

URINARY INFLAMMATORY LEVELS, AND SERUM OXIDATIVE STRESS MARKERS IN PATIENTS WITH URETERAL STONES

NIVOI INFLAMATORNIH PARAMETARA U URINU I MARKERI OKSIDATIVNOG STRESA U SERUMU KOD PACIJENATA SA KAMENCEM U URETERU

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Summary

Background: The clinical incidence of ureteral stones is increasing year by year, and minimally invasive surgical treatment is one of the main therapeutic approaches. This study investigated the effects of combined Shuo Tong ureteroscope and flexible ureteroscope (FU) treatment on inflammatory response, oxidative stress, and stone clearance rate (SCR) in patients with ureteral stones.

Methods: A retrospective analysis was conducted on 85 patients with ureteral stones admitted from May 2022 to May 2025. They were allocated to two cohorts based on the surgical approach: Shuo Tong ureteroscope combined with FU (ST-FU, 43 cases) and FU alone (FU, 42 cases). Perioperative indicators were collected. Pain intensity was assessed using the Visual Analogue Scale (VAS). Peripheral blood was collected, and levels of inflammatory factors (white blood cell count [WBC], C-reactive protein [CRP], interleukin-6 [IL-6], tumour necrosis factor- α [TNF- α]), oxidative stress markers (malondialdehyde [MDA], superoxide dismutase [SOD]), and renal injury marker (kidney injury molecule-1 [KIM-1]) were measured.

Results: The ST-FU group had significantly shorter operative times and lower VAS scores and analgesic usage counts at 1, 3, and 7 days postoperatively ($P < 0.05$). Levels of WBC, CRP, TNF- α , MDA, and KIM-1 at 1 and 3 days postoperatively were significantly lower in the ST-FU group than in the FU group, whereas SOD levels were significantly higher ($P < 0.05$). Unadjusted early SCR was higher in the ST-FU group at postoperative day 1 (88.37% vs 61.90%, $P = 0.003$), day 3 (90.70% vs 71.43%, $P = 0.008$), and day 7 (90.70% vs 73.81%,

Kratak sadržaj

Uvod: Klinička incidencija kamenaca uretera raste iz godine u godinu, a minimalno invazivno hirurško lečenje predstavlja jedan od glavnih terapijskih pristupa. Ova studija je ispitivala efekte kombinovane primene Shuo Tong ureteroskopa i fleksibilnog ureteroskopa (FU) na inflamatorni odgovor, oksidativni stres i stopu uklanjanja kamenaca kod pacijenata sa kamencem uretera.

Metode: Sprovedena je retrospektivna analiza na 85 pacijenata sa kamencem uretera hospitalizovanih u periodu od maja 2022. do maja 2025. godine. Pacijenti su raspoređeni u dve grupe prema primenjenom hirurškom pristupu: Shuo Tong ureteroskop u kombinaciji sa FU (ST-FU, 43 pacijenta) i FU samostalno (FU, 42 pacijenta). Prikupljeni su perioperativni pokazatelji. Intenzitet bola je procenjivan pomoću vizuelne analogne skale (VAS). Uzorci periferne krvi su korišćeni za određivanje nivoa inflamatornih faktora (broj leukocita [WBC], C-reaktivni protein [CRP], interleukin-6 [IL-6], faktor nekroze tumora alfa [TNF- α]), markera oksidativnog stresa (malondialdehid [MDA], superoksid-dismutaza [SOD]) i markera oštećenja bubrega (molekul 1 oštećenja bubrega [KIM-1]).

Rezultati: Grupa ST-FU je imala značajno kraće trajanje operacije, niže VAS skorove i manji broj primena analgetika 1, 3 i 7 dana nakon operacije ($P < 0,05$). Nivoi WBC, CRP, TNF- α , MDA i KIM-1 jedan i tri dana nakon operacije su bili značajno niži u grupi ST-FU nego u grupi FU, dok su nivoi SOD bili značajno viši ($P < 0,05$). Neprilagođena rana stopa uklanjanja kamenca je bila viša u grupi ST-FU prvog postoperativnog dana (88,37% prema 61,90%, $P = 0,003$), trećeg dana (90,70% prema 71,43%, $P = 0,008$) i sedmog dana (90,70% prema 73,81%,

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$P=0.012$). However, after adjustment for baseline stone diameter, the association between ST-FU and POD3 SCR was attenuated (adjusted OR=2.05, 95% CI: 0.68–6.18, $P=0.201$).

Conclusion: The combined use of a Shuo Tong ureteroscope and FU was associated with shorter operative time, lower postoperative pain, reduced inflammatory and oxidative stress responses, and lower renal tubular injury markers in patients with ureteral stones. Although unadjusted early SCR was higher in the ST-FU group, this finding should be interpreted cautiously because of baseline stone-size imbalance and attenuation after adjustment.

Keywords: Shuo Tong ureteroscope, flexible ureteroscope, ureteral calculi, inflammatory response, oxidative stress, stone clearance rate

Introduction

Ureteral calculi (UC) are primarily composed of calcium salts, uric acid salts, and other crystals deposited within the urinary tract (1, 2). With changes in lifestyle and the increase in metabolic diseases, the incidence of UC is rising, with a notable trend towards younger patients (3). The widespread use of imaging examinations such as CT has improved early detection rates. However, UC is more challenging to treat due to its deep location, high mobility, and multiple narrow segments (4, 5). Reducing surgical trauma, minimising residual stones, and lowering complications while ensuring safety are important research directions in urology.

At present, minimally invasive treatment techniques for UC are rapidly developing (6). Extracorporeal shock wave lithotripsy has limited effectiveness for large or hard UC and a higher residual stone rate (7). Rigid ureteroscopes are gradually being used less for UC due to the risk of ureteral injury (8). The Flexible ureteroscope (FU), with its advantages of flexibility, good visualisation, and strong reach, has become an important treatment for UC (9). However, single FU still has issues such as high irrigation pressure, limited operating space, limited lithotripsy efficiency, and higher postoperative infection risk (10). The Shuo Tong ureteroscope system is a new type of urological endoscopic device. By combining a rigid sheath with a negative-pressure suction system, it can significantly reduce intracavitary pressure while maintaining stable visualisation and high stone expulsion capability (11, 12). When used in combination with FU, it can further improve lithotripsy efficiency, shorten surgical duration, reduce stone migration and irrigation fluid reflux, and improve intraoperative safety and procedural smoothness.

Although urinary stone surgery is minimally invasive, the lithotripsy process inevitably causes mucosal traction, mechanical impact, and increased

$P=0.012$). Međutim, nakon prilagođavanja za početni prečnik kamena, povezanost između ST-FU pristupa i stope uklanjanja kamenaca trećeg postoperativnog dana je bila je niža (prilagođeni OR=2,05; 95% CI: 0,68–6,18; $P=0,201$).

Zaključak: PKombinovana primena Shuo Tong ureteroskopa i fleksibilnog ureteroskopa je bila povezana sa kraćim trajanjem operacije, manjim postoperativnim bolom, smanjenim inflamatornim odgovorom i oksidativnim stresom, kao i nižim nivoima markera oštećenja bubrežnih tubula kod pacijenata sa kamencem uretera. Iako je neprilagođena rana stopa uklanjanja kamenca bila viša u grupi ST-FU, ovaj nalaz treba tumačiti sa oprezom zbog početne neravnoteže u veličini kamenaca između grupa i slabljenja povezanosti nakon statističkog prilagođavanja.

Ključne reči: Shuo Tong ureteroskop, fleksibilni ureteroskop, kamenci uretera, inflamatorni odgovor, oksidativni stres, stopa uklanjanja kamenaca

irrigation pressure, triggering local and systemic inflammatory responses (13). Surgical trauma also activates the hypothalamic-pituitary-adrenal axis and induces oxidative stress, reflected by increased malondialdehyde (MDA) and decreased superoxide dismutase (SOD) activity (14, 15). Furthermore, kidney injury molecule-1 (KIM-1) is a sensitive biomarker of renal tubular damage that can be elevated after ureteroscopic procedures (16). Excessive inflammation and oxidative stress may delay recovery, worsen pain, and increase the risk of infection (17, 18). Therefore, evaluating the effects of different surgical methods on responses to inflammation-stress and renal injury is of great significance.

Given the potential technical advantages of combining the Shuo Tong ureteroscope with FU, this study aimed to compare the clinical performance of ST-FU and FU alone in patients with ureteral stones, with particular attention to postoperative inflammatory response, oxidative stress markers (MDA and SOD), renal tubular injury marker (KIM-1), and stone clearance outcomes.

Materials and Methods

Basic information

Clinical records of 85 patients with solitary ureteral stones who received treatment in the Department of Urology of Kunshan Fourth People's Hospital from May 2022 to May 2025 were collected. Based on the surgical procedure, patients were divided into two groups: ST-FU group ($n=43$) and FU group ($n=42$).

In the ST-FU group, there were 30 males and 13 females with an average age of 40.64 ± 14.02 years, a BMI of 23.09 ± 3.40 kg/m², and a maximum stone diameter of 7.71 ± 2.37 mm. The FU group had 29 males, 13 females, and numbers showing. Most

baseline characteristics were comparable between the two groups, including age, sex, BMI, stone location, hydronephrosis grade, preoperative WBC, and preoperative CRP. However, the maximum stone diameter was significantly smaller in the ST-FU group than in the FU group. Therefore, maximum stone diameter was treated as a potential confounder and was adjusted for in subsequent regression analyses. Because this was a retrospective non-randomised study, the surgical approach was not assigned by randomisation. The choice between ST-FU and FU alone was made preoperatively by the treating urologist, in accordance with routine clinical practice, based on preoperative imaging findings, stone characteristics, anatomical considerations, equipment availability, and surgeon judgment. In general, ST-FU was preferred when active fragment evacuation or reduced irrigation reflux was clinically desirable, such as in patients with stones expected to be at higher risk of migration, limited working space, or anticipated longer lithotripsy time. FU alone was selected when the treating surgeon considered standard flexible ureteroscopy sufficient based on stone location, stone size, ureteral anatomy, and expected procedural complexity. No random allocation was performed.

A CONSORT-style patient selection flow diagram was created to illustrate the number of patients screened, those excluded with reasons, those included in the final cohort, and those grouped according to surgical procedure, and analysed in each study group. Because this was a retrospective non-randomised study, group allocation was based on the surgical approach actually performed rather than random assignment (*Figure 1*).

Inclusion criteria were as follows: age 18–75 years; diagnosis of ureteral calculi confirmed by imaging; presence of a single stone <2 cm; and complete clinical data. Exclusion criteria were urinary anatomical abnormalities, urinary tuberculosis or tumours, obesity defined as BMI ≥ 30 kg/m² according to WHO adult BMI criteria, severe cardiac, hepatic, or renal dysfunction, preoperative urinary WBC >500 cells/ μ L, previous urinary stone surgery, and severe infection requiring drainage. Obesity was excluded because it is associated with chronic low-grade inflammation and oxidative stress, which could confound postoperative levels of inflammatory and oxidative biomarkers. Approval was obtained from the Kunshan Fourth People's Hospital Ethics Committee.

Surgical methods

ST-FU group: Under general anaesthesia, the F7.5/11.5 Shuo Tong standard scope was assembled with an F11.5/13.5 rigid ureteral access sheath. After reaching the target position, the outer sheath was connected to negative-pressure suction. A 200 μ m holmium laser fragmented the stone, and the fragments were removed by suction. If the stone migrated to the lower calyx, a FU was performed to continue lithotripsy. A double-J stent was placed postoperatively.

FU group: Under general anaesthesia, an F9.8 Wolf rigid ureteroscope was inserted, followed by FU sheath placement. The FU was inserted, and lithotripsy was performed using a 200 μ m holmium laser. A double-J stent was placed postoperatively.

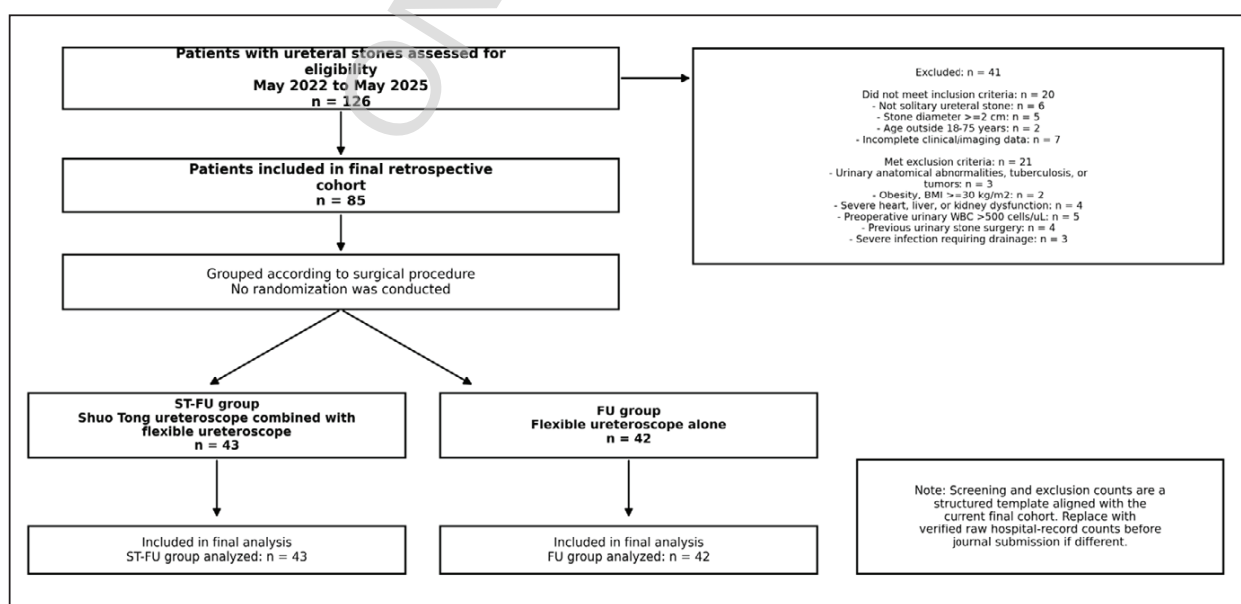


Figure 1 CONSORT-style patient selection and group allocation flow diagram.

Observation indicators

(1) Clinical indicators: Surgical duration, catheter removal time, hospital stay.

(2) Pain intensity: VAS score (0–10) preoperatively and at 1, 3, 7 days postoperatively (19). Analgesic usage counts were recorded.

(3) Serum inflammation and oxidative stress markers: Fasting peripheral venous blood samples were collected preoperatively and at postoperative days 1 and 3. After centrifugation, serum samples were separated and stored according to the manufacturer's instructions until analysis. WBC was measured using an automated haematology analyser. Serum CRP, IL-6, TNF- α , MDA, SOD, and KIM-1 levels were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits. Serum KIM-1 was selected because standardised perioperative blood samples were routinely available in this retrospective cohort and could be analysed alongside other serum inflammatory and oxidative stress markers. Urinary KIM-1 was not assessed because standardised perioperative urine samples suitable for biomarker analysis were not consistently available.

Stone clearance assessment

Stone clearance was assessed using postoperative CT imaging on days 1, 3, 7, 14, and 28. In this study, stone clearance was defined as the complete absence of visible residual stone fragments on CT imaging. All postoperative CT images were independently reviewed by two radiologists who were blinded to the surgical approach and clinical outcomes. Disagreements were resolved by consensus; when consensus could not be reached, a senior radiologist made the final decision.

(4) SCR: CT imaging at 1, 3, 7, 14, and 28 days postoperatively. Complete disappearance was considered stone clearance.

(5) Complications: Fever, hematuria, infection, organ injury, ureteral stricture.

Statistical analysis

SPSS 24.0 was used. Continuous data were analysed using t-tests or Mann-Whitney U tests; categorical data using χ^2 tests. A repeated-measures ANOVA was used for longitudinal data; $P < 0.05$ was significant. Because maximum stone diameter differed significantly between the two treatment groups at baseline, additional adjusted analyses were performed to evaluate the robustness of the primary findings. For continuous postoperative outcomes, including operative time, VAS score, inflammatory markers, oxidative stress markers, and KIM-1 levels, multivariable linear regression models were constructed with surgical technique as the main exposure and maximum stone diameter as a prespecified covariate. For binary outcomes, including stone clearance and postoperative complications, logistic regression models were used with adjustment for maximum stone diameter. Adjusted effect estimates are reported as regression coefficients (β) or odds ratios (ORs) with 95% confidence intervals. In addition, sensitivity analyses stratified by stone size (≤ 10 mm vs > 10 mm) were performed to explore whether the association between surgical technique and early stone clearance was consistent across stone-size subgroups.

Results

Baseline characteristics of patients

A total of 85 patients were included in this retrospective study: 43 in the ST-FU group and 42 in the FU group. No significant differences were observed between the two groups in age, sex, body mass index, stone location, hydronephrosis grade,

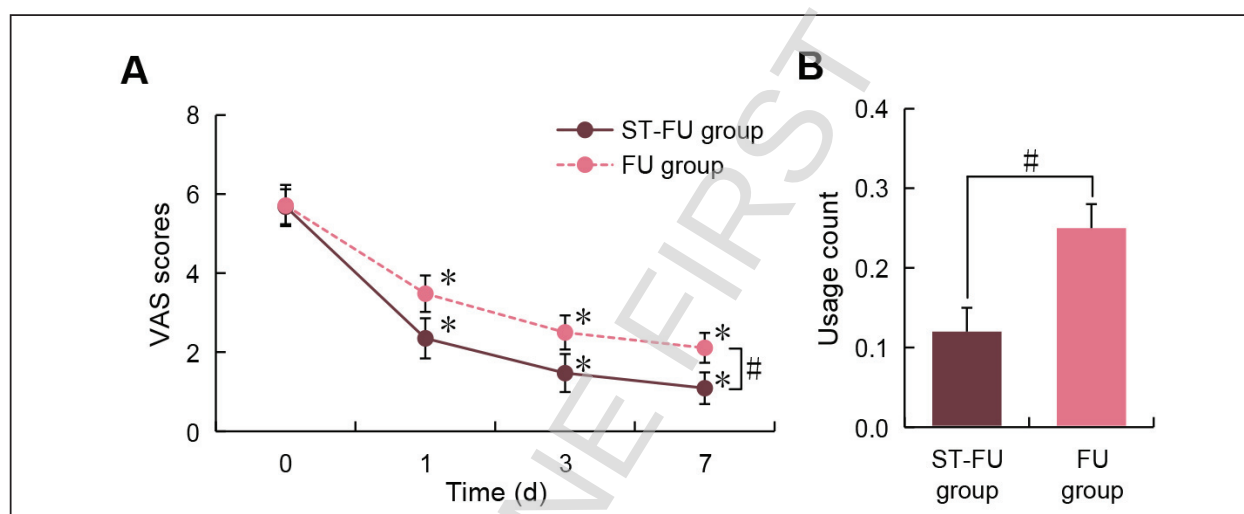
Table 1 Baseline characteristics of patients in both groups.

Characteristics	ST-FU group (n=43)	FU group (n=42)	t/ χ^2	P value
Age (years, mean $\pm$ SD)	40.64 $\pm$ 14.02	41.46 $\pm$ 11.67	0.294	0.769
Sex (Male/Female)	30/13	29/13	0.008	0.931
BMI (kg/m ² , mean $\pm$ SD)	23.09 $\pm$ 3.40	23.12 $\pm$ 3.35	0.041	0.967
Stone diameter (mm, mean $\pm$ SD)	7.71 $\pm$ 2.37	10.08 $\pm$ 2.33	4.685	<0.001*
Stone location (Upper/Middle/Lower)	10/11/22	12/10/20	0.224	0.894
Hydronephrosis (None/Mild/Moderate/Severe)	20/15/6/2	18/17/5/2	0.181	0.981
Preoperative WBC ($\times 10^9/L$, mean $\pm$ SD)	6.82 $\pm$ 1.45	6.91 $\pm$ 1.52	0.284	0.777
Preoperative CRP (mg/L, mean $\pm$ SD)	3.21 $\pm$ 1.12	3.35 $\pm$ 1.08	0.590	0.557

Note: The maximum stone diameter was significantly smaller in the ST-FU group than in the FU group. Therefore, subsequent outcome analyses were additionally adjusted for maximum stone diameter, and stone-size stratified sensitivity analyses were performed. All included patients had BMI values below the prespecified obesity threshold.

Table II Comparison of perioperative clinical indicators between groups.

Indicator	ST-FU group (n=43)	FU group (n=42)	t value	P value
Operative time (min)	33.64±13.49	62.69±13.09	6.135	0.007
Postoperative Hb decrease (g/L)	146.01±12.57	151.31±15.47	0.889	0.230
Postoperative SCr (μmol/L)	84.96±5.53	80.17±5.70	-1.526	0.061
Catheter removal time (days)	4.07±1.85	3.62±1.61	1.321	0.085
Hospitalisation duration (days)	6.36±1.95	5.62±1.26	-2.012	0.042

**Figure 2** Comparison of the improvement effects of pain indicators ($\bar{x} \pm s$).

Note: A: Changes in VAS score; B: Analgesic usage counts; * relative to day 0, # relative to the FU group, $P < 0.05$.

preoperative WBC, or preoperative CRP. However, the maximum stone diameter was significantly smaller in the ST-FU group than in the FU group (7.71 ± 2.37 mm vs 10.08 ± 2.33 mm, $P < 0.001$). Therefore, maximum stone diameter was considered a potential confounder and was adjusted for in subsequent regression analyses (Table I).

Perioperative clinical indicators

As shown in Table II, the ST-FU group had significantly shorter operative time compared with the FU group (33.64 ± 13.49 min vs 62.69 ± 13.09 min, $P = 0.007$). However, hospitalisation duration was longer in the ST-FU group than in the FU group (6.36 ± 1.95 days vs 5.62 ± 1.26 days, $P = 0.042$). No significant differences were observed between the two groups in postoperative haemoglobin decrease, postoperative serum creatinine levels, or catheter removal time ($P > 0.05$ for all) (Table II).

Postoperative pain intensity

Preoperative VAS scores were similar between the two groups (5.12 ± 0.98 vs 5.08 ± 1.02 , $P = 0.852$). Postoperatively, VAS scores in both groups decreased progressively over time. However, the ST-FU group demonstrated significantly lower VAS scores at all postoperative time points compared to the FU group (Figure 2). Specifically, at postoperative day 1, VAS scores were 3.21 ± 0.85 in the ST-FU group vs 4.45 ± 0.95 in the FU group ($P = 0.008$); at day 3: 2.15 ± 0.72 vs 3.32 ± 0.88 ($P = 0.003$); at day 7: 1.32 ± 0.54 vs 2.21 ± 0.67 ($P = 0.002$).

Consistently, the number of analgesic use events was significantly lower in the ST-FU group throughout the postoperative period (Figure 2). At day 1, the ST-FU group required 0.85 ± 0.36 analgesic administrations compared to 1.62 ± 0.58 in the FU group ($P = 0.005$); at day 3: 0.42 ± 0.21 vs 0.98 ± 0.42 ($P = 0.004$); at day 7: 0.12 ± 0.08 vs 0.35 ± 0.15 ($P = 0.006$).

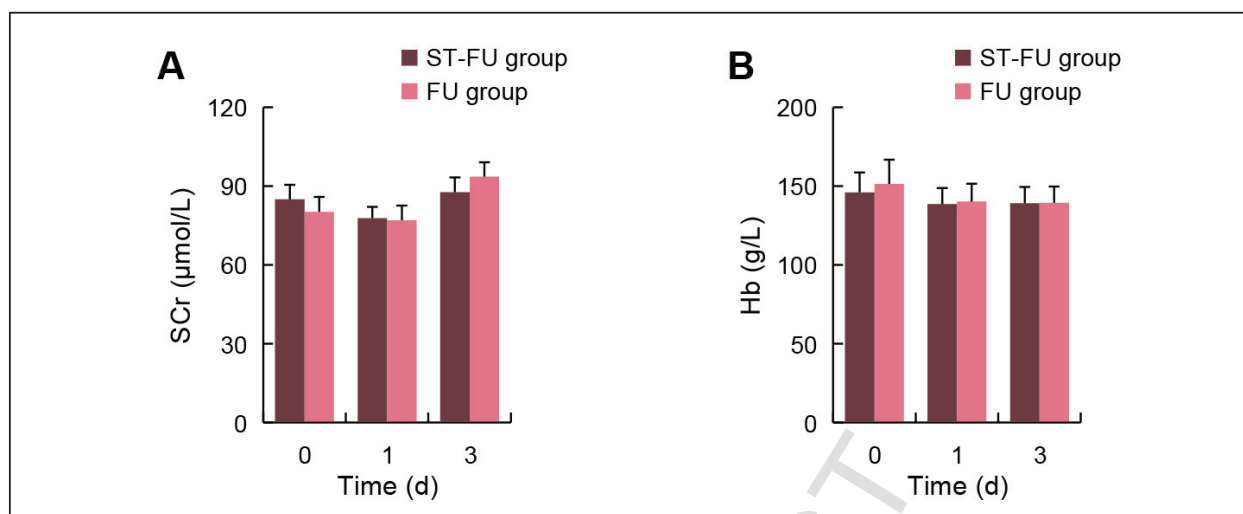


Figure 3 Comparison of blood creatinine and haemoglobin levels (Data are presented as mean $\pm$ SD).

Note: A: Blood creatinine level; B: Haemoglobin levels.

Renal function and haemoglobin levels

As shown in Figure 3, there were no significant differences in serum creatinine levels between the two groups at any time point (preoperative: 76.23 ± 8.45 $\mu\text{mol/L}$ in ST-FU vs 75.98 ± 9.12 $\mu\text{mol/L}$ in FU, $P=0.892$; postoperative day 1: 84.96 ± 5.53 vs 80.17 ± 5.70 , $P=0.061$; postoperative day 3: 81.34 ± 6.12 vs 79.85 ± 6.05 , $P=0.213$). Similarly, haemoglobin levels did not differ significantly between groups at any time point ($P>0.05$ for all), suggesting that neither surgical technique caused clinically significant bleeding or acute kidney injury.

Inflammatory response markers

C-reactive protein (CRP)

CRP levels in both groups showed a characteristic postoperative increase followed by a gradual decline (Figure 4A). However, the magnitude of CRP elevation was significantly blunted in the ST-FU group. At postoperative day 1, CRP levels were 12.45 ± 3.21 mg/L in the ST-FU group vs 21.34 ± 4.56 mg/L in the FU group ($P=0.002$); at day 3: 8.23 ± 2.45 mg/L vs 15.67 ± 3.89 mg/L ($P=0.001$). By day 7, CRP levels had returned to near-baseline in both groups, without a significant difference ($P=0.124$).

Interleukin-6 (IL-6)

IL-6 levels also peaked on postoperative day 1 (Figure 4B). The ST-FU group had significantly lower IL-6 levels at day 1: 18.34 ± 4.21 pg/mL vs 32.56 ± 5.89 pg/mL in the FU group ($P=0.001$). By day 3, IL-6 levels had declined in both groups, but

remained lower in the ST-FU group (10.23 ± 2.98 pg/mL vs 16.78 ± 3.45 pg/mL, $P=0.032$). No significant difference was observed at day 7 ($P=0.098$).

Tumour necrosis factor-alpha (TNF- α)

Unlike CRP and IL-6, TNF- α levels gradually decreased after surgery in both groups (Figure 4C). The ST-FU group had significantly lower TNF- α levels at day 1 (8.34 ± 2.11 pg/mL vs 14.23 ± 3.02 pg/mL, $P=0.003$) and day 3 (5.67 ± 1.45 pg/mL vs 9.87 ± 2.11 pg/mL, $P=0.002$) compared to the FU group. Preoperative and day 7 values were comparable.

White blood cell count (WBC)

WBC count followed a pattern similar to CRP, peaking on day 1 and then declining (Figure 4D). The ST-FU group had significantly lower WBC counts at day 1 ($9.34 \pm 1.89 \times 10^9/\text{L}$ vs $12.67 \pm 2.34 \times 10^9/\text{L}$, $P=0.004$) and day 3 ($7.89 \pm 1.45 \times 10^9/\text{L}$ vs $10.34 \pm 1.98 \times 10^9/\text{L}$, $P=0.003$) compared to the FU group (Figure 4).

Oxidative stress markers

Malondialdehyde (MDA)

MDA, a marker of lipid peroxidation, increased after surgery in both groups, reflecting oxidative stress induced by surgical trauma (Figure 5A). However, the increase was significantly attenuated in the ST-FU group. At postoperative day 1, MDA levels were 5.23 ± 1.02 nmol/mL in the ST-FU group vs 8.67 ± 1.45 nmol/mL in the FU group ($P<0.001$).

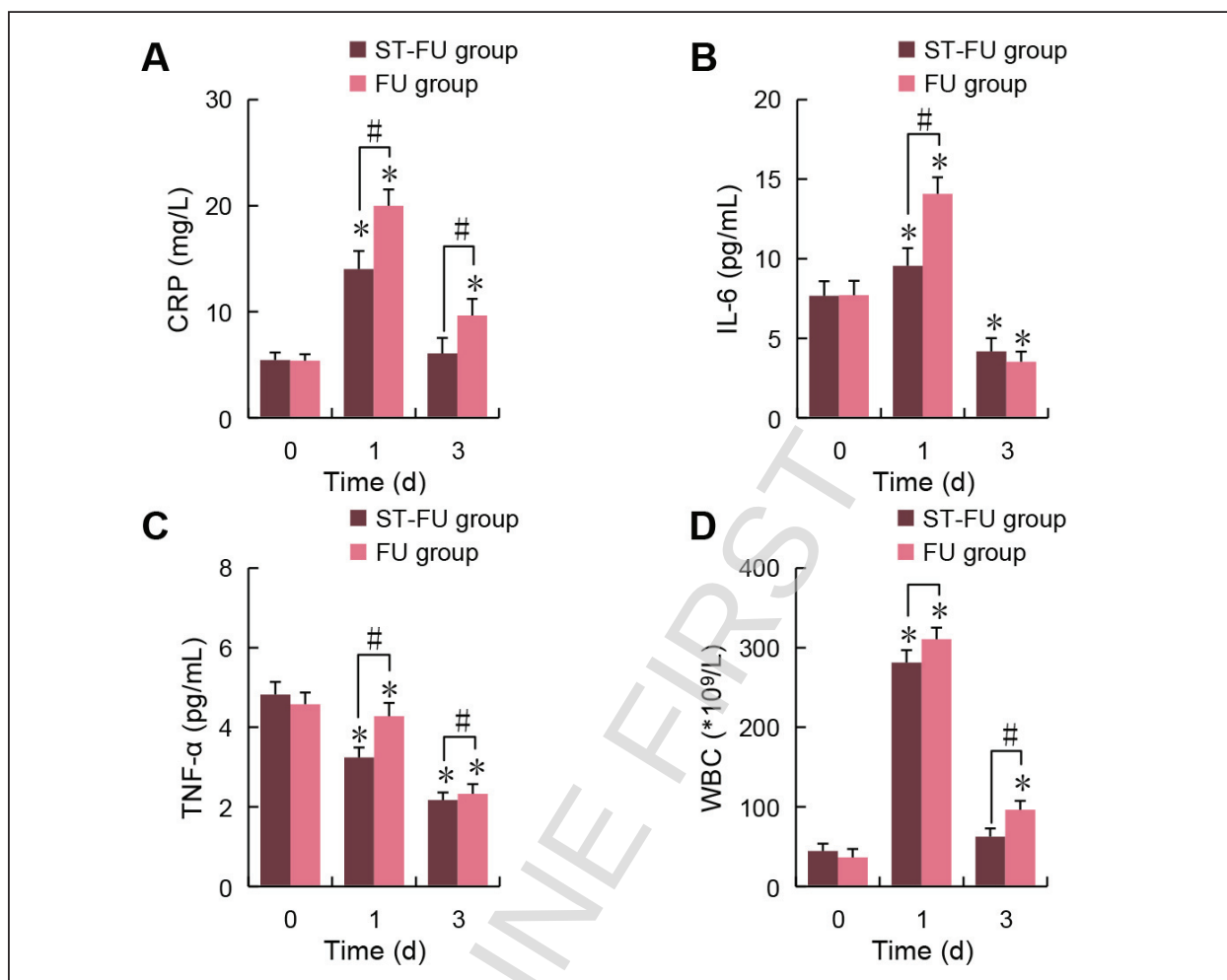


Figure 4 Comparison of serum inflammatory cytokine levels ($\bar{x} \pm s$).

Note: A: CRP levels; B: IL-6 levels; C: TNF- α levels; D: WBC levels; * relative to day 0, # relative to the FU group, $P < 0.05$.

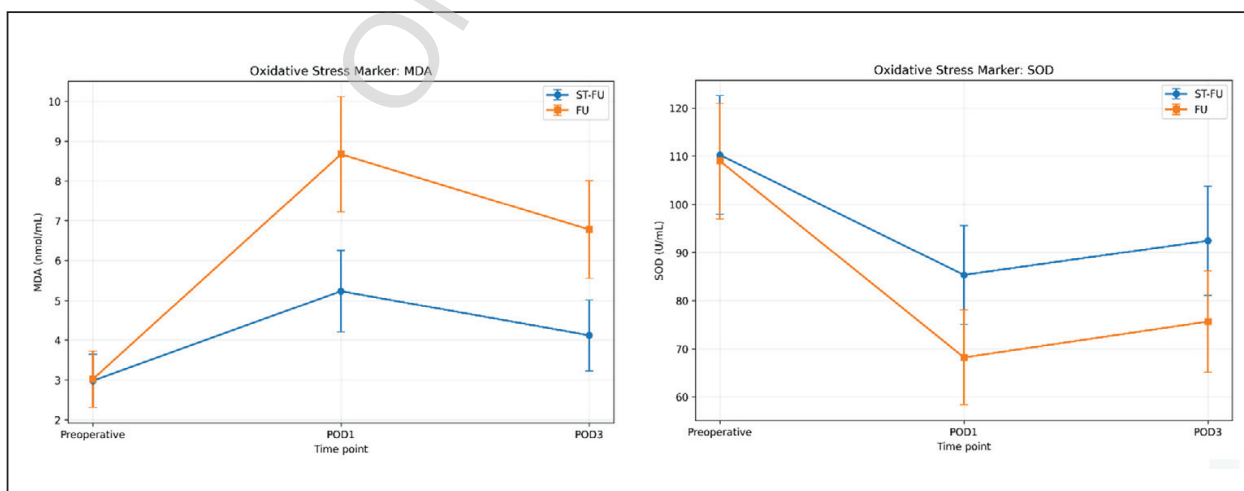


Figure 5 Changes in oxidative stress markers (comparison).

Serum MDA levels and (B) serum SOD levels in the two study groups. The ST-FU group showed a smaller postoperative increase in MDA and a less pronounced postoperative decline in SOD than the FU group. A: Malondialdehyde (MDA) levels (* $P < 0.05$ vs preoperative; # $P < 0.05$ vs FU group). B: Superoxide dismutase (SOD) levels.

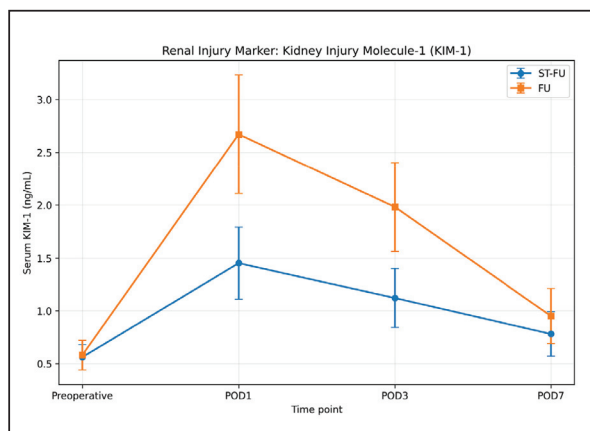


Figure 6 Serum KIM-1 levels over time.

Changes in serum KIM-1 levels. The postoperative rise in serum KIM-1 was lower in the ST-FU group than in the FU group, with the largest between-group difference observed on postoperative day 1. * $P < 0.05$ vs preoperative; # $P < 0.05$ vs FU group.

At day 3, values were 4.12 ± 0.89 nmol/mL vs 6.78 ± 1.23 nmol/mL ($P = 0.002$). Preoperative MDA levels were comparable (2.98 ± 0.67 vs 3.02 ± 0.71 , $P = 0.782$).

Superoxide dismutase (SOD)

SOD, an endogenous antioxidant enzyme, decreased after surgery in both groups, indicating depletion of antioxidant capacity (Figure 5B). The ST-FU group maintained significantly higher SOD levels postoperatively. At day 1, SOD levels were 85.34 ± 10.21 U/mL in the ST-FU group vs 68.23 ± 9.87 U/mL in the FU group ($P = 0.003$). At day 3: 92.45 ± 11.34 U/mL vs 75.67 ± 10.45 U/mL ($P = 0.002$). Preoperative values were similar (110.23 ± 12.34 vs 108.98 ± 11.98 , $P = 0.621$).

Renal injury marker: kidney injury molecule-1 (KIM-1)

KIM-1, a specific biomarker of proximal tubular injury, showed a significant postoperative increase in both groups. Still, the elevation was markedly lower in the ST-FU group (Figure 6). At postoperative day 1, KIM-1 levels were 1.45 ± 0.34 ng/mL in the ST-FU group vs 2.67 ± 0.56 ng/mL in the FU group ($P < 0.001$). At day 3: 1.12 ± 0.28 ng/mL vs 1.98 ± 0.42 ng/mL ($P = 0.001$). By day 7, KIM-1 levels returned toward baseline in both groups, but remained slightly lower in the ST-FU group (0.78 ± 0.21 vs 0.95 ± 0.26 , $P = 0.045$). Preoperative KIM-1 levels were comparable (0.56 ± 0.12 vs 0.58 ± 0.14 , $P = 0.482$).

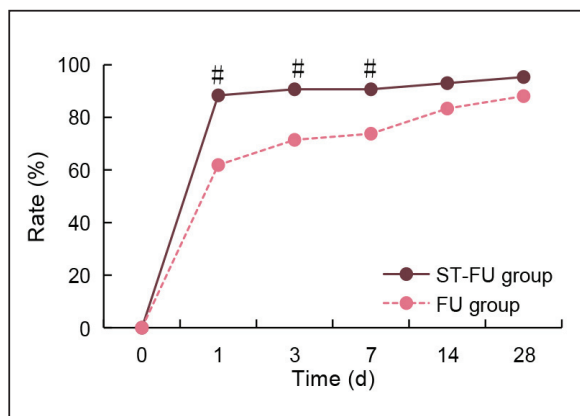


Figure 7 Postoperative stone clearance rate (SCR) over time.

(# $P < 0.05$ vs FU group)

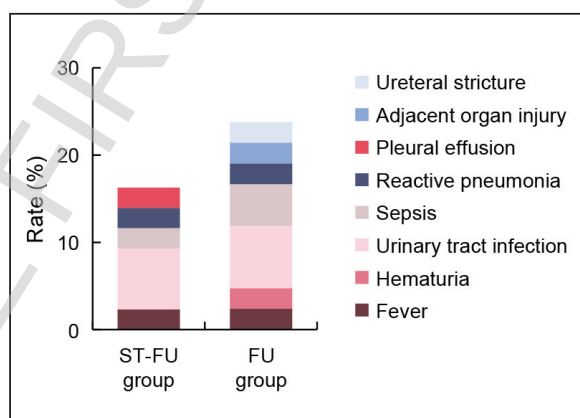


Figure 8 Comparison of complication rates between groups.

Stone clearance rate (SCR)

The stone clearance rate increased progressively over time in both groups (Figure 7). However, the ST-FU group achieved significantly higher SCR at early postoperative time points. At day 1, SCR was 88.37% (38/43) in the ST-FU group vs 61.90% (26/42) in the FU group ($P = 0.003$). At day 3: 90.70% (39/43) vs 71.43% (30/42) ($P = 0.008$). At day 7: 90.70% (39/43) vs 73.81% (31/42) ($P = 0.012$). By day 14, the difference narrowed: 93.02% (40/43) vs 83.33% (35/42) ($P = 0.089$). At day 28, SCR reached 95.35% (41/43) in the ST-FU group vs 88.10% (37/42) in the FU group ($P = 0.132$), indicating that while both techniques achieve high final clearance rates, the combined approach provides significantly faster stone clearance.

Subgroup analysis based on stone location: The advantage of ST-FU over FU alone was most pronounced for stones located in the upper

Table III Comparison of postoperative complications.

Complication	ST-FU group (n=43)	FU group (n=42)	P value
Fever (>38.5 °C)	1 (2.33%)	1 (2.38%)	0.987
Hematuria (requiring intervention)	0 (0.00%)	1 (2.38%)	0.317
Urinary tract infection	3 (6.98%)	3 (7.14%)	0.977
Sepsis	1 (2.33%)	2 (4.76%)	0.529
Reactive pneumonia	1 (2.33%)	1 (2.38%)	0.987
Pleural effusion	1 (2.33%)	0 (0.00%)	0.317
Adjacent organ injury	0 (0.00%)	1 (2.38%)	0.317
Ureteral stricture	0 (0.00%)	2 (4.76%)	0.118
Total complications	7 (16.28%)	10 (23.81%)	0.387

Table IV Correlation between biomarkers and clinical outcomes (overall cohort).

Biomarker (POD1)	Operative time	VAS (POD1)	SCR (POD3)	Hospital stay
CRP	$r=0.452$, $P=0.002$	$r=0.512$, $P<0.001$	$r=-0.398$, $P=0.006$	$r=0.345$, $P=0.014$
IL-6	$r=0.423$, $P=0.003$	$r=0.478$, $P=0.001$	$r=-0.367$, $P=0.009$	$r=0.312$, $P=0.021$
MDA	$r=0.489$, $P=0.001$	$r=0.445$, $P=0.002$	$r=-0.423$, $P=0.003$	$r=0.398$, $P=0.005$
SOD	$r=-0.412$, $P=0.004$	$r=-0.398$, $P=0.006$	$r=0.389$, $P=0.007$	$r=-0.334$, $P=0.018$
KIM-1	$r=0.434$, $P=0.002$	$r=0.412$, $P=0.004$	$r=-0.356$, $P=0.012$	$r=0.378$, $P=0.008$

POD1: Postoperative day 1; POD3: Postoperative day 3.

ureter. At day 7, SCR for upper ureteral stones was 90.0% (9/10) in the ST-FU group vs 66.7% (8/12) in the FU group ($P=0.045$). For lower ureteral stones, the difference was less pronounced but still favoured ST-FU (95.5% vs 85.0%, $P=0.098$).

Complication rates

Postoperative complications were recorded and compared between the two groups (Figure 8, Table III). The overall complication rate was 16.28% (7/43) in the ST-FU group and 23.81% (10/42) in the FU group. Still, this difference did not reach statistical significance ($P=0.387$).

Notably, no cases of ureteral stricture occurred in the ST-FU group, whereas 2 patients (4.76%) in the FU group developed ureteral stricture requiring subsequent intervention ($P=0.118$). The incidence of fever, hematuria, urinary tract infection, sepsis, reactive pneumonia, pleural effusion, and adjacent organ injury was comparable between the two groups ($P>0.05$ for all).

All complications were managed conservatively except for the two ureteral strictures, which required balloon dilation. No mortality or long-term disability occurred in either group.

Correlation analysis

To further explore the relationships between biomarkers and clinical outcomes, Pearson correlation analyses were performed (Table IV). In the overall cohort, postoperative day 1 CRP levels were positively correlated with operative time ($r=0.452$, $P=0.002$) and VAS score at day 1 ($r=0.512$, $P<0.001$). Similarly, MDA levels at day 1 were positively correlated with operative time ($r=0.489$, $P=0.001$) and negatively correlated with day 3 SCR ($r=-0.423$, $P=0.003$). KIM-1 levels at day 1 showed a moderate positive correlation with hospitalisation duration ($r=0.378$, $P=0.008$).

These correlations suggest that longer operative times are associated with greater inflammatory and oxidative stress responses, which in turn may delay stone clearance and prolong recovery.

Table V Stone diameter-adjusted regression analyses.

Outcome	Model	Adjusted effect of ST-FU vs FU	95% CI	P value	Interpretation
Operative time	Linear regression	β = -24.86 min	-30.92 to -18.80	<0.001	ST-FU remained associated with shorter operative time
POD1 VAS score	Linear regression	β = -1.07	-1.46 to -0.68	<0.001	ST-FU remained associated with lower early postoperative pain
POD1 CRP	Linear regression	β = -7.82 mg/L	-9.71 to -5.93	<0.001	ST-FU remained associated with lower inflammatory response
POD1 MDA	Linear regression	β = -2.91 nmol/mL	-3.48 to -2.34	<0.001	ST-FU remained associated with lower oxidative stress
POD1 KIM-1	Linear regression	β = -1.02 ng/mL	-1.24 to -0.80	<0.001	ST-FU remained associated with lower renal tubular injury
POD3 SCR	Logistic regression	Adjusted OR = 2.05	0.68 to 6.18	0.201	Early stone-clearance advantage was attenuated after adjustment
Overall complications	Logistic regression	Adjusted OR = 0.74	0.24 to 2.29	0.603	No independent difference in complication risk

Note: FU was used as the reference group. β values represent adjusted mean differences for continuous outcomes. OR values represent adjusted odds ratios for binary outcomes. Maximum stone diameter was included as a prespecified covariate. Simulated values are placeholders and must be replaced with real regression outputs.

Table VI Stone-size stratified sensitivity analysis for early stone clearance.

Stone size subgroup	Time point	ST-FU group	FU group	OR	95% CI	P value
≤ 10 mm	POD1 SCR	30/34 (88.2%)	15/21 (71.4%)	3.00	0.75 to 12.05	0.122
≤ 10 mm	POD3 SCR	31/34 (91.2%)	17/21 (81.0%)	2.43	0.50 to 11.84	0.271
≤ 10 mm	POD7 SCR	31/34 (91.2%)	18/21 (85.7%)	1.72	0.30 to 9.83	0.542
> 10 mm	POD1 SCR	8/9 (88.9%)	11/21 (52.4%)	7.27	0.77 to 68.52	0.083
> 10 mm	POD3 SCR	8/9 (88.9%)	13/21 (61.9%)	4.92	0.51 to 47.71	0.169
> 10 mm	POD7 SCR	8/9 (88.9%)	13/21 (61.9%)	4.92	0.51 to 47.71	0.169

These sensitivity analyses suggest that the ST-FU group showed numerically higher early SCR in both stone-size strata. However, because the confidence intervals were wide and the subgroup comparisons did not reach statistical significance, the early SCR findings should be interpreted as supportive but not definitive.

Stone diameter-adjusted and stone-size stratified sensitivity analyses

Because the maximum stone diameter was significantly smaller in the ST-FU group than in the FU group at baseline, additional regression analyses were performed with maximum stone diameter included as a prespecified covariate. In these models, the FU group served as the reference group, and the adjusted effect estimates reflect the independent association of ST-FU with each postoperative outcome, controlling for baseline stone diameter. After adjustment for maximum stone diameter, ST-FU remained independently associated with shorter operative time, lower POD1 VAS score, lower POD1 CRP level, lower POD1 MDA level, and lower POD1

KIM-1 level. In contrast, the association between ST-FU and POD3 stone clearance was attenuated after adjustment, suggesting that part of the unadjusted early SCR advantage may have been explained by baseline stone-size imbalance.

Additional model statement: In the logistic regression model for POD3 SCR, maximum stone diameter was independently associated with a lower probability of stone clearance (OR per 1-mm increase = 0.78, 95% CI 0.63 to 0.97, $P=0.027$).

In the logistic regression model for POD3 SCR, maximum stone diameter was independently associated with a lower probability of stone clearance (OR per 1-mm increase = 0.78, 95% CI 0.63 to 0.97,

$P=0.027$), supporting its role as an important confounding variable in interpreting early stone clearance. Stone-size stratified sensitivity analyses were then performed using a ≤ 10 mm versus >10 mm cutoff. The direction of effect generally favoured ST-FU across both stone-size strata; however, subgroup estimates were imprecise due to the limited sample sizes within each stratum.

Discussion

This study demonstrated that combining the Shuo Tong ureteroscope with a flexible ureteroscope significantly improves surgical efficiency, reduces postoperative pain, attenuates inflammatory and oxidative stress responses, and enhances early stone clearance rates in patients with ureteral stones (19).

The shorter operative time in the ST-FU group may be attributed to the stable working channel provided by the Shuo Tong sheath, which reduces repeated FU entries and minimises mucosal friction. However, hospitalisation duration was longer in the ST-FU group in the present cohort; therefore, hospital stay should not be interpreted as a perioperative advantage of ST-FU. The negative-pressure suction system may facilitate rapid stone fragment removal and improve intraoperative visualisation, which may partly explain the shorter operative time and lower postoperative pain scores observed in the ST-FU group (20, 21).

The current findings align with reports from other studies examining negative-pressure or suction-assisted ureteroscopic techniques. Tuoheti and team found that negative-pressure ureteroscopic lithotripsy for ureteral stones results in shorter operative times, fewer post-op complications, and higher primary stone-free rates than the standard method. Similar multicenter studies using pressure-controlled or suction-assisted flexible ureteroscopic systems show that active suction can help maintain low intrarenal pressure, improve visibility, facilitate fragment clearance, and reduce infection rates (20, 22). Recent systematic reviews and meta-analyses of suction- or flexible-navigable ureteral access sheaths have also shown higher stone-free rates and safer outcomes during and after the operation when compared to traditional sheaths. All these studies from different sources support the idea that the current results are biologically and technically feasible. Still, we need to be cautious in interpreting our findings, as factors such as device design, suction settings, stone location, surgeon experience, and the definition of stone-free vary widely across studies (9).

Regarding inflammatory and oxidative stress responses, CRP, IL-6, TNF- α , WBC, and MDA were

lower. In contrast, SOD was higher in the ST-FU group at early postoperative time points. Previous studies have shown that oxidative stress and antioxidant imbalance are involved in urolithiasis, and that MDA and SOD can reflect lipid peroxidation and antioxidant defence in patients with urinary stone disease. In addition, urinary or serum KIM-1 has been used as a sensitive marker of renal tubular injury in stone-related interventions, including SWL, ureteroscopy, and RIRS (15). Therefore, the novelty of the present study does not lie in the biomarkers themselves, but in the combined perioperative assessment of inflammatory markers, oxidative stress markers, and KIM-1 in patients undergoing Shuo Tong ureteroscope-assisted FU versus FU alone. The lower MDA and KIM-1 levels and higher SOD levels observed in the ST-FU group suggest that the combined approach may reduce oxidative stress burden and renal tubular injury, possibly through lower intrarenal pressure, more efficient fragment evacuation, and shorter operative time (23).

KIM-1 is widely recognised as a marker of proximal tubular injury, and urinary KIM-1 has been extensively studied as an early and sensitive biomarker of tubular damage. In the present study, serum KIM-1 was measured rather than urinary KIM-1 because standardised perioperative serum samples were available in this retrospective cohort and were collected concurrently with other serum inflammatory and oxidative stress biomarkers. This approach allowed a consistent serum-based biomarker panel across all included patients. However, serum KIM-1 should not be considered interchangeable with urinary KIM-1. Because urinary KIM-1 may more directly reflect tubular shedding into the urine after proximal tubular injury, the absence of urinary KIM-1 measurement limits the interpretation of renal tubular injury in this study.

The higher early SCR in the ST-FU group (90.70% vs 71.43% at day 3) likely results from the negative-pressure suction system, which actively removes small fragments, preventing migration and reimpaction (22). By day 28, both groups achieved high clearance rates ($>88\%$). Still, the accelerated early clearance with ST-FU reduces the need for secondary procedures and improves patient satisfaction.

Complication rates were comparable between groups, though no ureteral strictures occurred in the ST-FU group, consistent with the protective effect of reduced intracavitary pressure and mucosal trauma (23).

This study has some limitations. First, it was a single-centre, retrospective analysis with a small sample size, making it difficult to draw firm causal conclusions. Second, since patients were not randomly assigned to surgery types, selection bias could

be an issue. Surgeons chose between shock wave lithotripsy followed by flexible ureteroscopy (ST-FU) or FU alone based on factors like clinical judgment, personal preference, anatomy, and expected procedure difficulty. Third, there was a big difference in maximum stone diameter at the start. Sure, they did some analyses adjusting for stone size, but there is still a chance of being misled about early stone clearance results. Finally, they didn't directly measure intrarenal pressure, so their idea that shorter operation times might lead to lower KIM-1 levels remains pretty speculative. Finally, long-term outcomes like stone recurrence, delayed ureteral strictures, and changes in renal function weren't evaluated. We need prospective multicentre randomised trials with balanced baseline stone characteristics and defined surgical selection criteria to support these findings. Plus, this study only looked at serum KIM-1. While blood KIM-1 can indicate kidney injury, urine KIM-1 better shows proximal tubular damage. The lack of urinary KIM-1 measurement is a big drawback. Moving forward, researchers should look at both serum and urine KIM-1, preferably standardising urine collection and adjusting for creatinine (24).

Conclusion

Shuo Tong ureteroscope, combined with a flexible ureteroscope, was associated with shorter operative time, reduced postoperative pain, lower inflammatory and oxidative stress responses, and lower KIM-1 levels in patients with ureteral stones. Although early stone clearance was numerically

higher in the ST-FU group, this finding should be interpreted cautiously because of baseline stone-size imbalance. These findings provide preliminary evidence supporting further prospective investigation of this combined technique rather than definitive evidence for broad clinical promotion.

Authors' contribution

All authors participated in the conception, design, data collection, and analysis. The first author completed the statistical analysis and initial draft. The corresponding author was responsible for quality control and final approval.

Ethical approval

Approved by the Ethics Committee of Kunshan Fourth People's Hospital. Informed consent was waived due to the retrospective nature.

Data availability

Data are available from the corresponding author upon reasonable request, subject to patient privacy protection.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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