Evaluation of the effectiveness and safety of UAS in the treatment of upper urinary tract stones with flexible ureteroscopy lithotripsy: a meta-analysis and systematic review

Wei Guo  
Department of Urology, Qilu Hospital of Shandong University

Zeyan Li  
Department of Urology, Qilu Hospital of Shandong University

Keqiang Yan  
Department of Urology, Qilu Hospital of Shandong University

Zhiqing Fang  
Department of Urology, Qilu Hospital of Shandong University

Yidong Fan  
Department of Urology, Qilu Hospital of Shandong University

Research Article

Keywords: Ureteral tract stone, Meta-analysis, Ureteral access sheath, Flexible ureteroscopy

Posted Date: June 26th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3055544/v1

License: ☔️ This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Objective

To investigate the effectiveness and safety of ureteral access sheaths (UAS) in flexible ureteroscopic lithotripsy of upper urinary tract stones through a comprehensive systematic review and meta-analysis.

Methods

We conducted a meta-analysis and systematic review of the UAS in flexible ureteroscopy lithotripsy on April 12, 2023 (PROSPERO ID: CRD42022368459). The main outcomes of the meta-analysis included stone-free rate (SFR), intra and post-operation complications, hospitalization duration, and operation time.

Results

Twenty-one studies with 11335 patients satisfied the inclusion criteria. The results showed that compared with the UAS group, the non-UAS group had a higher stone-free rate (SFR) (OR = 0.76, 95%CI 0.60–0.95, P = 0.01) and shorter operation time (MD = 11.21, 95% CI 5.66–16.76, P < 0.00001), but no significant difference in postoperative complications (OR = 1.20, 95% CI 0.79–1.82, P = 0.38), intraoperative complications (OR = 1.20, 95%CI 0.85–1.70, P = 0.57), and hospitalization duration (MD = -0.03, 95%CI -0.30–0.24, P = 0.84).

Conclusion

Our findings indicate that UAS usage results in unfavorable surgical outcomes with no benefit in preventing surgical complications. Therefore, we recommend re-evaluating the usage of UAS as a surgical aid in patients with large stones.

1 Introduction

Upper urinary tract calculi are common worldwide and have a significant impact on the quality of life of patients. It may cause renal colic, urinary tract infection, and even hydronephrosis, with the most serious results being chronic renal function loss and even renal failure. For urinary stones of different sizes and locations, there are many surgical methods such as extracorporeal shock wave lithotripsy (ESWL), ureteroscopy lithotripsy (URL), percutaneous nephrolithotomy (PCNL) and laparoscopy or open surgery. ESWL can effectively remove small stones (less than 2 cm); however stones may become stuck in the physiological stricture of the ureter during removal, causing trauma to patients. PCNL and laparoscopic lithotomy, both of which are open surgeries, have a good effect on removing large or staghorn stones, but patients require a long time to recover. With the development of endoscopic technology, the treatment for urinary calculi has gradually changed from open surgery to endoscopic treatment. Urologists can reach the patient's stone site through the retrograde urethrogram with the help of a rigid, semi-rigid, or flexible ureteroscope, and then perform lithotripsy by laser or other methods allowing for effective and safe interventions and diminishing patient trauma or discomfort. Currently, for most patients with uncomplicated urinary calculi, the combination of laser and flexible ureteroscopy is the most advanced and widely used technology for urinary calculi and is accepted by most urologists and patients.

To further improve the safety and efficacy of flexible ureteroscopic lithotripsy, scientists have developed many types of auxiliary instruments and technical means, including ureteral access sheaths (UAS). The first UAS put into clinical usage was developed in 1974 and was invented by Takayasu et al. They used the UAS as a guide channel for the subsequent insertion of a safety guide wire and flexible ureteroscope to reduce damage to the ureter caused by repeated insertion of surgical instruments. To date, different sizes, models, materials, and accessories of the UAS have been developed. With the help of these different types of UAS, urologists can reduce intrapelvic pressure, avoid damage to the ureteral wall, provide a channel for collecting dusted renal or ureteral stones, and protect precious surgical instruments during ureteroscopy lithotripsy.

However, as an auxiliary instrument that needs to be continuously inserted during the operation, there is no conclusive evidence regarding the effect of the UAS on the surgical outcome. Some clinical cohort studies have evaluated the effect of the UAS in flexible ureteroscopic lithotripsy; however their conclusions are also controversial. The 2022 guidelines of the European Association of Urology, provide explanation of the UAS procedure. The guidelines state that UAS can help in reducing intrarenal pressure, improving intraoperative visual acuity, and potentially reducing operation time, especially in patients with multiple stones or a high stone burden. We conducted a meta-analysis and systematic analysis to explore the potency and safety of UAS in the treatment of upper urinary tract calculi.

2 Material and methods
2.1 Search Strategy

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[3]. The protocol for this review is available on PROSPERO (CRD42022368459; https://www.crd.york.ac.uk/prospero/). We performed a systematic literature search of PubMed, Embase, Cochrane Library, and Web of Science databases updated before April 12, 2023. The following Medical Subject Heading (MeSH) terms combined with free terms for "ureteroscopy" and "ureteral access sheath" were searched in different databases. No restriction on title or abstract and language was employed in the search strategy to avoid literature omission. The references of included articles were manually reviewed to identify relevant articles.

2.2 Inclusion and Exclusion Criteria

Based on the PICOS principle, articles that met the following criteria were included: (1) Participants (P): Patients diagnosed with upper urinary tract calculi (ureteral and renal stones) and treated using flexible ureteroscopy; (2) Intervention (I) and comparison (C): Exploring the effects of UAS during flexible ureteroscopy; (3) Outcomes (O): Inclusion of at least one of the following outcomes: stone-free rate (SFR), intraoperative and postoperative complications, operative time, and hospitalization duration; and (4) Study design (S): RCTs or retrospective/prospective cohort studies with the relevant data. Articles that met the following criteria were excluded: (1) Letters, comments, review articles, laboratory studies, case reports and experimental animal studies. (2) Lack of key data, such as sample size, 95% CI, and P-value, or this value could not be calculated. (3) Study design without a comparative group. (4) Duplicated articles.

2.3 Data Extraction

Two authors (Guo W and Li ZY) independently reviewed all the articles based on the search strategy. Any disagreement in the review process was resolved by an independent third party (Fan YD). The following data were independently extracted from each article: author, title, country, sample size, procedures performed, study period, follow-up time, article type, general patient characteristics, UAS size, stone burden, operative characteristics, and outcomes. If necessary, we would contact the original author of the article to obtain the required data. The primary outcome was SFR and the secondary outcomes included intraoperative and postoperative complications, operative time, and hospitalization duration.

2.4 Quality Assessments

The Newcastle-Ottawa scale (NOS) [4] was used to assess the quality of the included studies. Studies with seven stars or greater on the scale were considered high quality. The average NOS score was 6.62 for all included studies.

2.5 Statistical Analysis

Review Manager software (Review Manager (RevMan) [Computer program]. Version 5.4. The Cochrane Collaboration, 2020) and STATA 16.0 (Stata Corporation, College Station, USA) were used to analyze relevant data. Due to the lack of data in a few studies, we used the algorithm proposed by Luo et al. to input the missing data[5]. Pooled odds ratios (ORs) and mean differences (MDs) were calculated respectively as summary statistics for dichotomous and continuous variables with 95% confidence intervals (CIs). The Z test was used to analyze pooled effects, and a P-value 0.05 was considered statistically significant. Between-study heterogeneity was evaluated by Q-test and I²-statistics. An I²>50% was considered to indicate significant heterogeneity and a random-effects model was used. Otherwise, a fixed-effects model was used to assess the summary statistics. The source of between-study heterogeneity was explored using sub-group and sensitivity analyses. Subgroup analyses were performed according to patient age, study design, size of UAS, and SFR definition to reduce heterogeneity. Sensitivity analysis was performed by omitting one study at a time. In addition, the Egger linear regression test [6, 7] and non-parametric trim-and-fill method [8, 9] were used to explore publication bias for the primary outcome.

3 Results

3.1 Literature search

The entire systematic search process under the guidance of PRISMA is shown in Fig. 1. The initial search identified 1674 potentially relevant studies, and no potentially relevant studies were screened manually. Using the automatic deduplication function in Endnote, 936 duplicate entries were excluded from the analysis. Titles and abstracts were screened to exclude irrelevant studies, case reports, in vitro experiments, non-comparative studies, and reviews. The full texts of the remaining studies were examined, and 14 irrelevant entries were excluded. In addition, one study was excluded because of the lack of original text. Eventually, 21 studies[10–30] involving 11335 patients and 11360 procedures were identified.

3.2 Study characteristics and quality assessment
Twenty-one included trials were published between 2005 and 2022, with sample sizes ranging from 43 to 5316. There were one RCT\cite{25}, five prospective cohort studies \cite{12, 14, 15, 17, 27} and 15 retrospective cohort studies\cite{10, 11, 13, 16, 18\textendash}24, 26, 28\textendash}30] between the UAS and non-UAS groups. The quality of the included studies was scored between 5 and 8. One of the trails was related to stone management in pediatric patients \cite{28} and 6 of them\cite{11, 13, 23, 25, 28, 29} involved distal ureteral calculi. The baseline characteristics of the included literature \cite{10\textendash}30} are presented in Table 1.
Table 1
Characteristics of included studies

<table>
<thead>
<tr>
<th>References</th>
<th>Enrollment period</th>
<th>Country</th>
<th>Sample size (UAS/non-UAS)</th>
<th>SFS (UAS/non-UAS)</th>
<th>Study design</th>
<th>Stone type</th>
<th>Definition of SFS</th>
<th>Quality (NOS)</th>
<th>Size of UAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berquet 2014[11]</td>
<td>2009.05-2012.01</td>
<td>France</td>
<td>157/123</td>
<td>135/107</td>
<td>retrospective study</td>
<td>kidney or ureteral stone</td>
<td>residual &lt; 3mm</td>
<td>7</td>
<td>12/14F</td>
</tr>
<tr>
<td>Bozzini 2021[12]</td>
<td>2017.01-2017.12</td>
<td>Italy</td>
<td>92/89</td>
<td>90/82</td>
<td>prospective randomized study</td>
<td>kidney stone (1-2cm)</td>
<td>residual &lt; 3mm</td>
<td>8</td>
<td>10/12F</td>
</tr>
<tr>
<td>Cristallo 2022*[13]</td>
<td>2018.01-2020.05</td>
<td>Argentina</td>
<td>43/198</td>
<td>NA</td>
<td>retrospective study</td>
<td>upper ureter and kidney stone</td>
<td>absence of residual stone</td>
<td>6</td>
<td>12/14F</td>
</tr>
<tr>
<td>Damar 2021[14]</td>
<td>2017.02-2017.11</td>
<td>Turkey</td>
<td>30/30</td>
<td>28/28</td>
<td>prospective study</td>
<td>kidney stone</td>
<td>residual &lt; 3mm</td>
<td>7</td>
<td>9.5/11.5F</td>
</tr>
<tr>
<td>Ecer 2022[15]</td>
<td>NR</td>
<td>Turkey</td>
<td>40/20</td>
<td>37/17</td>
<td>prospective randomized study</td>
<td>kidney stone</td>
<td>residual &lt; 3mm</td>
<td>8</td>
<td>11/13F</td>
</tr>
<tr>
<td>Geavlete 2021[16]</td>
<td>2019.01-2020.12</td>
<td>Romania</td>
<td>144/144</td>
<td>110/125</td>
<td>retrospective study</td>
<td>kidney stone</td>
<td>NR</td>
<td>6</td>
<td>12/14F</td>
</tr>
<tr>
<td>Geraghty 2016[17]</td>
<td>2012.03-2014.10</td>
<td>UK</td>
<td>40/28</td>
<td>33/25</td>
<td>prospective study</td>
<td>large kidney stone &gt; 2cm</td>
<td>residual &lt; 2mm</td>
<td>6</td>
<td>9.5/11.5F or 12/14</td>
</tr>
<tr>
<td>Gunseren 2021[18]</td>
<td>2010-2019</td>
<td>Turkey</td>
<td>114/461</td>
<td>96/382</td>
<td>retrospective study</td>
<td>kidney stone 20mm</td>
<td>NR</td>
<td>5</td>
<td>9.5F</td>
</tr>
<tr>
<td>Karaaslan 2019**[19]</td>
<td>2016.01-2018.10</td>
<td>Ankala</td>
<td>81/48</td>
<td>NA</td>
<td>retrospective study</td>
<td>kidney stone</td>
<td>NR</td>
<td>6</td>
<td>12/14F</td>
</tr>
<tr>
<td>Lildal 2018***[21]</td>
<td>2013.11-2016.02</td>
<td>Denmark</td>
<td>88/92</td>
<td>NA</td>
<td>retrospective study</td>
<td>kidney stone</td>
<td>NR</td>
<td>7</td>
<td>10/12F</td>
</tr>
<tr>
<td>Lima 2020[22]</td>
<td>2012.03-2018.07</td>
<td>UK</td>
<td>203/135</td>
<td>177/125</td>
<td>retrospective study</td>
<td>kidney stone</td>
<td>residual &lt; 2mm</td>
<td>8</td>
<td>9.5/11.5F or 12/14F</td>
</tr>
</tbody>
</table>

Abbreviation:
UAS, ureteral access sheath; SFS, stone-free status; SFR, stone-free rate; NA, not available; NR, not reported; RCT, random control study; NOS, Newcastle-Ottawa scale.

*: SFR was not calculated because they did not have a standardized protocol in place for post-operative imaging during the study.

**: The study provided an overall result (68/129, SFR = 52.7%) rather than comparative data of UAS and non-UAS.

***: No available SFR data was provided.

****: Here was the raw data provided by the study. Postoperative imaging was available for 47.6% of patients to assess SFS.
### References

<table>
<thead>
<tr>
<th>References</th>
<th>Enrollment period</th>
<th>Country</th>
<th>Sample size (UAS/non-UAS)</th>
<th>SFS (UAS/non-UAS)</th>
<th>Study design</th>
<th>Stone type</th>
<th>Definition of SFS</th>
<th>Quality (NOS)</th>
<th>Size of UAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meier 2021[23]</td>
<td>2016.06-2018.07</td>
<td>USA</td>
<td>1969/3260 (881/1292)****</td>
<td>612/1021</td>
<td>retrospective study</td>
<td>kidney or ureteral stone</td>
<td>absence of residual stone</td>
<td>6</td>
<td>NR</td>
</tr>
<tr>
<td>Ozimek 2022[24]</td>
<td>2013.09-2017.06</td>
<td>Germany</td>
<td>98/185</td>
<td>59/146</td>
<td>retrospective study</td>
<td>kidney stone</td>
<td>NR</td>
<td>7</td>
<td>12/14F</td>
</tr>
<tr>
<td>Tracy 2018[26]</td>
<td>2013.01-2015.06</td>
<td>USA</td>
<td>168/89</td>
<td>133/75</td>
<td>retrospective study</td>
<td>kidney stone</td>
<td>absence of residual stone</td>
<td>7</td>
<td>12/14F</td>
</tr>
<tr>
<td>Traxer 2015[27]</td>
<td>2010.01-2012.10</td>
<td>Global</td>
<td>1422/727</td>
<td>1051/602</td>
<td>prospective study</td>
<td>kidney stone</td>
<td>residual &lt;1mm</td>
<td>5</td>
<td>NR</td>
</tr>
<tr>
<td>Xi 2017[10]</td>
<td>2015.09-2017.09</td>
<td>China</td>
<td>133/57</td>
<td>108/43</td>
<td>retrospective study</td>
<td>kidney stone (1-2cm)</td>
<td>residual &lt;3mm</td>
<td>8</td>
<td>12/14F</td>
</tr>
<tr>
<td>Yitgin 2021[29]</td>
<td>2019.02-2020.05</td>
<td>Turkey</td>
<td>51/62</td>
<td>46/58</td>
<td>retrospective study</td>
<td>kidney or ureteral stone</td>
<td>residual &lt;2mm</td>
<td>6</td>
<td>10/12F</td>
</tr>
</tbody>
</table>

**Abbreviation:**

UAS, ureteral access sheath; SFS, stone-free status; SFR, stone-free rate; NA, not available; NR, not reported; RCT, random control study; NOS, Newcastle-Ottawa scale.

*: SFR was not calculated because they did not have a standardized protocol in place for post-operative imaging during the study.

**: The study provided an overall result (68/129, SFR = 52.7%) rather than comparative data of UAS and non-UAS.

***: No available SFR data was provided.

****: Here was the raw data provided by the study. Postoperative imaging was available for 47.6% of patients to assess SFS.

### 3.3 Primary outcomes

#### 3.3.1 Stone-free rate

In summary, compared to the UAS group, the non-UAS group had a higher SFR, indicating that the surgical treatment effect without UAS was better. The included studies have defined the SFR differently. Six studies [13, 20, 23, 25, 26, 28] identified SFR as absent calculi on the initial postoperative imaging and one study[24] determined SFR intraoperatively by an endourologist using intraoperative fluoroscopy. One of the articles [27] recognized it as a residual stone less than 1 mm, while three [17, 22, 29] defined it as having a residual stone fragment that is less than 2 mm, and five [10–12, 14, 15] described it as residual stone less than 3 mm. Postoperative radiological re-evaluation with ultrasonic examination, non-contrast computed tomography (NCCT), or delayed kidney, ureter, and bladder (KUB) radiography were always performed. Eighteen studies [10–12, 14–18, 20, 22–30] compared the differences in SFR between UAS and non-UAS groups. The result demonstrated a higher SFR (OR = 0.76, 95%CI 0.60–0.95, P = 0.01, Fig. 2) in the non-UAS group than in the UAS group summarized with a random effects model and a moderate heterogeneity (Q = 35.07, P = 0.01, I² = 51.53%, Fig. 2). This is supported by the Labbe plot(Fig. 3). In
the sensitivity analysis, an appreciable decrease was performed in heterogeneity when the L’Esperance et al cohort was omitted\cite{20}, and aggregate results did not change (OR = 0.68, 95%CI 0.56–0.82, P < 0.00001; Q = 23.12, P = 0.11, I² = 31%).

### 3.3.2 Subgroup analysis

Subgroup analyses were conducted based on age, study design, year of study, size of the UAS, and definition of SFR to further estimate the efficiency of the UAS in SFR. Finally, no significant results were obtained in any of the subgroup analyses (Table 2).

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Studies</th>
<th>Heterogeneity</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>Subgroup Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td>17</td>
<td>34.25</td>
<td>0.77 (0.61–0.98)</td>
<td>0.03</td>
<td>1.34 0.25 25.2</td>
</tr>
<tr>
<td>Children</td>
<td>1</td>
<td>Not applicable</td>
<td>0.41 (0.14–1.17)</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Definition of SFS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NR</td>
<td>4</td>
<td>8.31</td>
<td>0.67 (0.39–1.14)</td>
<td>0.14</td>
<td>0.33 0.57 0</td>
</tr>
<tr>
<td>Residual &lt; 3mm</td>
<td>14</td>
<td>26.70</td>
<td>0.80 (0.61–1.04)</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Study Design</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT</td>
<td>1</td>
<td>Not applicable</td>
<td>0.18 (0.01–3.94)</td>
<td>0.28</td>
<td>1.24 0.54 0</td>
</tr>
<tr>
<td>Retrospective study</td>
<td>12</td>
<td>26.42</td>
<td>0.76 (0.57–1.00)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Prospective study</td>
<td>5</td>
<td>7.52</td>
<td>0.98 (0.46–2.09)</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>Year of study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-2015</td>
<td>5</td>
<td>14.84</td>
<td>0.68 (0.56–0.82)</td>
<td>&lt; 0.00001</td>
<td>0.04 0.85 0</td>
</tr>
<tr>
<td>2015-</td>
<td>13</td>
<td>20.15</td>
<td>0.66 (0.57–0.77)</td>
<td>&lt; 0.00001</td>
<td></td>
</tr>
<tr>
<td>Size of UAS*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.5 or 9.5/11.5F</td>
<td>2</td>
<td>0.01</td>
<td>1.10 (0.64–1.88)</td>
<td>0.74</td>
<td>8.01 0.16 37.5</td>
</tr>
<tr>
<td>10/12F</td>
<td>2</td>
<td>2.83</td>
<td>1.49 (0.25–8.72)</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td>12/14F</td>
<td>7</td>
<td>10.61</td>
<td>0.69 (0.47–1.02)</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>NR</td>
<td>2</td>
<td>0.03</td>
<td>0.60 (0.51–0.69)</td>
<td>&lt; 0.00001</td>
<td></td>
</tr>
</tbody>
</table>

* Only subgroups containing two or more studies were listed here.

Abbreviation: UAS, ureteral access sheath; SFR, stone-free rate; SFS, stone-free status; NA, not available; NR, not reported; RCT, random control study; OR, Odds ratio; CI, confidence interval.

### 3.3.3 Publication bias of SFR

Based on the SFR, there was no evidence of significant publication bias (z = 1.06, P = 0.2873) in the Egger test. All the studies were evenly distributed on both sides of the combined effect of the funnel plots (Fig. 2). Furthermore, we conducted a sensitivity analysis using the trim-and-fill method in STATA software, and one study was added to the new funnel plot (Fig. 2), but the overall result remained unchanged (OR = 0.74, 95%CI 0.58–0.93, P = 0.01). Based on the above, the results obtained are encouraging.

### 3.4 Secondary outcomes

#### 3.4.1 Post-operation complication

We did not find any differences in post-operation complications between the UAS group and non-UAS groups. Postoperative complications refer to problems, manifestations, symptoms, and corresponding complications, which are related to the operation. Seventeen studies\cite{10–19, 22, 24, 26–30} provided effective post-operation complication data, such as bleeding, fever, colic pain, urinary tract infection, lung
embolism, and urosepsis. With the random-effect model, the combined effect result did not show a higher incidence in the UAS group than non-UAS group (OR = 1.20, 95% CI 0.79–1.82, P = 0.38; Q = 49.48, P < 0.0001, I² = 67.66%; Fig. 3). Most studies have not reported the incidence of complications associated with different UAS sizes. There were five UAS sizes that could be used for sub-group analysis: 9.5F or 9.5/11F, 10/12F, 11/13F, 12/14F, and 14/16F. We conducted further analysis to evaluate the impact of different UAS sizes on post-operative complications. The results showed no statistically significant difference in the incidence of complications among the UAS of different sizes.

### 3.4.2 Infra-operation complication

The UAS also did not reflect a reduction in intraoperative complications. Compared with postoperative complications, intraoperative complications refer to unexpected circumstances during the operation. Three studies [10, 12, 15] provided intra-operative complication data using the Post-Ureteroscopy Lesion Scale (PULS), a surgical video-based grading system for assessing ureter wall trauma[31]. Urologists started with a view of the ureteropelvic junction and ended with the ureteral orifice, showing the postoperative ureter along its entire length, and graded potential trauma as grade 0–5. In the included studies, all reported outcomes were of Grades 0–3. Additionally, four studies[23, 25, 27, 28] provided data on intra-operative complications due to symptoms, such as bleeding and perforation. The result of the conducted SFR in the UAS Group do not show a significant difference compared to the non-UAS Group (OR = 1.20, 95% CI 0.85–1.70, P = 0.26; Fig. 3). The subgroup analysis results in this part showed that OR in PULS and Clavien-Dindo [32] classifications were 1.43 (95% CI 0.86–2.37, P = 0.95; Fig. 3) and 1.13 (95% CI 0.60–2.14, P = 0.08; Fig. 3), respectively, and both grading approaches reached no significant heterogeneity(Q = 0.32, P = 0.57, I² = 0; Fig. 3). Therefore, we had reason to believe that UAS would not increase the intra-operative complication incidence analogously to the non-UAS group.

### 3.4.3 Operation time

Patients in the UAS group had a longer operative time than those in the non-UAS group. A total of 12 [10, 11, 13, 14, 18, 19, 21, 22, 24, 25, 27, 29] studies provided data on operative time, two [24, 25] of which provided a range of operative time rather than mean and standard deviation values. To complete the data summary analysis, we used the online calculation tool provided by Luo et al. [5] to calculate the mean and standard deviation of the raw data. Finally, effective data was obtained and showed a significant difference between groups (MD = 11.21, 95% CI 5.66–16.76, P < 0.00001; Fig. 4) with a severe heterogeneity (Q = 147.60, P < 0.00001, I² = 92.55%; Fig. 4).

### 3.4.4 Hospitalization duration

There was no obvious effect on the duration of hospitalization in patients with UAS. Data on hospitalization duration were be found in five articles[11, 14, 15, 22, 27], one of which [14] provided invalid data that could not be included in the summary analysis. The results of the remaining four articles showed no significant difference in hospitalization duration between the UAS and non-UAS groups (MD = -0.03, 95% CI -0.30–0.24, P = 0.84; Q = 4.71, P = 0.19, I² = 36.36%, Fig. 4).

### 4 Discussion

Current published clinical studies have provided different opinions regarding the effect of UAS usage on SFR and have proposed different recommendations for the treatment of urinary stones. Our comprehensive quantitative review of 21 studies and 11335 patients provided a potential explanation for the inconsistent findings. In consciousness, we found that the use of UAS during surgery may not be as effective as expected. In the subgroup analysis, we varied several factors such as age, study design, size of UAS, and definition of SFR to explore possible sources of heterogeneity, but no significant results emerged. The purpose of inserting UAS during surgery was to improve efficacy, but the actual situation was contrary to expectations. In Meier’s [23] and Ozimek’s [24] studies, the use of UAS in patients reduced the SFR (69.5% vs. 79.0% and 60.2% vs. 78.9%). It was not possible to fully attribute the reduction in SFR solely to the use of UAS, as there is a potential for bias due to the operational burden in their opinions. In a multi-center and large-sample retrospective clinical study by Traxer et al. [27], the group that did not UAS performed better on SFR (73.9% vs. 82.8%), and there was no significant difference in stone burden between the two groups. These results suggest the need to re-examine the effectiveness of UAS in patients.

During the data analysis process, we noticed several confounding factors in the results, including the size of the UAS, distribution of stone locations, and whether the ureter was stented before surgery. Due to incomplete raw data, we were unable to conduct further analysis and research on this part of the data, which required to carefully explain our synthesized results. Among the 21 studies included, eight different UAS sizes were involved, with the most widely used being 12/14F (7/21), followed by 10/12F (2/21). In some studies, such as Geraghty et al. [17] and Lima et al. [22], researchers used multiple UAS sizes for surgery and did not calculate the stone-free rate separately based on different UAS sizes. Only Tracy et al. [26] calculated the SFR for different sizes of UAS, and according to their research, there was no statistically significant change in SFR when using different sizes of UAS (no UAS 87.6% vs. 12/14F 78.1% vs. 14/16F 81.3%). The location of the stones described in the relevant literature can generally be divided into the following types: ureter, upper renal pole, mid renal pole,
lower renal pole and renal pelvis. Berquet et al. [11] studied the SFR of stones at different locations and found better performance in the ureter, renal pelvis, mid-pole and upper pole; however, there was no statistical difference in the results.

To explore the potential impact of these uncontrollable confounding factors, researchers used multivariable analysis to study the independent predictors of the SFR. Taking Meier et al. [23] as an example, the independent predictors of SFR included the use of UAS, location of stones in the kidney, and size of stones. In the included studies, the results of the multivariate analysis indicated that pre-stenting could not be used as an independent predictor. Currently, the necessity for pre-stenting remains controversial. Due to the lack of relevant data, we were unable to explore the correlation between pre-stenting and SFR as a grouping factor in the meta-analysis process. We further reviewed the relevant literature and found that Fahmy [33] and Chang [34] et al. concluded that higher SFR and initial insertion success rate are correlated with pre-stenting, but the relationship between the incidence of complications and pre-stenting is not statistically significant.

The UAS was designed to keep the ureteral wall away from stone debris and allow repeated insertion and removal of surgical instruments. However, based on current clinical research, we did not observe a protective effect of the UAS. Whether it was based on the PULS evaluation method [31] or the common symptom report, there was no significant difference between UAS and non-UAS in the incidence of intraoperative complications. Based on our meta-analysis, we could not find conclusive evidence to support the protective effect of UAS in reducing short-term postoperative complications such as fever and colic pain. In a study by Wang [28], 90-day post-operation emergency department (ED) visits and 90-day post-operation symptoms were mentioned to explore short-term complications, and no significant differences between the groups were observed. Within the scope of references, the UAS provides the advantages of acting as a stone drainage pipe during the operation [1], reducing the pressure [35, 36] in the infrarenal region caused by flushing, and improving the surgical field of vision and visibility [36]. In addition, in some in vitro model experiments, the use of UAS alleviated the rise in renal temperature caused by laser lithotripsy [37, 38]. A few studies have described whether UAS can protect renal function (such as serum creatinine levels). Ecer et al. [15] compared the changes in serum creatinine levels at 4 hours and 14 days after the operation and found that the level of serum creatinine was not statistically significant whether UAS was used or not.

Some in vitro studies also suggested that the use of UAS would compress the ureteral wall and cause ischemia [39], which may lead to ureteral scarring or stenosis, however, Delvecchio et al. did not find a correlation between the use of the UAS and ureteral stricture [40] during a 3-month follow-up. Although several studies [10, 12, 15] had evaluated the condition of postoperative ureteral injury in patients by PULS, they had not reported secondary ureteral stricture in patients with relatively severe injury. A study assessing the association between high-grade ureteral injury and ureteral stricture or hydronephrosis showed that the use of UAS would not lead to significant clinical sequelae (1/56) [41]. However, a recent retrospective study of 1001 RIRS operations showed that 3% of patients were diagnosed with ureteral strictures during a 3-month follow-up. In the subsequent multivariate analysis, the use of UAS was considered an independent related factor [27]. In sum up, there is insufficient evidence regarding the safety of UAS in terms of intraoperative complications, and short or long-term post-operation complications.

Our analysis showed that the operative time in the UAS group was significantly longer than that in the non-UAS group. It is worth noting that, in the research by Pardalidis [25] and Ozimek [24], the UAS data was calculated suing algorithm, which may differ from the real situation. Regarding the hospitalization duration, the number of studies that could be included in the calculation was relatively small, the synthesis of the meta-analysis revealed the same effect between the groups, and the heterogeneity was high.

Super-pulsed Thulium Fiber Laser (TFL) is the latest laser treatment for urinary stones, and several clinical studies have compared its curative effect with the traditional holmium laser [42–45], and only Enikeev et al. [44] studied the role of UAS in TFL lithotripsy but did not obtain statistically significant results. Owing to the obvious differences in the location, size, density, and other parameters of the stones between these studies, we could not observe the advantages and disadvantages of UAS in TFL lithotripsy.

Alpha-receptor blockers are commonly used in urology, such as tamsulosin and silodosin, which can relax the urethral smooth muscle, thus reducing the difficulty in inserting the UAS during surgery. Meier et al. [23] reviewed the effects of preoperative use of alpha-blockers on outcome indicators (emergency department visit, hospitalization, and stone-free status) but did not reach meaningful results. In a prospective randomized trial of 77 patients undergoing retrograde intrarenal surgery [46], the impact of a three-day silodosin administration prior to surgery was evaluated with the systematic use of a UAS. The results showed no presentation, and ureteral injury involving the smooth muscle layer (PULS Grades 3 to 5) occurred significantly less frequently in the silodosin group than in the control group (9.3% vs. 27.3%, P = 0.031). However, this finding was not observed in another retrospective study [47]. At present, the effect of alpha-blockers on the use of UAS is unclear.
As the newest meta-analysis on the impact of UAS on ureteroscopic lithotripsy, this study had the following limitations. First, owing to the small number of related RCTs, most of the studies included in this review were prospective and retrospective clinical cohort studies, leading to an unavoidable high risk of bias. Second, for the primary outcome, SFR, the definition and evaluation methods of SFR in different studies were not completely consistent, which was an important source of heterogeneity. Finally, there is still no recognized standard for the use of the UAS. The conditions for the use of UAS had not been fully described in various studies, which may lead to unmeasured confounding factors that may have a potential impact on the results.

The application conditions for flexible ureteroscopes have been clearly explained by the consensus of various authoritative urological societies and experts, such as the European Association of Urology. There is no uniform standard for the use of UAS. Therefore, we need a more standardized process for the use of UAS to minimize the impact of confounding factors, and reach a more convincing conclusion, to ensure that more patients with urinary stones can receive better treatment effects and smaller residual stone sizes.

5 Conclusion

This is the latest meta-analysis of the impact of UAS in flexible ureteroscopic lithotripsy, and our results show that the use of UAS prolongs the operation time and reduces SFR but has no impact on intraoperative complications, postoperative complications, and hospitalization duration. Based on the current evidence, we need to carefully consider the use of UAS because it may not be suitable for all patients undergoing flexible ureteroscopic lithotripsy. Therefore, more RCTs to evaluate the real impact of UAS are needed to benefit more patients eligible for UAS.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: All authors unanimously agree consent for publication.

Availability of data and materials: The original contributions presented in the study are included in the article.

Competing interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding: This work was supported by grants of from the Department of Science and Technology of Jinan City (Grant no.201805030).

Authors’ contributions: Wei Guo (First Author): Conceptualization, Methodology, Data Curation, Investigation, Formal Analysis, Visualization, Writing - Original Draft; Zeyan Li: Investigation, Data Curation, Writing - Original Draft; Keqiang Yan: Visualization; Zhiqing Fang: Methodology; Yidong Fan(Corresponding Author): Conceptualization, Supervision, Writing - Review & Editing.

References


Figures
Figure 1

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of the present study.
Figure 2

The forest plot, funnel plot and imputed funnel plot of SFR. UAS, ureteral access sheath; OR, odds ratio; CI, confidence interval.
Figure 3

a: Forest plot of post-operation complications. b: Forest plot of intra-operation complications. UAS, ureteral access sheath; PULS, Post-Ureteroscopy Lesion Scale; OR, odds ratio; CI, confidence interval.
Figure 4

a: Forest plot of operation time. b: Forest plot of hospitalization duration. UAS, ureteral access sheath; SD, standard difference; OR, odds ratio; CI, confidence interval; MD, mean difference.