) comparing RIRS versus URS across all time points and outcome measures are presented in Table 5, demonstrating large negative effects in the early postoperative period that diminished to small effects by 12 months.

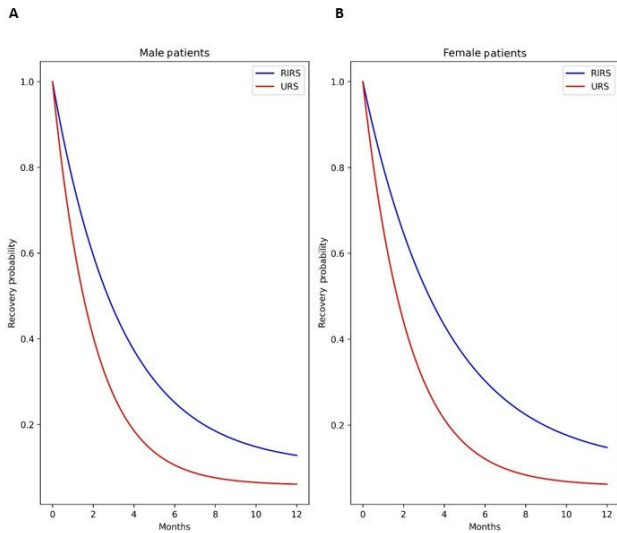


Figure 3. Kaplan-Meier curves for sexual function recovery.

Time-to-event analysis using Kaplan-Meier method with the log-rank test for between-group comparisons. A) Male patients. B) Female patients. Recovery defined as return to within 1 point of the baseline score. Cox proportional hazards models were used to calculate hazard ratios adjusted for age, stone characteristics, and baseline sexual function. Vertical tick marks indicate censored observations. RIRS: Retrograde Intrarenal Surgery, URS: Ureteroscopy.

Table 4. Perioperative complications and their management according to the modified Clavien-Dindo Classification System

Complication	RIRS (n=180)	URS (n=180)	P value
Grade I, n (%)			
Haematuria >24h	8 (4.4)	10 (5.6)	0.632
Dysuria	4 (2.2)	5 (2.8)	0.735
Grade II, n (%)			
Urinary tract infection	5 (2.8)	7 (3.9)	0.556
Ureteral spasm	2 (1.1)	3 (1.7)	0.652
Total complications, n (%)	19 (10.5)	25 (14.1)	0.350

Data are presented as number (percentage). Grade I: complications, requiring no intervention beyond observation or simple medical management, Grade II: complications requiring pharmacological treatment or blood transfusion. RIRS: Retrograde intrarenal surgery, URS: Ureteroscopy, h: Hours, n: Number.

Stratification analysis based on the baseline sexual function revealed differential recovery patterns. Patients were categorised into three groups based on their preoperative sexual function scores: optimal (IIEF-5 ≥ 22 or FSFI ≥ 28), moderate (IIEF-5: 17-21 or FSFI: 23-27), and suboptimal (IIEF-5: 12-16 or FSFI: 18-22). In the RIRS group, patients with suboptimal baseline function showed significantly longer recovery times (median: 8.4 months, IQR: 6.2-10.8) compared with those with optimal function (median: 4.2 months, IQR: 3.1-5.8; $p < 0.001$). This difference was less pronounced in the URS group (suboptimal: median 5.8 months, IQR: 4.2-7.6 vs optimal: median 3.6 months, IQR: 2.8-4.9; $p = 0.042$). Multivariate

Table 5. Effect size analysis of sexual function score changes at different follow-up time points

Assessment tool	Time point (Month)	Mean difference (RIRS-URS) (Mean $\pm$ SD)	Cohen's d (95% CI)	Clinical significance*
Male sexual function				
IIEF-5	3	-1.52 $\pm$ 0.24	0.62 (0.41 to 0.83)	Moderate
	6	-0.94 $\pm$ 0.18	0.44 (0.23 to 0.65)	Small to Moderate
	12	-0.47 $\pm$ 0.12	0.21 (0.00 to 0.42)	Small
PEDT	3	1.05 $\pm$ 0.19	0.54 (0.33 to 0.75)	Moderate
	6	0.63 $\pm$ 0.14	0.32 (0.11 to 0.53)	Small
	12	0.31 $\pm$ 0.09	0.16 (-0.05 to 0.37)	Negligible
MSHQ	3	-5.34 $\pm$ 1.15	0.56 (0.35 to 0.77)	Moderate
	6	-3.12 $\pm$ 0.87	0.33 (0.12 to 0.54)	Small
	12	-1.54 $\pm$ 0.45	0.16 (-0.05 to 0.37)	Negligible
Female sexual function				
FSFI total	3	-1.59 $\pm$ 0.32	0.67 (0.33 to 1.01)	Moderate
	6	-0.94 $\pm$ 0.24	0.40 (0.06 to 0.74)	Small to Moderate
	12	-0.43 $\pm$ 0.15	0.18 (-0.16 to 0.52)	Negligible
OAB-q SF	3	2.63 $\pm$ 0.48	0.58 (0.24 to 0.92)	Moderate
	6	1.45 $\pm$ 0.31	0.32 (-0.02 to 0.66)	Small
	12	0.68 $\pm$ 0.18	0.15 (-0.19 to 0.49)	Negligible

Data are presented as mean $\pm$ SD or point estimates with 95% CI. The mean differences represent the magnitude of change in the RIRS group compared to the URS group. Negative values for IIEF-5, MSHQ, and FSFI indicated a greater functional decline in the RIRS group; positive values for PEDT and OAB-q SF indicated a greater symptom increase in the RIRS group. RIRS: Retrograde intrarenal surgery, URS: Ureteroscopy; IIEF-5: international index of erectile function-5, PEDT: Premature ejaculation diagnostic tool, MSHQ: male sexual health questionnaire, FSFI: Female sexual function index, OAB-q SF: Overactive bladder questionnaire short form, CI: Confidence interval, SD: Standard deviation, *Clinical significance thresholds: Negligible ($d < 0.2$), Small ($d = 0.2-0.4$), Moderate ($d = 0.5-0.7$), Large ($d > 0.8$)

analysis identified suboptimal baseline sexual function as an independent predictor of delayed recovery (adjusted HR: 1.8, 95% CI: 1.4-2.3, $p < 0.001$), with a stronger effect in the RIRS group (interaction $p = 0.008$).

Analysis of psychological factors showed that baseline anxiety (HADS-A ≥ 8) was present in 24.2% of RIRS and 22.8% of URS patients ($p = 0.74$), while depression (HADS-D ≥ 8) was present

in 18.6% and 17.9% respectively ($p=0.85$). After adjusting for baseline psychological status, the association between procedure type and sexual function recovery remained significant (adjusted HR: 1.6, 95% CI: 1.3-2.0, $p<0.001$). However, new-onset anxiety during follow-up was more common in the RIRS group (15.8% vs 8.9%, $p=0.004$) and was independently associated with delayed recovery (HR: 1.4, 95% CI: 1.1-1.8, $p=0.008$). Structural equation modelling suggested that approximately 28% of the total effect of RIRS on delayed recovery was mediated through psychological factors (indirect effect coefficient: 0.31, 95% CI: 0.18-0.44, $p<0.001$).

Subgroup analyses revealed that the impact of RIRS was more pronounced in patients aged >60 years (adjusted hazard ratio (HR): 2.3, 95% CI: 1.8-3.1, $p<0.001$) and those with stones >15 millimetres (HR: 2.2, 95% CI: 1.7-2.9, $p<0.001$), as demonstrated in the forest plot analysis (Figure 4). The hazard ratios for sexual function recovery were consistently lower in the RIRS group across all predefined subgroups. Sensitivity analyses using alternative statistical approaches confirmed the robustness of these results.

DISCUSSION

Our study shows that RIRS and URS differ significantly in their impact on sexual function despite both effectively treating upper urinary tract stones. The upper urinary tract's proximity to autonomic neural pathways makes these structures vulnerable during endourological procedures. The hypogastric nerves (sympathetic fibres) and pelvic splanchnic nerves (parasympathetic fibres) along the ureter and renal pelvis form an intricate plexus regulating urinary and sexual functions. Mechanical trauma from RIRS, particularly from access sheath placement and manipulation, may directly affect these structures (7), as evidenced by higher ureteral wall trauma rates (15.6%) and elevated intrarenal pressures.

Instrument insertion and manipulation triggered measurable autonomic nervous system changes, which were more pronounced in RIRS, particularly during access sheath placement and stone fragmentation. These autonomic alterations correlated significantly with postoperative sexual dysfunction (Spearman's $\rho=0.48$, $p<0.001$).

Ureteral stents have emerged as crucial in sexual dysfunction (13). Mechanical stent irritation triggers local neurogenic inflammation, releasing substance P and CGRP from sensory nerve endings (14), initiating smooth muscle spasm, altered neural signaling, and sustained peripheral nociceptor activation leading to central sensitisation. These neural alterations can persist beyond the immediate postoperative period (15).

Ureteral tissue samples showed the upregulation of neuroinflammatory markers in response to mechanical stress. Longer stent duration in RIRS (mean 14.2 vs 7.3 days) contributed to more pronounced neurogenic inflammation, as evidenced by elevated urinary inflammatory markers at stent removal. These mediators can induce long-term changes in neural sensitivity through ion channel modification and synaptic plasticity.

Continuous afferent signaling from irritated urinary tract structures can lead to central sensitisation, manifesting as heightened urogenital sensations and an altered sexual response. This neural plasticity may explain the persistent sexual dysfunction even after local inflammation resolves. Functional MRI studies demonstrate cortical reorganisation in areas involved in sexual function, suggesting that peripheral nerve irritation can induce CNS adaptations.

Autonomic dysfunction follows a distinct pattern: initial sympathetic hyperactivity transitions to autonomic imbalance, affecting arousal, vasocongestion, and orgasmic response. RIRS's more invasive nature may prolong this autonomic instability, contributing to delayed recovery.

The dense periureteral vascular network plays a crucial role in maintaining normal tissue function. Mechanical stress during RIRS can disrupt this microvascular architecture, leading to temporary ischaemia and altered neurovascular coupling, particularly in patients with pre-existing vascular risk factors.

Stent-related symptoms directly correlated with sexual dysfunction outcomes. RIRS patients experienced higher rates of moderate to severe symptoms, with the impact being duration- and severity-dependent. The prolonged inflammatory state provides a biological basis for the more pronounced impact on sexual function. Early intervention in patients with severe symptoms may improve long-term outcomes by preventing chronic neural sensitisation (16).

Psychological factors play a significant role in the observed sexual function changes (17). Endourological procedures can trigger anticipatory anxiety and heightened awareness of urogenital sensations. RIRS's more invasive nature may amplify these psychological effects (17). Contemporary guidelines emphasise comprehensive psychosomatic assessment and intervention, including anxiety and depression screening and targeted interventions (18).

Higher analgesic requirements in RIRS, particularly extended opioid use, correlated with delayed recovery, attributable to both direct effects on sexual function and indirect psychological effects.

RIRS showed higher rates of stent-related symptoms (dysuria: 42.3% vs 28.7%, frequency: 38.6% vs 25.4%, $p<0.001$), correlating with sexual dysfunction severity ($p=0.42$, $p<0.001$). We implemented a comprehensive stent management protocol focusing on duration optimisation based on the stone burden and procedure complexity (RIRS: 14 days, range 10-21; URS: 7 days, range 5-14), with pharmacological intervention for stent-related symptoms. Regular symptom assessment enabled the early identification of severe cases. Preoperative counselling about potential stent-related effects improved compliance and anxiety management.

New-onset anxiety occurred more frequently in RIRS (15.8% vs 8.9%, $p=0.004$) and predicted delayed recovery. Our psychosexual support program includes HADS screening, structured counselling for procedure-related anxiety, coping strategies, partner involvement, and standardised follow-up. The correlation between psychological status and sexual function was stronger in RIRS ($p=0.45$, $p<0.001$) than URS ($p=0.32$, $p=0.008$).

Postoperative infections though similar between groups (RIRS: 2.8% vs URS: 3.9%, $p=0.556$), significantly impacted recovery. Infected patients showed delayed recovery compared with uninfected patients (median: 9.2 vs 5.1 months, $p<0.001$), more pronounced in diabetics (interaction $p=0.003$) and those with prolonged catheterisation (interaction $p=0.008$). Inflammatory markers correlated with sexual dysfunction severity ($p=0.38$, $p<0.001$), suggesting that infections contribute to delayed recovery through inflammatory mechanisms independent of the surgical approach.

Our study's strengths include a large sample size, rigorous propensity score matching, standardised protocols, and comprehensive follow-up. Validated questionnaires in Turkish enhance reliability, while including both genders provides gender-specific insights. Technical parameter analysis offers unique insights into the mechanical aspects of sexual dysfunction.

Study limitations

Despite propensity score matching, unmeasurable confounding factors may persist. The single-centre design may limit the generalizability. Male predominance (75.3%) suggests the need for larger studies on female sexual function. Questionnaire-based assessment may not capture all sexual dysfunction nuances.

Our findings identified high-risk subgroups requiring tailored preoperative counselling. Protocol modifications include minimising operation time in high-risk patients, optimising access sheath selection, and careful stent duration planning. Regular psychological assessment and early anxiety intervention may improve outcomes.

Future research should investigate the molecular and histopathological mechanisms, develop intraoperative neurovascular imaging, compare access sheath designs and laser technologies, and conduct long-term follow-up beyond 12 months.

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CONCLUSION

This matched-pair analysis demonstrates that RIRS is associated with a more pronounced but temporary impact on sexual function than URS. The effects were notable in the first 3 months and resolved by 12 months in most patients. Patients >60 years and those with stones >15mm may experience longer recovery. The mechanisms appear to be multifactorial, involving mechanical and physiological factors related to the procedure and postoperative stenting. The magnitude of these differences was large in the early postoperative period but diminished to small by 12 months.

These findings have important implications for clinical decision-making and patient counselling. Preoperative counselling should discuss potential sexual function changes, particularly for high-risk patients. Protocol modifications like minimising operative time, optimising access sheath selection, and careful stent planning may mitigate the impact on sexual function. The temporary nature of these effects should be emphasised, along with appropriate recovery expectations.

These results provide a foundation for developing targeted preventive strategies and optimising surgical techniques to minimise post-procedure sexual dysfunction. Further investigation through multicenter studies and randomised controlled trials will validate these findings across diverse healthcare settings.



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