Tip bendable suction ureteral access sheath versus traditional sheath in retrograde intrarenal stone surgery: an international multicentre, randomized, parallel group, superiority study

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Summary

Background Retrograde intrarenal surgery (RIRS) is the main treatments for upper urinary tract stones. The Ureteral Access Sheath (UAS) serves as a supplementary tool, facilitating direct kidney access during RIRS. High quality of evidence comparing tip bendable suction ureteral access sheath (S-UAS) with traditional UAS in RIRS for the treatment of renal and ureteral stones is lacking. The purpose of the study is to compare the efficacy and safety of S-UAS with traditional UAS in RIRS for the treatment of renal or ureteral stones ≤30 mm.

Methods An international, multicenter, and superiority randomized controlled trial included 320 intention-to-treat patients across 8 medical centers in China, the Philippines, Malaysia and Turkey from August 2023 to February 2024. The inclusion criteria were patients ≥18 years old with renal or ureteral stones ≤30 mm. RIRS was performed using either S-UAS or traditional UAS. The primary outcome was the immediately stone-free rate (SFR). Secondary outcomes included SFR 3 months after operation, operating time, hospital stay, auxiliary procedures, complications (using the Clavien–Dindo grading system), and improvement in the Quality of Life (QoL) score. Differences between proportions [risk difference (RD)]/means [mean difference (MD)] and 95% confidence intervals (CI) were presented. This study is registered at ClinicalTrials.gov: NCT05952635.

Findings The S-UAS group demonstrated a significantly higher immediately SFR (81.3% versus 49.4%; RD 31.9%; 95% CI 22.5%–41.7%; p = 0.004) compared to the traditional UAS group, as determined by the one-side superiority test. Additionally, the S-UAS group exhibited a higher SFR at 3 months post-operation (87.5% versus 70.0%; RD 17.5%; 95% CI 8.7%–26.3%; p < 0.001), lower postoperative fever rate (RD −11.9%; 95% CI −18.7% to −4.9%; p < 0.001), reduced use of stone baskets (RD −70.6%; 95% CI −77.8% to −63.5%; p < 0.001), and better QoL improvement (MD 7.25; 95% CI 2.21–12.29; p = 0.005). No statistically significant differences were observed in operation time, hospital stay, or the need for second-stage RIRS.

Interpretation In RIRS for upper urinary tract stones ≤30 mm, S-UAS exhibited superior performance compared to traditional UAS, demonstrating higher SFR, reduced postoperative fever rate, and improved QoL outcomes. S-UAS emerges as a prudent and advantageous alternative to traditional UAS for RIRS.

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Keywords: Retrograde intrarenal stone surgery; Ureteral access sheath; Suction; Tip bendable; Randomized controlled trial

Research in context

Evidence before this study

Retrograde intrarenal surgery (RIRS) is the main treatments for upper urinary tract stones. The Ureteral Access Sheath (UAS) serves as a supplementary tool, facilitating direct kidney access during RIRS. To improve the safety and efficiency of RIRS, the tip bendable suction ureteral access sheath (S-UAS) was developed. However, high quality of evidence comparing S-UAS with traditional UAS in RIRS for the treatment of renal and ureteral stones is lacking.

Added value of this study

We performed an international, multicenter, and superiority randomized controlled trial including 320 intention-to-treat patients across 8 medical centers in China, the Philippines, Malaysia and Turkey from August 2023 to February 2024. We found that the application of S-UAS in RIRS achieved a superior stone-free rate (SFR) compared to traditional UAS, accompanied by notable improvements in Quality of Life. Furthermore, the adoption of S-UAS leads to a decreased necessity for stone basket utilization and a reduction in postoperative fever rates.

Implications of all the available evidence

In RIRS for upper urinary stones ≤30 mm, S-UAS exhibited superior performance compared to traditional UAS, demonstrating higher SFR, reduced postoperative fever rate, and improved QoL outcomes. Consequently, S-UAS emerges as a prudent and advantageous alternative to traditional UAS for RIRS.

Introduction

Urolithiasis represents a prevalent chronic condition worldwide.[1–3] The prevalence of urolithiasis in the U.S. is 11%, affecting approximately one in every 9 individuals.[1] Among the various treatment modalities for ureteral and renal stones, Retrograde Intrarenal Stone Surgery (RIRS) has emerged as a common choice due to its less invasive nature compared to percutaneous nephrolithotomy (PCNL) and its superior versatility over shock wave lithotripsy (SWL).[4] The European Association of Urology (EAU) recommends RIRS as the primary choice for renal stones ≤2 cm or proximal ureteral stones ≥1 cm.[5]

Despite its widespread adoption, real-world outcomes of RIRS paint a less sanguine picture. The reported stone-free rate (SFR) of RIRS is 45.6%–96.7%.[6,7] This wide variation in SFR suggests that 3.3%–54.4% patients still retain residual stones. The limited efficacy in achieving a stone-free state, the necessity for multiple surgical sessions, and the potential for life-threatening complications related to intra-renal pelvic pressure (IPP) pose significant challenges for RIRS, particularly in the management of larger stones.

The Ureteral Access Sheath (UAS) serves as a supplementary tool, facilitating direct kidney access during RIRS. To improve the safety and efficiency of RIRS, the tip bendable suction ureteral access sheath (S-UAS) was developed.[8–10] The S-UAS is a novel UAS characterized by excellent flexibility and deformability at the tip, enabling passive bending (angle >90°) in sync with the bending of flexible ureteroscope. Additionally, it can be connected to a vacuum suction device. Initial studies suggest that S-UAS can successfully navigate the ureteropelvic junction (UPJ), reaching the renal pelvis and calices in tandem with the flexible ureteroscope.[8,9] Positioned close to the stone, S-UAS has demonstrated the potential to achieve complete stone-free status in RIRS. However, further clinical investigations and comparisons with existing techniques are imperative. Thus, a large multicenter randomized control trial (RCT) was undertaken to assess and compare the efficacy and safety of S-UAS with traditional UAS in RIRS. This study aims to contribute higher-quality evidence for more informed conclusions and recommendations.

Methods

Trial design and participants

A prospective, international, multicentre, randomized, single-blinded, superiority study was conducted across 8 urological departments with a notable caseload of urinary stones (five in China, one in Malaysia, one in the Philippines, one in Turkey) from August 2023 to February 2024 (ClinicalTrials.gov, NCT05952635). The trial completed the enrolment of all patients in November 2023 and concluded the follow-up work in February 2024. Each participating center routinely conducted over 300 RIRS annually. The study adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.[11] Table 1 outlines the detailed inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
• Adults aged ≥18 years; • American Society of Anesthesiology score 1–3; • Upper urinary stones (renal or upper ureteral) diameter of ≤3 cm confirmed by CT; • Capable of giving written informed consent, which includes adherence with the requirements of the trial.	• Patients with abnormal urinary tract anatomy (such as horseshoe kidney or ileal conduit); • Patients with uncontrolled urinary tract infection; • Patients with health or other factors that are absolute contraindications to RIRS; • Patients unable to understand or complete trial documentation.

Table 1: **Inclusion and exclusion criteria in the study.**

Randomization and masking

Parallel randomization was conducted using a stratified approach based on the participating centers. Each of the eight centers enrolled 40 participants, randomized in a 1:1 ratio to either the S-UAS group or the traditional UAS group. Electronic generation of the randomization sequence took place before patient inclusion. Consecutively numbered, sealed envelopes were utilized for random sequence allocation and concealment. During UAS placement, the sealed envelope was opened by a designated nurse, revealing the assigned UAS for use. Subsequently, at the conclusion of the procedure, the same individual automatically recorded the operative data.

Procedures and quality control

A standardized operating methodology, sanctioned by the principal investigator at each center, was instituted and endorsed for uniformity. Monthly protocol monitoring visits were conducted across all participating centers to ensure adherence to the established procedures.

2 mm non-contrast computed tomography (CT) scan and ultrasonography were performed in all patients before the operation. Stone size and density were consistently measured using identical software across all centers. Patients who had negative urine culture took standard peri-operative antibiotic prophylaxis (single shot of cefuroxime 200 mg or levofloxacin 500 mg in cases of allergy) 30 min before intervention. Patients with positive preoperative urine culture were treated with suitable antibiotics based on the culture sensitivity result for 4–7 days before RIRS.

All the procedures were performed by one designated experienced surgeon (≥100 procedures per year in RIRS with S-UAS and traditional UAS) per center. General anesthesia was administered, and the lithotomy position was adopted for each procedure. A 5 F open-ended ureteral catheter was inserted into the ureter and a retrograde urography was performed to assess the upper urinary tract. A 0.035-inch guidewire was then placed into the renal pelvis. A 12/14 F or 11/13 F S-UAS or traditional UAS was employed (see Fig. 2). In instances where the UAS could not be placed due to a narrow ureter, a smaller UAS (10/12 F) was attempted. Traditional UAS was positioned at UPJ while the S-UAS was maneuvered into upper, middle, or lower calyces by the flexible ureteroscope to the vicinity of the stones.

Either an 8.5 F or 7.5 F disposable flexible ureteroscope was chosen for the RIRS based on the UAS size: 8.5 F scope for 12/14 F UAS and 7.5 F scope for 11/13 F or 10/12 F UAS. In the traditional UAS group, employed syringe manual irrigation was employed using a 50 cc syringe. In the suction UAS group, an irrigation pressure pump was utilized to ensure adequate irrigation during surgery, thereby facilitating faster stone aspiration. The irrigation flow rate was set as 50–100 ml/min. The suction pressure was controlled to a setting of 80–120 mmHg. The stone was fragmented by a holmium laser with a 200 μm laser fiber (with energy setting less than 30 W). In the S-UAS group, stone fragments smaller than the gap between the flexible ureteroscope and UAS were automatically aspirated; larger fragments were gradually suctioned out via the S-UAS during the withdrawal of the flexible ureteroscope (Supplementary Video 1). If the sheath could not reach the stone, and fragments could not be aspirated, a nitinol stone basket was employed to remove the fragments. Conversely, for the traditional UAS group, stone fragmenting was performed, and all fragments were removed using a nitinol stone basket. The status of residual stones was evaluated routinely by endoscopy.

At the end of each procedure the UAS was removed along with the ureteroscope. Ureteral injuries were visually assessed and classified according to the endoscopic classification of the lesions.[12] A 6 F indwelling double-J stent was placed for 1–2 weeks if no ureter injury occurred. Postoperative Foley catheter was not placed regularly.

Kidney-ureter-bladder X-ray (KUB) and ultrasonography were performed within postoperative 24 h to evaluate the immediately stone-free status. Blood routine examination and serum procalcitonin were performed within 2 h after operation to monitor the infection. If the patient had no significant post-operative discomfort, they were discharged on the next day after surgery. The stone composition was analyzed using the same infrared spectrometer and methodology in all centers.[13] Low-dose CT, with a 2-mm section thickness, was obtained for all patients at the 3-month follow-up to evaluate the final stone-free status.

Outcomes

The primary endpoint of the study was the immediately stone-free rate (SFR) assessed through endoscopy, kidney-ureter-bladder X-ray (KUB), and ultrasonography

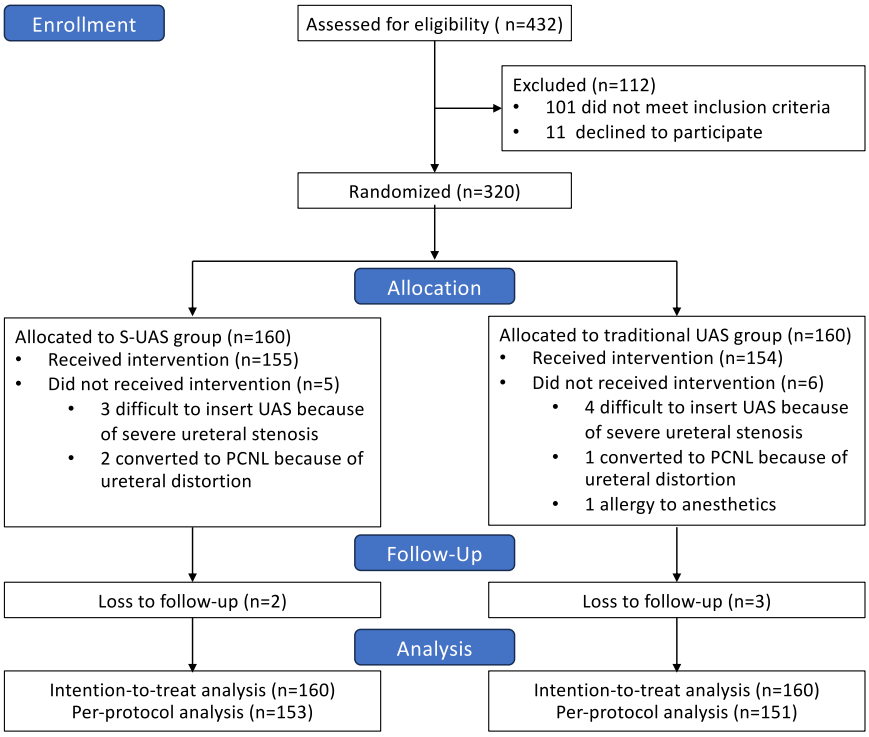

Fig. 1: **Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the trial outlining enrolment, randomisation, allocation, follow-up, and analysis according to intention-to-treat and per-protocol standards**. UAS, Ureteral access sheath; S-UAS, Tip bendable suction ureteral access sheath; PCNL, Percutaneous nephrolithotomy.

within 24 h postoperatively. The immediately stone-free status was defined as having no residual stone fragments observed intraoperatively under endoscopy, and no residual stones or fragments smaller than 2 mm detected on a KUB and ultrasound. If there were discordant results from the three means of ascertaining clearance, it was considered that the stone has not been cleared. Secondary endpoints included the SFR at 3 months postoperatively assessed by low-dose CT scan with a 2-mm section thickness. This interval was chosen to allow time for patients to pass remaining stone fragments spontaneously. Stone-free status at 3 months postoperatively was defined as the absence of residual stones or any stone fragments larger than 2 mm as detected by CT scans. The radiologists assessing the post-operative imaging (KUB/ultrasoundgraphy/CT) were blinded to the intervention.

Other secondary endpoints were operating time, hospital stay, auxiliary procedures, complications (using the Clavien–Dindo grading system[14]), and improvement in the Quality of Life (QoL) score. QoL score was recorded preoperatively and at one month postoperatively using Wisconsin Stone QoL questionnaire.[15–17] The QoL improvement score was calculated as the difference between the QoL score one month postoperatively and the preoperative QoL score (QoL post-op minus QoL pre-op).

Patients' characteristics and clinical outcomes were meticulously recorded on a pre-established case report form. Stone size was defined as the largest diameter for a single stone and the sum of the largest diameters for multiple stones. Operative time was characterized as the duration from the insertion of the endoscope into the urethra to the completion of stent placement. Hospital stay was rounded to the nearest whole day and calculated from the day of surgery to the day of discharge. Septic shock was identified according to clinical criteria involving persisting hypotension necessitating vasopressor therapy to maintain a mean arterial pressure of ≥65 mmHg and a serum lactate level of ≥2 mmol/l despite adequate fluid resuscitation.[18]

Statistical analysis

The original sample size calculations were based on the trial's superiority design. To determine the sample size, we conducted a retrospective analysis involving 180 patients from three out of eight centers (Guangzhou, Shanghai, and Zhejiang in China), with 90 cases using S-UAS and 90 cases using traditional UAS before the study. The findings suggested an estimated immediately SFR of approximately 85% (P1) in the S-UAS arm and 55% in the traditional UAS arm. A superiority margin of 15% (P1–P2 > 15%) was deemed acceptable. Through

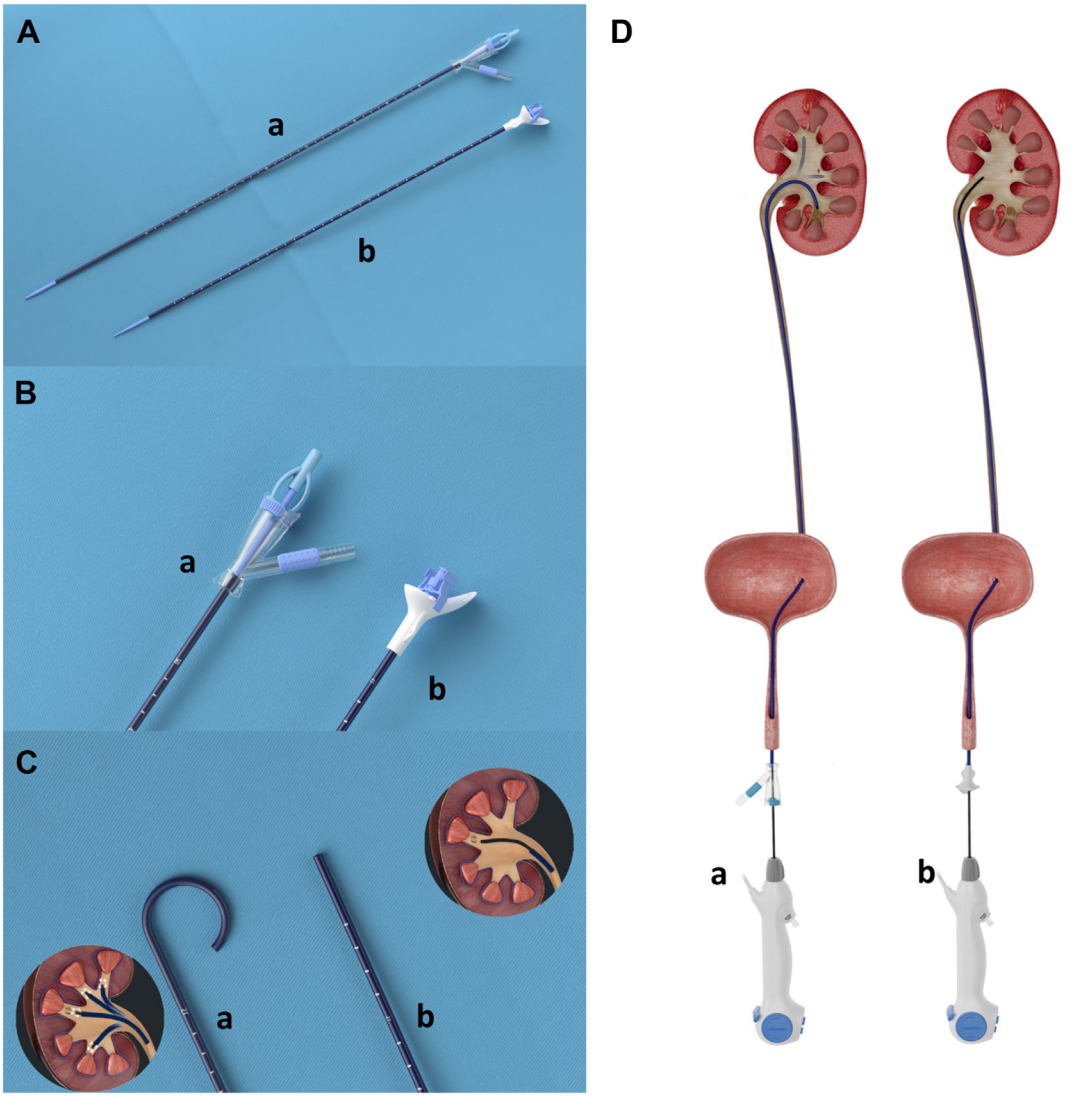

Fig. 2: **Structural diagrams of the tip bendable suction ureteral access sheath (S-UAS) and traditional ureteral access sheath (UAS).** (A) Whole view of the S-UAS (a) and traditional UAS (b); (B) Diagram of the distal end of the S-UAS (a) and traditional UAS (b); (C) Diagram of the proximal end of the S-UAS (a) and traditional UAS (b); (D) Illustration highlighting the differences in RIRS procedures between S-UAS (a) and traditional UAS (b).

simulations designed for this purpose and executed in Stata, the sample size was estimated. With 90% power, an alpha level set at 0.025, 143 participants per group (286 in total) were initially required. To accommodate potential loss to follow-up and study withdrawals, this number was increased to 160 per group (320 in total).

Statistical analysis was performed using SPSS 20.0 and SAS 9.4. Main analyses of the primary and secondary outcomes were analyzed on an intention-to-treat (ITT) basis, and sensitivity analyses were conducted on per-protocol (PP) population. Kolmogorov–Smirnov test was used to determine whether continuous data follows normal distribution. Continuous variables with a normal distribution were presented as mean (standard deviation) and compared between groups using the independent t-test. Non-normally distributed variables were reported as median (first quartile, third quartile) and compared using the Mann–Whitney U-test. Categorical variables were presented with frequencies and percentages and were analysed using fisher's exact or chi-square test. A one-side superiority test (Mantel–Haenszel test with a 15% superiority margin and a one-sided alpha level of 0.025) was used to evaluate whether S-UAS had a superiority immediately SFR to traditional UAS in RIRS. Differences between proportions (risk difference)/means (mean difference) and 95%

confidence intervals (CI) were presented. A post-hoc sensitivity analysis was performed to adjust for stone diameter and study centers by using multivariate linear regression and the Mantel–Haenszel test. A p value of <0.05 was considered statistically significant.

Ethics statement

At study entry, all patients provided a written informed consent. The protocol, including any amendments, and all necessary clinical trial documentation, were approved by the independent ethics committee of each investigational study site before the trial was initiated.

Role of the funding source

The funders had no role in the study design, data collection, data analysis, data interpretation, manuscript writing, or publication decisions. Guohua Zeng and Wei Zhu had access to the dataset and held the final responsibility for the decision to submit the manuscript for publication.

Results

Patient recruitment and baseline characteristics

Out of the 432 patients assessed for eligibility, 320 received randomly assigned intervention, constituting the ITT population (160 in the S-UAS group and 160 in the traditional UAS group; refer to Fig. 1). Three patients in S-UAS group and four patients in traditional UAS group failed to have the UAS placed due to severe ureteral stenosis. Additionally, two patients in S-UAS group and one patient in traditional UAS group were converted to PCNL because of ureteral distortion. One patient in the traditional UAS group failed to undergo RIRS due to anesthetics allergy. Excluding cases lost to follow-up, the PP population included 153 patients in the S-UAS group and 151 in the traditional UAS group. Patient demographics are summarized in Table 2. The distributions of patients' age, gender, BMI, fitness status, comorbidities, preoperative hydronephrosis, and pre-stenting were similar between the two groups. However, the stone diameter was significantly larger in the S-UAS group (14 mm versus 11 mm, p = 0.002). Despite this, the stone volumes between the two groups were similar (985.4 mm^3 versus 932.9 mm^3, p = 0.204). Other stone characteristics, such as multiplicity, location, and Hounsfield Unit, were comparable between the two groups.

Table 3 delineates the operative characteristics between the groups. The most frequently utilized UAS size in both groups was 11/13F in both groups (63.9% versus 70.4%, p = 0.421). A 7.5Fr disposable ureteroscope was utilized in 83.6% of patients in the traditional UAS group and 81.6% of patients in the S-UAS group (p = 0.638). The irrigation fluid volume during RIRS was higher in the S-UAS group compared to the traditional group (73.13 ± 16.24 versus 60.70 ± 19.02 ml/min; mean difference 12.43 ml/min; 95% CI 8.53–16.34; p < 0.001). There was no significant difference in the follow-up time between the two groups for evaluating the immediately SFR (15 versus 17 h, p = 0.380) and the 3-month SFR (89 versus 91 days, p = 0.253) (Supplementary Table S1).

Efficacy

The S-UAS group demonstrated a significantly superior immediately SFR (81.3% versus 49.4%; risk difference 31.9%; 95% CI 22.5%–41.7%; p = 0.004) compared to the traditional UAS group, as determined by the one-side superiority test. Additionally, the S-UAS group maintained a significantly higher SFR at 3 months (87.5% versus 70.0%; risk difference 17.5%; 95% CI 8.7%–26.3%; p < 0.001) compared to the traditional UAS group (Table 4). QoL score improvement after surgery was higher in S-UAS group as compared to traditional group (38.36 ± 23.09 versus 31.11 ± 22.71; mean difference 7.25; 95% CI 2.21–12.29; p = 0.005). The S-UAS group had fewer patients requiring the use of stone baskets for stone removal compared to traditional UAS group (28.1% versus 98.6%; risk difference –70.6%; 95% CI –77.8% to –63.5%; p < 0.001). There was no significant difference between the groups in operative time (45.0 ± 23.2 versus 40.9 ± 19.1 min; mean difference 4.11 min; 95% CI –0.56 to 8.78; p = 0.085). A PP sensitivity analysis was conducted including only patients who completed the trial (excluding n = 16; 5%). Results of the PP sensitivity analysis were similar to those obtained with the ITT analysis (Table 4).

A post hoc sensitivity analysis adjusted for stone diameter and study centers were also indicative of S-UAS benefit in efficacy (Supplementary Table S2). The results showed that the S-UAS group had a significantly higher immediately SFR (risk difference 36%; 95% CI 26%–45%; p < 0.001) and SFR at 3 months (risk difference 20%; 95% CI 12%–29%; p < 0.001) compared to traditional UAS group. Additionally, the S-UAS group had less use of stone baskets (risk difference –73%; 95% CI –79% to –66%; p < 0.001) and greater improvement in QoL score (mean difference 7.63; 95% CI 2.51–12.75; p = 0.004).

Subgroup analyses according to the stone locations showed that the S-UAS significantly improved the immediately SFR for kidney stones (78.7% versus 34.7%; risk difference 44.0%; 95% CI 32.0%–56.1%; p < 0.001) and the SFR at 3 months (86.1% versus 57.4%; risk difference 28.7%; 95% CI 17.0%–40.3%; p < 0.001) (Supplementary Table S3). However, its advantages in SFR were not significant for smaller ureteral stones. The immediately SFR and SFR at 3 months for ureteral stones in the two groups were 86.5% versus 74.6% (p = 0.089) and 90.4% versus 91.5% (p = 0.546), respectively (Supplementary Table S3). The effects of S-UAS on the primary outcome (immediately SFR) were

	Traditional UAS (n = 160)	S-UAS (n = 160)	p value
Age (yr)	52.0 (40.0, 61.8)	53.0 (45.0, 64.0)	0.150
Gender, n (%)			0.430
Male	96 (60.0)	89 (55.6)	
Female	64 (40.0)	71 (44.4)	
BMI (kg/m^2)	24.2 (21.9, 27.0)	24.8 (22.4, 26.5)	0.318
ASA classification, n (%)			0.315
I	120 (75.0)	108 (67.5)	
II	29 (18.1)	36 (22.5)	
III	11 (6.9)	16 (10.0)	
Laterality, n (%)			0.242
Left	67 (41.9)	80 (50.0)	
Right	81 (50.6)	66 (41.3)	
Bilateral	12 (7.5)	14 (8.7)	
Stone type, n (%)			0.447
Single	98 (61.2)	87 (55.0)	
Multiple	56 (35.0)	65 (40.0)	
Staghorn	6 (3.8)	8 (5.0)	
Stone location, n (%)			0.400
Renal pelvis	11 (6.9)	18 (11.2)	
Upper calyx	5 (3.1)	2 (1.3)	
Middle calyx	2 (1.3)	2 (1.3)	
Lower calyx	21 (13.1)	13 (8.1)	
Proximal ureter	59 (36.9)	52 (32.5)	
Multiple or staghorn	62 (38.7)	73 (45.6)	
Stone diameter (mm)	11.0 (9.0, 16.0)	14.0 (10.0, 20.0)	0.002
Stone surface (mm^2)	61.6 (44.2,115.3)	81.8 (54.2, 131.5)	0.025
Stone volume (mm^3)	932.9 (502.2, 1808.6)	985.4 (605.7, 2231.5)	0.204
CT value of stone (HU)	897.5 (707.8, 1155.8)	932.0 (682.5, 1145.0)	0.879
Pre-op serum Cr level (μmol/l)	81.0 (65.1, 97.2)	81.5 (64.5, 104.8)	0.491
Comorbidities, n (%)	60 (37.5)	59 (36.9)	0.148
Hypertension	40 (25)	29 (18.1)	
Diabetes	9 (5.6)	7 (4.4)	
Hypertension and diabetes	10 (6.3)	19 (11.9)	
Hepatitis	1 (0.6)	4 (2.5)	
Initial positive urine culture, n (%)	18 (11.3)	30 (18.8)	0.060
Pre-stenting, n (%)	22 (13.8)	19 (11.9)	0.616
Grade of hydronephrosis, n (%)			0.619
G0	40 (25.0)	31 (19.4)	
Mild (G1 or G2)	90 (56.3)	93 (58.1)	
Moderate (G3)	24 (15.0)	28 (17.5)	
Severe (G4)	6 (3.8)	8 (5.0)	

BMI, body mass index; Cr, creatinine; CT, computed tomography; G0, grade 0; G1, grade 1; G2, grade 2; G3, grade 3; G4, grade 4; UAS, ureteral access sheath; S-UAS, tip bendable suction ureteral access sheath; ASA, American Society of Anesthesiologists. Data are presented as median (first quartile, third quartile), or number (proportion).

Table 2: **Characteristics of the intention-to-treat participant at baseline.**

similar across different countries in subgroup analyses (Supplementary Table S4).

Safety

The overall operative complication rates, using the Clavien-Dindo grading system, were higher in traditional UAS group as compared to S-UAS group (risk difference –11.3%; 95% CI –18.1% to –4.4%; p = 0.003) (Table 4). The incidence of postoperative fever (≥38.5 °C) was lower in S-UAS group compared to traditional UAS group (5.6% versus 17.5%; risk difference –11.9%; 95% CI –18.7% to –4.9%; p < 0.001). One patient in traditional UAS group developed septic shock who required intensive care unit treatment. Two patients in the traditional UAS group and one patient in the S-UAS group developed subcapsular haematoma which were managed conservatively. The incidence of postoperative fever remained lower in S-UAS group in a

	Intention to treat				Per protocol (Sensitivity analyses)			
	Traditional UAS (n = 160)	S-UAS (n = 160)	Difference (95% CI)	p value	Traditional UAS (n = 151)	S-UAS (n = 153)	Difference (95% CI)	p value
UAS size (Fr), n (%)				0.421				0.360
12/14	26 (16.4)	29 (18.4)	–	–	26 (17.2)	27 (17.6)	–	–
11/13	112 (70.4)	101 (63.9)	–	–	106 (70.2)	98 (64.1)	–	–
10/12	21 (13.2)	28 (17.7)	–	–	19 (12.6)	28 (18.3)	–	–
Flexible ureteroscope size (Fr), n (%)				0.638				0.922
8.5	26 (16.4)	29 (18.4)	–	–	26 (17.2)	27 (17.6)	–	–
7.5	133 (83.6)	129 (81.6)	–	–	125 (82.8)	126 (82.4)	–	–
Irrigation fluid volume (ml/min)	60.70 (19.02)	73.13 (16.24)	12.43[a] (8.53–16.34)	<0.001	60.67 (19.02)	72.97 (16.47)	12.30[a] (8.29–16.32)	<0.001

UAS, Ureteral access sheath; S-UAS, Tip bendable suction ureteral access sheath; CI, confidence interval. Data are presented as mean (standard deviation), or number (proportion). [a]Mean Difference.

Table 3: **Operative characteristics in intention-to-treat and per-protocol population.**

PP sensitivity analysis (5.2% versus 16.6%; risk difference –11.4%; 95% CI –18.2% to –4.4%; p = 0.002) (Table 4). A post hoc sensitivity analysis, adjusting for stone diameter and study centers, further confirmed that the incidence of postoperative fever remained lower in the S-UAS group (risk difference –13%; 95% CI –20% to –6%; p < 0.001) (Supplementary Table S2).

Fewer patients in S-UAS group had ureteral wall injury as compared to traditional UAS group (11.9% versus 35.0%; risk difference –23.1%; 95% CI –32.0% to –14.2%; p < 0.001). All injuries were grade 1 and managed conservatively (Table 4).

There were no significant differences found between the groups regarding postoperative hospital stays (22.3 ± 19.8 versus 23.5 ± 18.5 h; mean difference –1.26 h; 95% CI –5.48 to 2.95; p = 0.556) and the necessity for second-stage RIRS (5.0% versus 6.9%; risk difference –1.9%; 95% CI –7.0% to 3.3%; p = 0.478). All patients underwent stone analysis, revealing no significant differences in stone composition between the groups (p = 0.135) (Table 4).

Discussion

In recent years, the introduction of the S-UAS has aimed to enhance the clearance of stone fragments during RIRS However, a scarcity of high-level evidence exists to substantiate the potential improvement in the efficacy and safety of RIRS associated with S-UAS. This multicenter, randomized, controlled trial contributes robust findings, indicating that the application of S-UAS significantly enhances the SFR, improves QoL, reduces the utilization of stone baskets, and decreases postoperative fever rates in RIRS. To the best of our knowledge, this is the inaugural multi-center RCT that meticulously recruited a predetermined large sample of patients with upper urinary tract stones, adhering to stringent eligibility criteria and undergoing prolonged follow-up to investigate the hypothesis that S-UAS enhances the safety and efficacy of RIRS.

Despite the wide-spread use of RIRS, the presence of residual fragments after the procedure remains a critical challenge. Current literature indicates that up to 38% of renal units may have residual fragments bigger than 2 mm after RIRS when assessed by CT scan.[19,20] Such residual fragments can lead to renal colic and hematuria, necessitating additional procedures. It was reported that patients with >2 mm residual fragments after RIRS are nine times more likely to require repeat surgery than those with ≤2 mm residual fragments.[21,22] Even small residual fragments, considered as "clinically insignificant," can have noteworthy consequences, underscoring the importance of achieving complete stone-free status immediately after surgery. The application of S-UAS in RIRS accomplishes this more effectively than traditional UAS, removing not only small stone fragments but also thoroughly clearing stone. Therefore, patients underwent RIRS with S-UAS experience improved QoL, reflected in higher QoL scores after surgery.

In the study, we found that for renal stones, S-UAS significantly improves both the immediately and 3-months SFR compared to traditional UAS. However, for ureteral stones, the SFR of S-UAS is similar to that of traditional UAS, with both groups achieving high stone-free rates. An explanation for the lack of difference for ureteral stones is that the bendability S-UAS provides no additional benefit in stone evacuation since the ureter is typically straight. Furthermore, ureteral stones typically have a smaller stone burden, allowing for high stone clearance rates with traditional UAS combined with a stone removal basket. Additionally, the space for stone fragmentation in the ureter is more limited, making it less likely for stone fragments to migrate to other locations in the kidney during the fragmentation process.

Urinary tract infection is one of the most frequent complications in RIRS, reported at rates of 1.7%–18.8%.[23] Our study demonstrated that the application of S-UAS significantly reduces postoperative fever, suggesting a potential protective function in preventing infectious complications. IPP during RIRS is one of the

	Intention to treat				Per protocol (Sensitivity analyses)			
	Traditional UAS (n = 160)	S-UAS (n = 160)	Difference (95% CI)	p value	Traditional UAS (n = 151)	S-UAS (n = 153)	Difference (95% CI)	p value
Immediately SFR, n (%)	79 (49.4)	130 (81.3)	31.9%[a] (22.5%–41.7%)	0.004[b]	71 (47.0)	124 (81.0)	34.0%[a] (23.9%–44.1%)	<0.001[b]
3 months SFR, n (%)	112 (70.0)	140 (87.5)	17.5%[a] (8.7%–26.3%)	<0.001	104 (68.9)	134 (87.6)	18.7%[a] (9.7%–27.8%)	<0.001
Hb dropped (g/L)	7.6 (8.3)	6.9 (7.4)	−0.74[c] (−2.47 to 0.98)	0.397	7.7 (8.5)	6.9 (7.5)	−0.80[c] (−2.60 to 1.00)	0.383
Operative time (min)	40.9 (19.1)	45.0 (23.2)	4.11[c] (−0.56 to 8.78)	0.085	41.3 (19.2)	45.2 (23.5)	3.87[c] (−0.98 to 8.72)	0.117
Use of stone basket, n (%)	158 (98.6)	45 (28.1)	−70.6%[a] (−77.8% to −63.5%)	<0.001	150 (99.3)	44 (28.8)	−70.5%[a] (−77.9% to −63.3%)	<0.001
Degree of ureteral wall injury, n (%)			–	<0.001				<0.001
None	104 (65.0)	141 (88.1)	–	–	97 (64.2)	135 (88.2)	–	–
Grade I	56 (35.0)	19 (11.9)	−23.1%[a] (−32.0% to −14.2%)	–	54 (35.8)	18 (11.8)	−24.0%[a] (−33.2% to −14.8%)	–
Post-op hospital stays (hrs)	23.5 (18.5)	22.3 (19.8)	−1.26[c] (−5.48 to 2.95)	0.556	23.7 (18.8)	22.4 (20.2)	−1.30[c] (−5.70 to 3.11)	0.563
QoL score improvement	31.11 (22.71)	38.36 (23.09)	7.25[c] (2.21–12.29)	0.005	31.30 (23.09)	37.52 (22.83)	6.22[c] (1.04–11.40)	0.019
Second-stage RIRS, n (%)	11 (6.9)	8 (5.0)	−1.9%[a] (−7.0%–3.3%)	0.478	6 (4.0)	5 (3.3)	−0.7%[a] (−4.9%–3.5%)	0.742
Clavien-Dindo, n (%)			–	0.003			–	0.005
Grade I–II	27 (16.9)	9 (5.6)	−11.3%[a] (−18.1% to −4.4%)	–	24 (15.9)	8 (5.2)	−10.7%[a] (−17.5% to −3.9%)	–
Grade IIIa – IVa	1 (0.6)	0 (0)	–	–	1 (0.7)	0 (0)	–	–
Complications, n (%)								
Fever (>38.5 °C) (Clavien grade I)	28 (17.5)	9 (5.6)	−11.9%[a] (−18.7% to −4.9%)	<0.001	25 (16.6)	8 (5.2)	−11.4%[a] (−18.2% to −4.4%)	0.002
Blood transfusion (Clavien grade II)	1 (0.6)	0	–	1.00	1 (0.7)	0	–	0.995
Subcapsular haematoma (Clavien grade II)	2 (1.2)	1 (0.6)	–	1.00	2 (1.3)	1 (0.7)	–	0.991
Urinary extravasation (Clavien grade II)	0	1 (0.6)		1.00	0	1 (0.7)		1.00
Septic shock (Clavien grade IVa)	1 (0.6)	0	–	1.00	1 (0.7)	0	–	0.995
Stone composition, n (%)				0.135				0.093
Calcium oxalate	122 (76.3)	114 (71.3)	–	–	115 (76.2)	108 (70.6)	–	–
Calcium phosphate	2 (1.3)	0	–	–	2 (1.3)	0	–	–
Uric acid	7 (4.4)	14 (8.8)	–	–	6 (4.0)	14 (9.2)	–	–
Infection stone (struvite or carbonate apatite)	29 (18.1)	32 (20.0)	–	–	28 (18.5)	31 (20.2)	–	–

CI, Confidence interval; SFR, Stone-free rate; Hb, Hemoglobin; QoL, Quality of life; UAS, Ureteral access sheath; S-UAS, Tip bendable suction ureteral access sheath. Data are presented as mean (standard deviation), or number (proportion). [a]Risk Difference = PT– PS; PT (proportion of test group): S-UAS group; PS (proportion of standard group): traditional UAS group. [b]Mentel–Haenszel test (a 15% superiority margin at one-sided alpha level of 0.025 was used). [c]Mean Difference.

Table 4: **Primary and secondary outcomes in intention-to-treat and per-protocol population.**

major factors causing infection complications. Some studies demonstrated that the application of negative pressure technology during RIRS could decrease infection complications by lowering the IPP.[24,25] Differing from traditional UAS positioned at the UPJ, the S-UAS can be adjustable to the renal pelvis, targeting specific renal calices as necessary to ensure sufficient irrigation-suctioning space. This adjustment helps prevent the blockage of the UAS opening by the mucous membrane of the ureteropelvic junction and maintains a low IPP. The integration of S-UAS with a vacuum device facilitates a continuous irrigation-suctioning cycle, improving intrarenal fluid outflow and sustaining reduced IPP.

The S-UAS offers mechanical stone debris removal without the need for baskets, thereby reducing the cost of surgical consumables. The device's capability to enter upper and middle calyces allows stone fragments to be removed with suction force. For stones in lower calyx where the S-UAS entry may be challenging, baskets can be employed to relocate stones to middle/upper calyx or remove the stone fragments directly.

Our study reveals a higher incidence of ureteral wall injuries in the traditional UAS group. Our experience with the S-UAS showed that the placement of the S-UAS is smoother with less resistance due to its soft and collapsible tip. We believe that there is definitely potential for further studies to assess if this contributes to reducing the incidence of ureteric wall injury.

Contrary to other studies, our findings indicate no significant difference in operative time between the two groups.[10] Ding et al.[9] reported that application of S-UAS possess a higher efficacy in stone removal comparing with traditional UAS. However, the suctioning process with the S-UAS, in practice, still requires time. In contrast, the use of basket for stone removal may not be time-consuming, but they can be challenging for complete removal of very small fragments.

In this study, one case in the S-UAS group developed a subcapsular hematoma, and one patient experienced urinary extravasation postoperatively. We speculate that these occurrences were due to increased intrarenal pressure during the procedure. When using S-UAS, the accumulation of small stone fragments between the scope and the sheath may obstruct the reflux of irrigation fluid (even in the presence of negative pressure suction), ultimately leading to elevated intrarenal pressure. Therefore, when using a S-UAS, if stone fragments were sucked into the sheath, the surgeon should promptly withdraw the flexible ureteroscope to allow the stone fragments to be sucked out, thereby avoiding the elevated intrarenal pressure. The recently introduced S-UAS, with irrigation and pressure monitoring attached, can potentially solve this issue. It will alert the urologist promptly when the UAS is clogged by stone fragments, causing an elevation of intra-renal pressure.

There are several limitations in our study. First, due to potential risks of radiation exposure and ethical concerns, patients did not undergo CT assessment for stone clearance within 24 h postoperatively; instead, CT examination was conducted three months after the procedure to evaluate the final SFR. Second, endoscopy, KUB, and ultrasound within 24 h after RIRS were used to determine the primary outcome of stone clearance. This timing was not typically used in routine clinical practice, raising concerns about the external validity of our findings. In addition, the three-month follow-up may limit the assessment of long-term complications such as ureteral stricture. Furthermore, it is important to note that our study did not encompass a comprehensive cost analysis, an aspect that could have offered deeper insights into the economic ramifications associated with the utilization of S-UAS in comparison to the conventional combination of a stone basket and traditional UAS. We believe that our prospective investigation lays a foundational framework for future research endeavors aimed at conducting meticulous cost analyses. Finally, the surgeons who participated in the trial were expert surgeons experienced with the use of S-UAS. Although these factors may limit the generalizability to real world scenarios, we believe that a homogenous skillet among surgeons is necessary to reduce surgeon biases when comparing the outcomes of S-UAS versus traditional UAS.

In conclusion, our study provided evidence that the application of S-UAS achieved a superior SFR compared to traditional UAS, accompanied by notable improvements in QoL. Furthermore, the adoption of S-UAS leads to a decreased necessity for stone basket utilization and a reduction in postoperative fever rates. Consequently, S-UAS emerges as a prudent and advantageous alternative to traditional UAS for RIRS.

Contributors

Guohua Zeng and Kemal Sarica contributed to study supervision; Guohua Zeng and Kemal Sarica contributed to study concept and design; Wei Zhu, Shusheng Liu, Jianwei Cao, Hao Wang, Hui Liang, Kehua Jiang, Yu Cui, Chu Ann Chai, Emre Sahinler, Albert Aquino, Giorgio Mazzon, Wen Zhong, Zhijian Zhao, Lin Zhang, Jie Ding, Qing Wang, Yizhou Wang, Kelven Weijing Chen, Yongda Liu, Simon Choong, Kemal Sarica, and Guohua Zeng contributed to acquisition of data; Wei Zhu, Shusheng Liu, and Guohua Zeng contributed to analysis and interpretation of data; Wei Zhu and Guohua Zeng contributed to drafting of the manuscript; Chu Ann Chai, Kelven Weijing Chen, Simon Choong, and Kemal Sarica contributed to critical revision of the manuscript for important intellectual content; Wei Zhu, Shusheng Liu, and Guohua Zeng contributed to statistical analysis; Wei Zhu, Hui Liang, and Guohua Zeng contributed to obtaining funding; Wei Zhu, Hao Wang, Jianwei Cao, Hui Liang, Kehua Jiang, Yu Cui, Chu Ann Chai, Emre Sahinler, and Albert Aquino contributed to administrative, technical, and material support.

Data sharing statement

Data are not available for sharing due to privacy and ethical or legal issues. Summary statistical data will be available from the corresponding author on reasonable request.

Declaration of interests

All authors met the ICMJE authorship criteria. All authors made substantial contributions to the manuscript submitted for publication, read

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102724.

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