Operative outcomes 24 hours after retrograde intrarenal surgery for solitary renal calculi using a flexible and navigable suction ureteral access sheath. A prospective global multicenter study by the European Association of Urology Section on Urolithiasis

Minerva Urology and Nephrology (formerly: Minerva Urologica e Nefrologica)
EDIZIONI MINERVA MEDICA

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Reply letter with the authors' point-by-point response

Notes from the Chief Editor

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Notes to the authors: please consider recent MUN papers during your revision

REPLY. Thank you very much for your comment. We have added the following papers recently published in MUN in the reference list: PMID: 33016029; PMID: 30230298; PMID: 30567423; PMID: 33016033

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Comment 1

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General comment (originality, scientific accuracy, strengths and/or weaknesses): The topic of the multicentre study is innovative and up-to-date. The CT evaluation 24 hours after RIRS is a valid tool in order to evaluate early SFR. The number of patients is not very high, but this should push towards deepening the quality of the reported results.

REPLY. Thank you very much for appreciating our study.

Major corrections (main criticisms): The study, being multi centric, implies a number of biases:

1) 5 different kinds of FANS-UAS have been used: are you sure that they are equivalent in terms of physical features (friction, elasticity, bendability, et cetera). This issue should be discussed.

REPLY. Thank you very much for your important comment. You are right but this is beyond the scope of this study and we do not have the experimental information on this. According to your valuable comment, we have added the following sentence in study limitation section "*Yet,* *we have employed in our study five different FANS-UAS which are probably not equivalent in terms of physical features (i.e. friction, elasticity, and bendability) but we do not have the experimental information on this.*"

2) gravity, intermittent manual syringe irrigation and the Traxerflow were used as irrigation: all these elements interfere very differently with the intrarenal pelvic pressure, which should find the right balance with the suction of the FANS-UAS. Did someone ever measure values of IRPP in a test-case for each kind of irrigation? How did you deal with this bias? Please explain and discuss.

REPLY. Thank you very much for your important comment. Indeed, we agree with you that gravity, intermittent manual syringe irrigation and the Traxerflow have different impact on intrarenal pressure. However, the use of suction during surgery allowed to reduce the intrarenal pressure. Unfortunately, we could not test the value of intrarenal pressure during surgery in any case as we did not have the means to do the same. We have added this limitation as you rightfully suggest in the main text as follows "*In future, perhaps our limitation of not being able to assess intrarenal is a an important consideration to further improve outcomes when using FANS-UAS*"

3) I fully realize that with 16 centers, 15 countries and 20 urologists it is not possible to detail the kind of ureteroscope used by each one, but again, the ratio between FANS-UAS diameter and diameter of the fURS would be relevant for the infrarenal pelvic pressures, along with the irrigation flow. These data should be mentioned (the disposable scopes are not so many).

REPLY. Thank you very much for your relevant comment. Indeed, as it has been highlighted by recent studies apart from intrarenal pressure, even the ratio between the scope and UAS size and its direct influence on both 24 hours and long term FANS-UAS outcomes will need to be evaluated

Unfortunately we are not able to provide this data because we did not gather.

4) The exit strategy after RIRS is heterogeneous: also this element can interfere with the presence/absence of stone fragments 24 hours after RIRS, therefore, also the exit strategy should be standardized. Please detail (how long were the JJ stents left in place afterwards?) and discuss.

REPLY. Thank you very much for your important comment. Indeed, the exit strategy was inhomogeneous because it was left to treating surgeon's decision. Stent duration can usually vary across patients according to each case (i.e. presence of large RFs, ureteral/PCS lesions and so on) and cannot be truly standardized. The stent itself does not actually interfere much with CT evaluation of RFs because large fragments are easily visible. Unfortunately, we did not gather data of indwelling time of ureteral stent. However, we have implemented Methods as follows "*The choice of energy source for RIRS and perioperative decisions such as pre-stenting and postoperative exit strategy and stent dwelling time were at the respective surgeon's own discretion*"

5) Lasers should also be specified: TFL, but especially Ho:YAG, where the devices can be different with extremely variable features depending upon the power, the settings and the pulse modulation. Settings (J, Hz, resulting W, pulse duration) should be specified, being the outcomes/risks different in relationship with the entity of the irrigation flow.

REPLY. Thank you very much for your important comment. Laser machine manufactures have been specified in Methods as follows "*Lithotripsy was performed using either Thulium fiber laser (Fibre dust, Quanta System, Varese, Italy or Soltive, Olympus, Hamburg, Germany or*

Urolase SP 60W, IPG Photonics, Oxford, MA) or Holmium laser (Lumenis Pulse™ 100H, Boston Scientific, Marlborough, MA or Medilas H Solvo, Dornier, Weßling, Germany or Cyber Ho 60 Quanta System, Varese, Italy)". We are sorry but we cannot provide data of laser settings because the same was not gathered for this study.

6) There is no mention of the stone composition, which should be ideally homogeneous for the kind of evaluation the study aims at.

REPLY. Thank you very much for your important comment. We agree with you but unfortunately we did not gather this data

In the Results TFL is the reported laser used. In Table 2 it looks like

REPLY. Thank you very much for your comment. Rest of cases were done using Holmium laser and this was amended in the text with the following sentence "*Thulium fiber laser was used in 44.4% of cases, whereas Holmium laser was employed in the other ones*."

Minor corrections (page, paragraph, line where the author must make the corrections): - Title: access sheath = I would add ureteral (access sheath); Section and Urolithiasis = I would put capital first letters.

REPLY. Thank you very much for your comment. We have made the suggested changes.

- Abstract and Text: FANS = FANS-UAS? in Italian FANS means Farmaci Antiinfiammatori Non Steroidei, equivalent to NSAID, Non Steroidal AntiInflammatory Drugs. This might create some confusion in Italian urologists.

REPLY. Thank you very much for your comment. According to your valuable suggestion, we have replaced FANS with FANS-UAS in both abstract and main text

- Abstract, Methods: "A multivariable logistic regression analysis model to assess their significance as independent of Grade A SFR" = there is no verb in this sentence, and additionally it is not overall very clear.

REPLY. Thank you very much for your comment. We do apologies for this oversight. This sentence has been rephrased as "*A multivariable logistic regression analysis model was performed to assess factors associated with the odds of having Grade A stone-free status*".

- Abstract, Conclusions: The meaning of the first sentence (imaging and clinical evidence favor excellent preoperative outcomes...) is not very clear: did you mean "demonstrate" or something like that?

REPLY. Thank you very much for your comment. We do apologies for this oversight. Yes, we mean what you said. Therefore, this sentence has been rephrased as "*Imaging and clinical evidence demonstrate excellent perioperative outcomes just 24 hours post RIRS with FANS-UAS.*."

- Abstract, Conclusions: what do you mean with "dismal infective complications"? May be the term dismal is not fully appropriate.

REPLY. Thank you very much for your comment. We do apologies for this oversight. Dismal has been replace with "*a low rate of*"

- Results: 11-13 Ch FANS-UAS: did you have prestented patients? in case not how many failures in their application?

REPLY. Thank you very much for your important comment. we only collected data on those patients in whom FANS-UAS was successfully deployed.

- Conclusions: the last sentence is really not very clear, please rephrase.

REPLY. Thank you very much for your comment. We apologies for not being clear. That sentence has been rephrased for more clarity as follows "*Indeed, comparing FANS-UAS with traditional UAS may further enhance key features of this new technology. However, our findings provide a platform for future studies to improve RIRS outcomes*"

- reference 2 is incomplete, please add the missing data.

REPLY. Thank you very much for pointing out this. Reference has been amended as follows "De Stefano V, Castellani D, Somani BK, Giulioni C, Cormio A, Galosi AB, et al. Suction in Percutaneous Nephrolithotripsy: Evolution, Development, and Outcomes from Experimental and Clinical studies. Results from a Systematic Review. Eur Urol Focus. 2024 Jan;10(1):154–68"

- reference 17 is also not written correctly, please correct.

REPLY. Thank you very much for pointing out this. Reference has been amended as follows "Osther PJS, Pedersen K V, Lildal SK, Pless MS, Andreassen KH, Osther SS, et al. Pathophysiological aspects of ureterorenoscopic management of upper urinary tract calculi. Curr Opin Urol. 2016 Jan;26(1):63–9."

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Comment 2

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General comment (originality, scientific accuracy, strengths and/or weaknesses): The authors have produced a good collaborative study.

REPLY. Thank you very much for appreciating our study.

Minor points: They stated that this is the first global study using FANS. However, to my knowledge, the same group has previously published global results focusing on different patient groups.

REPLY. Thank you very much for your comment. Indeed, even though this is the first study to measure the 24 hours outcomes of RIRS using, it is not the first multicenter study on FANS-UAS. According to your suggestion, we have deleted that sentence in the revised version of the manuscript.

Is a structured discussion with subheadings, bullets, and numbers appropriate within the context of this journal? I leave this decision to the journal rules editing. Discussion first paragraph.

REPLY. Thank you very much for your comment. Discussion is already structured with subheadings, bullets, and numbers. First paragraph of discussion has been deleted as you suggested in your previous comment.

Major corrections (main criticisms): No

REPLY. Thank you very much for your comment

Minor corrections (page, paragraph, line where the author must make the corrections): Discussion first paragraph second line.

REPLY. Thank you very much for your comment. We do apologies for being not clear. That sentence has been rephrased for more clarity as follows: "*Since it is not a routine practice, we decided to use a 24-hour NCCT with the bone window to discuss the rationale and objectives, as well as its impact on primary outcome assessment compared to the traditional method of reporting SFR at one month. We chose this approach for the following reasons*:"

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Running Title: 24-hour outcome of RIRS using FANS-UAS

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ABSTRACT

Background: Suction techniques showed potential to improve outcomes of retrograde intra-renal surgery (RIRS). We assessed the 24-hour stone-free rate (SFR) and complications after RIRS using flexible and navigable suction ureteral access sheaths (FANS-UAS).

Methods: Sixteen centers prospectively contributed to data (August 2023-October 2023). Inclusion criteria: age ≥18 years, single renal stone, pre and 24-hour post-RIRS CT scan. Exclusion criteria: ureteral stone, anomalous kidney, multiple stones. SFR: *Grade A*: no fragments; *Grade B*: fragments ≤2 mm; *Grade C*: fragments 2.1-4 mm; *Grade D*: fragments >4 mm. A multivariable logistic regression analysis model ~~was performed~~ to assess ~~their significance as independent~~ factors associated with the odds of having Grade A stone-free status. Data are expressed as median (interquartile range), absolute numbers and frequencies, odds ratio (OR), and 95% confidence interval (CI).

Results: 142 patients with a median age of 52 years (40-61) were enrolled. 61.3% were males. Median stone volume was 1165 mm^3 (656-1936). Median operative time was 48.5 (36.25-71.75) min. Transient fever (37°C-37.5°C) occurred in 10 (7%) patients. No sepsis case occurred. 96.5% of patients were stone-free (Grade A+B). Grade A SFR was 52.8%. All patients were discharged within 48 hours. Bone window (OR 3.156 95% CI 1.177-9.130,p=0.027) was the only factor significantly associated with higher odds of 100% SFR, while stone volume (OR 0.999, 95% CI 0.999-1.000,p=0.007) was significantly associated with lower odds.

Conclusions: Imaging and clinical evidence ~~favour~~ demonstrate excellent perioperative outcomes just 24 hours post RIRS with FANS-UAS. The technique demonstrates a good safety profile, ability for immediate high SFR, and ~~dismal~~ a low rate of infective complications.

Key words: Kidney Calculi; Flexible Ureteroscopy; Lithotripsy, Laser; Retrograde Intrarenal Surgery; Vacuum assisted surgery.

TEXT

1. INTRODUCTION

Vacuum-assisted techniques are revolutionizing the endourological management of urolithiasis by flexible ureteroscopy[1] and percutaneous nephrolithotripsy[2,3]. The main aim of a successful retrograde intra-renal surgery (RIRS) as a minimally invasive approach is to render the patient stone-free with the least morbidity[4]. However, as has been reported by the FLEXOR study, despite best efforts in real-world practice, residual fragments (RFs) remain in 21.7% of patients and 51.5% of these patients have a second intervention[5].

To improve RIRS outcomes apart from more powerful lasers, dust, and fragment removal devices like the flexible and navigable suction ureteral access sheath (FANS-UAS)[6], direct in scope suction technique[7], and steerable post lithotripsy aspiration catheters[8] are some of the novel proposals. Of these, in a retrospective single-center study, FANS-UAS has shown a higher SFR when compared to a standard ureteral access sheath (UAS) with lower incidences of infectious and overall complications[9]. A few studies are reporting the outcomes of RIRS using FANS-UAS[9–11]. However, most of these are single-center and retrospective studies with a low number of cases and there is concern that sheath placement across the ureteropelvic junction and its movement within the collecting system may cause more injuries whilst attempting aspiration.

In this prospective study, we aimed to assess by using imaging and clinical outcomes within 24 hours of the procedure if FANS-UAS is safe, feasible, and helps to improve stone-free rate (SFR) in a multicenter real-world practice. The secondary outcome was to assess the utility of the sheath as an effective device for improving visibility, and the ability to navigate the sheath in different parts of the pelvic caliceal system (PCS), especially the lower pole, and document any specific or unique challenges encountered.

2. MATERIAL AND METHODS

2.1 Study design

This study was conducted under the auspices of the European Association of Urology Section of urolithiasis (EULIS). Twenty surgeons from 16 centers from 15 countries prospectively contributed to the data as per protocol designed by the primary site, the Asian Institute of Nephrology and Urology after obtaining institutional review board approval (#AINU 12/2022) and has been conducted in accordance with the principles set forth in the

Helsinki Declaration. Each participating center also obtained its own ethics board approval. Patients have given their informed consent for participation in the research study.

All contributing surgeons had prior experience of performing at least 250 RIRS cases, however, only 3 of the 20 surgeons had any prior experience of using a FANS-UAS. Hence a training video was provided[6], and all surgeons were asked to use the sheath in at least one trial case before starting the study. Study period was between 1st August 2023 and 31st December 2023. We report here an interim analysis assessing the 24-hour outcomes of the 142 patients enrolled until October 20th. Inclusion criteria were symptomatic and asymptomatic patients aged ≥18 years, single renal stone of any size and location in the pelvicalyceal system deemed suitable for RIRS under fluoroscopy guidance by the treating surgeon and pre and post-RIRS non-contrast computed tomography (NCCT) scan. Exclusion criteria were children, multiple stones, isolated or concomitant ureteral stone, endoscopic combined intra-renal surgery, same-sitting bilateral procedure, staged surgery for residual fragments, previous ureteric injury or known ureteric anomalies or past ureteric reconstruction, patients who had incidental on table renal or ureteric pathology and concomitant intervention for same, and patients mentally unable to provide a written informed consent or unfit for general or spinal anaesthesia.

2.2 FANS-UAS and Surgical Procedure

NCCT scan with 2.5 mm slice thickness was performed in each case before RIRS to calculate the stone volume as per EAU urolithiasis guidelines[12]. Any positive urine culture was treated preoperatively as per the center's own antibiogram/protocol. Any antiplatelet or anticoagulation was stopped for 5 days before surgery and 5 days after surgery if deemed feasible and to be documented likewise. Baseline and operative characteristics were collected.

The following FANS-UAS were employed according to local practice provided by any company depending on the region of practice: Clearpetra (Welllead Medical, Panyu, Guangzhou, China), Negative Pressure Ureteral Access Sheath (Innovex Medical, Shanghai, China), Elephant second generation (Zhejiang YiGao Medical Technology, Hangzhou, China), Suction UAS (SEPLOU, Beijing, China), Disposable Ureteral Guide Sheath (ZSR Biomedical Technology, Dongguan, Guangdong China China). Size and type of scope and laser were as per surgeons' own choice and available resources. Irrigation was performed using gravity assisted with either intermittent manual syringe irrigation or the

TRAXERFLOW Dual Port Gravity Line (Rocamed, Southborough, Massachusetts) as per availability of each center. Pressure bags were not used in any of the cases.

All surgeons were asked to follow the steps for the procedure as per the step-by-step video published[6]. One-dose antibiotic prophylaxis was given in all cases at induction according to local protocols.

RIRS was to be performed under any anesthesia and fluoroscopy guidance. This included positioning the patient in the lithotomy position, followed by a retrograde pyelogram and diagnostic semi-rigid ureteroscopy to ascertain that there were no ureteric abnormalities and delineating the pelvicalyceal system before placement of the FANS-UAS.

Lithotripsy was performed using either Thulium fiber laser (Fibre dust, Quanta System, Varese, Italy or Soltive, Olympus, Hamburg, Germany or Urolase SP 60W, IPG Photonics, Oxford, MA) or Holmium laser (Lumenis Pulse™ 100H, Boston Scientific, Marlborough, MA or Medilas H Solvo, Dornier, Weßling, Germany or Cyber Ho 60 Quanta System, Varese, Italy).

The operative parameters were defined as follows: i) Operative time: Time from start of Cystoscopy to exit (stent or ureteric catheter or nil drainage); ii) Ureteroscopy time: Time from placement of UAS to removal of UAS for exit; iii) Lasing time: actual time recorded during laser lithotripsy as per that indicated on the machine; iv) Radiation time: Total time from the start of retrograde pyelogram to exit (as seen on radiation monitor screen).

On table decision to use accessories like baskets for stone extraction, the need to abandon the procedure, change to another UAS, or any malfunction was recorded. The choice of energy source for RIRS and perioperative decisions such as pre-stenting and postoperative exit strategy and stent dwelling time ~~was~~ were at the respective surgeon's own discretion. Intraoperative visual inspection of all calyces and stone-free assessment by the surgeon were recorded to correlate how these measures fare vis a vis post-operative imaging assessment. Surgeons were also asked to grade their experience of using the FANS-UAS at the end of each case using a 5-point LIKERT-type scale (1 excellent; 2: very good; 3: good 4: average; 5: difficult)[13]. As an objective evaluation, surgeons were asked to document if RIRS with FANS-UAS had contributed to a change or deviation in their exit strategy concerning stent placement after each case.

Patients were assessed postoperatively according to the study protocol using an NCCT scan with 2.5 mm slice thickness 24 hours after the surgery and RFs categorized into one of the following categories using the bone window[14]: i) *Grade A*: there were no visible fragments (100% SFR); ii) *Grade B*: fragments up to 2 mm; iii) *Grade C*: fragments 2.1-4 mm; iv) *Grade D*: fragments >4 mm. For our study purposes patients with Grade A and B were considered "stone-free" and would not need any further imaging or re-intervention unless mandated by the surgeon for other reasons. Only Grades C and D would require follow-up with imaging between 4 weeks and 3 months to plan subsequent intervention if needed. Other 24-hour outcomes included immediate peri and postoperative complications, such as bleeding, need for transfusion, ureteric or PCS injury, infective complications, persistent haematuria prolonging hospital stay, and loin pain. Loin pain was scored using the standard 10-point visual analogue scale (VAS)[15]. All patients with RF(s) were counseled for either observation or re-intervention based on surgeons' assessment and if planned for a late (>6 weeks within 3 months) surgical intervention. A repeat NCCT scan would be done to confirm the need for re-intervention. Outcomes for these would be followed up subsequently.

2.3 Statistical analysis

Continuous variables are expressed as medians and interquartile ranges while categorical variables are reported as absolute numbers and percentages. Variables were selected a priori and entered into a multivariable logistic regression model to assess their significance as independent of 100% SFR. Data are expressed as odds ratio (OR) and 95% confidence interval (CI) with a double-sided p-value <0.05 indicating statistical significance. All statistical tests were performed using R Statistical language, version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

2.4 Data availability

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

3. RESULTS

During the study period, 142 patients with loin pain as the most common reason for intervention were enrolled with a median age of 52 years (40-61) (Table 1). There were 87 (61.3%) males. 71.1% were first-time stone formers. Median stone volume was 1165 (656-1936) mm^3. Median stone size was 1-2 cm in 66.9% of the cases with interpolar/renal pelvis as the most common location in 41.5% of cases followed by the lower pole as the next most common location in 34.6% of cases. Median Hounsfield unit was 1070 (890-1212). 49.3% of patients were pre-stented. 76.8% of patients received prophylactic antibiotics but only 21.8% of cases had a positive urine culture.

Preferentially, 11/13 Fr sheath in 44.4% of patients and a disposable scope in 77.5% was used under general anesthesia in 80.3% of cases (Table 2). Thulium fiber laser was used in 44.4% of cases, whereas Holmium laser was employed in the other ones. A basket was used in 15.5% of cases only to reposition stone fragments and nil was used for stone extraction. Pure dusting technique for lithotripsy was deployed in 45.8% but 52.1% of surgeons reported using a combination of dusting and fragmentation and none used popcorning. Median lasing, ureteroscopy, and overall operative times were 16.5 (10.31-26.82) min, 35.5 (25.00-59.75), and 48.5 (36.25-71.75) min, respectively. In 86.6% of the cases, the sheath was successfully navigated into all parts of the kidney and suction could be deployed successfully without any issues in 97.2 % of cases. In only 2 cases the FANS-UAS needed to be downsized from 12-14 Fr to a 10-12 Fr sheath. As part of the exit strategy, in 84.5% of cases a double J stent and in 9.2% and 6.3% of patients an overnight ureteric catheter was placed, or no drainage was deployed, respectively. For the latter 2, a change from their routine exit strategy was reported by the surgeon in 12.7% of cases. No case was abandoned intra-operatively due to non-technical reasons and no patient was lost at follow-up so far. For 46.5% of cases, surgeons reported intraoperative visual complete clearance which correlated when confirmed by the 24-hour NCCT. Perioperative complications and outcomes within the first 24 hours are reported in Table 3. Intra-operatively by virtue of sheath manipulation mild PCS oozing was reported in 11 cases (7.7%) and transient fever (37°C -37.5°C, Clavien grade 1) was reported overnight in 10 (7%) patients. There were no cases of sepsis. All 5 patients with ureteric access sheath injury Traxer grade 1 (n=4), grade 2 (n=1) needed only a double J stent placement[16]. As the NCCT was done 24 hours after surgery, we were able to document the presence of some perinephric stranding and perinephric fluid in 4.9% and 2.1% cases respectively. Median VAS score for loin pain was 2 (1-2). Median LIKERT score was 2 (1-3) points for ease of using suction with the navigation sheath, manipulating the sheath and scope together, and improving visibility during the procedure by minimizing the snow globe effect.

Overall, 96.5% of cases were stone-free (Grade A+B). 100% SFR (Grade A) was seen in 52.8% of cases. Grade B SFR was 43.7%. Grades C and D SFR was 3.5% and these patients were planned for re-intervention by RIRS (Table 3). All 142 cases were discharged within 48 hours and may be followed up to 3 months post-operatively and intervention outcomes will be documented in those planned for re-intervention. The surgeons reported an estimated 100% SFR in 66 cases (46.5%) by visual examination of all calyces which had a 100% correlation with post-operative 24-hour NCCT imaging. At multivariable analysis (Table 4), using bone window (OR 3.156 95% CI 1.177-9.130, p=0.027) was the only factor significantly associated with higher odds of 100% SFR, while stone volume (OR 0.999, 95% CI 0.999-1.000, p=0.007) was significantly associated with lower odds.

4. DISCUSSION

4.1 The rationale and information gained using a 24-hour NCCT scan and bone window

~~To our knowledge, this is the first global multinational multicentre prospective study using FANS. As it is not a routine practice, in an attempt to discuss the rationale and aim of doing the NCCT at 24 hours and its effect on primary outcome assessment compared to the traditional reporting SFR at one month, we chose to use a 24-hour NCCT using the bone window for the following reasons~~:

Since it is not a routine practice, we decided to use a 24-hour NCCT with the bone window to discuss the rationale and objectives, as well as its impact on primary outcome assessment compared to the traditional method of reporting SFR at one month. We chose this approach for the following reasons:

1) A CT scan is the only true road map to determine the presence of RF, allows for accurate calculation of the size of RF, and must be advocated especially if a surgical re-intervention is planned as part of follow-up[17].
2) There is no definite consensus on the timing of the CT scan and guidelines advocate imaging anytime within 3 months of RIRS intervention[12,18]. Whilst this is acceptable, the only proof of correlating intraoperative findings like complete stone clearance, missed injury to the ureter and PCS along with post-operative outcomes such as the presence of the type of RFs (dust or pieces), evidence of PCS injury, manifestations of high intrarenal pressure due to pyelovenous and pyelolymphatic and retrorenal backflow seen as perinephric stranding or perinephric fluid extravasation[19] is possible only with visual imaging done within first 24 hours. These manifest clinically as loin pain, fever, and sepsis. All three were significantly and evidently low or negligible in our study. In future, perhaps our limitation of not being able to assess intrarenal is a an important consideration to further improve outcomes when using FANS-UAS.

3) A bone window was used as it is superior to abdomen window for measuring stone size, stone volume, and even RF size as well as for identifying stone dust[14]. In fact, Bhojani et al. observed that in comparison to endoscopic evaluation, an NCCT scan in the abdominal window underreports the number and size of residual stones as it is unable to detect multiple small stones lying close to one another[20]. Hence, we abide that stone volume and bone window are the better assessment tools in any lithotripsy. Indeed, the fact that our regression analysis also shows stone volume to be a significant predictor of lower odds of being stone-free SFR re-iterates predictions of Ito et al[21].

By virtue of having an evidence-based imaging correlation, we are emphatically able to say that indeed as a device designed to improve RIRS, FANS-UAS clearly showed that a high immediate single-stage SFR (96.5%) is achievable with negligible minor and nil significant morbidity in the first 24 hours. The low incidence of loin pain, absence of sepsis, and ability to discharge patients stone-free with imaging evidence elevates surgeons' confidence and patients' trust factor that indeed the procedure is safe and the possibility of re-intervention is less likely.

4.2 The rationale of using FANS-UAS in RIRS

The Trifecta for any surgery in managing urolithiasis patients including RIRS is to obtain complete stone clearance with minimal morbidity and improve the patient's quality of life. Well established as a first-line intervention in guidelines for stones up to 2 cm[12], the challenge in RIRS lies in achieving a complete clearance in a single stage, and if RFs persist, then deciding on what is the best management strategy for the same[22,23].

With a better understanding that apart from patient, stone, and technological factors[24], other physiological parameters contribute to intra-operative morbidity such as intra-renal pressure[25] and temperature[26], suction devices and techniques are advocated as possible game changers in RIRS management of kidney stone disease. Chen et al. showed in a porcine model that with FANS-UAS surgeons can actively regulate the intrarenal pressure that can be reduced to the desired range by adjusting the negative value under any irrigation fluid velocity[10]. By keeping the sheath across the pelvic-ureteral junction and close to the stone, one can achieve a complete stone-free status in RIRS. In a feasibility audit study using two different sheath and scope combinations, it was noted that using a 10 Fr sheath a 97.4% SFR could be achieved in 3 months with zero infectious complications[11]. Similarly, Zhang et al also reported a 24-hour SFR of 86.3% vs. 75.0% (p= 0.038) when using ultrasonography and/or KUB and a 91.2% vs. 81.3% (p=0.037) 30-day SFR using a FANS-UAS vis a vis a traditional UAS confirmed by ultrasonography and/or KUB and/or NCCT examination[9]. In our study, we achieved an overall 96.5% SFR which is multifactorial. Firstly, in terms of technique by applying a controlled suction, the snow globe effect was minimized during dusting which allowed for better stone lithotripsy and simultaneous removal of all dust not allowing it to sediment in calyces. This enables better visualization of larger hidden fragments if generated and when feasible they were successfully aspirated by navigating the sheath to the desired calyx. Laser was mainly needed to chip the remnant stones to make them fit into the sheath. This was feasible irrespective of stone composition and location including the lower pole. This obviated the need for unnecessary popcorning and hence was reportedly not used by any surgeon. Perhaps because of this higher frequency laser lithotripsy would have been avoided which further negated any inadvertent PCS injury or bleeding as is seen by our low intraoperative bleeding and peri-operative complications. In our series, within the first 24 hours, we have very few overall low-grade complications irrespective of the type of scope, laser, lasing technique, and size of the FANS-UAS sheath used. As reported, experienced surgeons were asked to participate but the majority were using FANS-UAS for the first time and yet reported a highly satisfactory operator experience. This indicates that in experienced hands the technique of performing FANS-UAS can be easily learned and safely deployed for stones in any location. We are limited by the fact that they are all solitary stones, and we do not have data of any less experienced surgeon using the same. Yet, our patients will be followed up and any readmissions within 30 days or late complications will be documented subsequently but the early intra and perioperative outcomes are very encouraging. Importantly as has been proposed by other single-centre retrospective studies[9–11], zero sepsis was indeed achievable. This is because suction prevents the intra renal intravasation, negates bacteriemia due to pyelovenous or pyelolymphatic reflux, and reduces the absorption of endotoxic substrates as debris and dust are immediately suctioned[9,19].

A clearer operative view of the PCS, allowing larger irrigation flow with effective aspiration, facilitates the aspiration of stone fragments and dust by selective calyceal targeting of the atraumatic flexible tip of FANS-UAS, especially for the lower renal pole, and deep and dilated calyces permitting surgeons to systematically perform a detailed visual inspection and they aspirate and remove any missed fragment or residue when needed. This contributes to the excellent stone-free results documented within the first 24 hours. Our 24-

hour SFR is higher than the other single series, 86.3% by Zhang et al[9]. Despite the movement of the sheaths inside the PCS, the good hydrophilic coating and soft tip collapsible design of the sheaths do not cause any friction trauma, are safe, and do not precipitate intraoperative bleeding[6]. In summary, a clear field, good irrigation, actively controlled suction, and aspiration are the key essentials to operative success when using the FANS-UAS both for stone-free and infective complications. This is why we had a zero-sepsis rate.

4.3 Study limitations and future directions

As alluded to before, a longer follow-up, higher volume of enrolment, and use in multiple stones will be needed to determine the real operative sequelae of using FANS-UAS in all ages and by surgeons of different levels of experience. We do not at this stage advocate the use of this without adequate training and expertise. Notably, from a technical standpoint and encouraged by a visual assessment of all calyces devoid of any dust and fragments few surgeons were prompted to alter their exit strategy by abstaining from stent placement or placing a temporary ureteric catheter overnight. Perhaps, this is a variable to investigate in depth in future studies, whilst not directly evaluated in our study, this could improve a patient's experience of RIRS, avoid stent-related pain and haematuria, and minimize ancillary procedures like stent removals. Our findings provide us an opportunity to design a patient-reported outcome measures study to better identify the nuances of FANS-UAS treatment outcomes. Yet, experienced surgeons (>250 cases) were asked to participate and this would definitely influence the good early outcomes we see but the majority were using FANS-UAS for the first time and yet reported a highly satisfactory operator experience. It is indeed possible expertise is in itself a very important variable to ensure good intra and immediate post-operative outcomes.

Further, how FANS-UAS is performed needs fluoroscopy assistance albeit the radiation and surgical times are short and within acceptable practices. We need more data to better evaluate radiation exposure and how to better adopt ALARA practices when using FANS, also considering that RIRS can be done safely without fluoroscopy guidance[27,28]. Our preliminary image-guided assessment in 24 hours of using FANS-UAS as an adjunct for RIRS indicates that it is safe and effective. Urologists could use this information to pre-operatively better counsel patients about what to realistically expect in the first 24 hours after RIRS. Yet, we have employed in our study five different FANS-UAS which are probably not equivalent in terms of physical features (i.e. friction, elasticity, and bendability) but we do not have the experimental information on this. Lastly, this study lacks a comparative group either against traditional UAS or non-flexible tip suction UAS but our results can be considered a landmark for planning future comparative studies.

Our study comprehensively supports the conclusion by Schoenthaler et al that technical and technological developments like FANS-UAS when used effectively are much needed to achieve a zero RF following RIRS without compromising safety[29]. Further, this paper challenges many conventional practices of RIRS such as how to place a UAS, the need for high power lasing or popcorning, the timing of SFR assessment, the need for accessories like baskets for repositioning and the role of post-operative stenting, re-assessment of factors that contribute to SFR and infective complications thus opening several avenues for future research.

5. CONCLUSIONS

Our results indicate that in the hands of experienced urologists, even as early as the first 24 hours of surgery, FANS-UAS showed significant promise both to improve SFR and minimize infective complications. Measuring stone volume and bone window in NCCT helps improve intra and immediate post-operative SFR assessment. ~~Indeed, comparing this technology with patients who did not have this used may further enhance key features of this technology but our outcomes provide a platform for many new studies to better improve RIRS outcomes~~.

Indeed, comparing FANS-UAS with traditional UAS may further enhance key features of this new technology. However, our findings provide a platform for future studies to improve RIRS outcomes

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Table 1. Patient baseline characteristics.

	Overall (N=142)
Age	52 [40-61]
Male gender	87 (61.3)
ASA score	
1	80 (56.3)
2	55 (38.8)
3	7 (4.9)
Body Mass Index, kg/m^2	26 [24-29]
Anticoagulants/antiplatelets	15 (10.6)
First-time stone former	101 (71.1)
Presentation	
Hematuria	6 (4.2)
Pain	114 (80.3)
Fever	4 (2.8)
Incidental	18 (12.7)
Urine culture positive	31 (21.8)
Preoperative antibiotics	109 (76.8)
Pre-stented patients	70 (49.3)
Right-sided kidney	59 (41.5)
Stone diameter	
<1cm	24 (16.9)
1-2cm	95 (66.9)
>2cm	23 (16.2)
Hounsfield units	1070 [890-1212]
Stone volume, mm^3	1165 [656-1936]
Stone location	
Upper pole	34 (23.9)
Interpolar/pelvis	59 (41.5)
Lower pole	49 (34.6)

Table note: Data are expressed as median [IQR] for continuous variables and n (%) for categorical variables. **ASA:** American Society of Anesthesiologists

Table 2: Intraoperative characteristics.

	Overall (N=142)
General anesthesia	114 (80.3)
Sheath size, French	
12-14	37 (26.1)
11-13	63 (44.4)
10-12	42 (29.5)
Type of Sheath	
Clearpetra	78 (54.9)
Negative Pressure Ureteral Access Sheath	9 (6.3)
Elephant	40 (28.2)
Others	15 (10.6)
Disposable scope	110 (77.5)
Scope size	
≥8 French	64 (48.1)
<8 French	78 (51.9)
Type of laser	
Holmium:YAG laser	79 (55.6)
Thulium fiber laser	63 (44.4)
Laser time, min	16.50 [10.31-26.82]
Ureteroscopy time, min	35.50 [25.00-59.75]
Total operation time, min	48.50 [36.25-71.75]
Radiation time, min	0.60 [0.34-1.50]
Radiation dose, mSv	7.40 [3.00-12.18]
Lithotripsy mode	
Dusting only	65 (45.8)
Popcorning only	0
Fragmentation only	3 (2.1)
Combination of techniques	74 (52.1)
Stone basketing	22 (15.5)
Need for sheath change	2 (1.4)
Sheath able to access all parts of the kidney	123 (86.6)
Working suction	138 (97.2)
Postoperative exit strategy	
Double J stent	120 (84.5)
Overnight ureteric catheter	13 (9.2)
No stent or ureteric catheter	9 (6.3)
Change of surgeon's routine practice (sheath/not stenting)	18 (12.7)
Likert scale rating for sheath performance	
Ease of suction	2 [1, 3]
Manipulation	2 [2, 3]
Visibility	2 [1, 3]

Table note: Data are expressed as median [IQR] for continuous variables and n (%) for categorical variables.

Table 3: Peri-operative complications and outcomes within the first 24 hours

	Overall (N=142)
Mild pelvic-caliceal system oozing due to sheath manipulation	11 (7.7)
Case abandoned	0
Transfusion	0
Ureteric injury	5 (3.5)
Traxer grade 1	4 (2.8)
Traxer grade 2	1 (0.7)
Pelvic-caliceal system injury	2 (1.4)
Fluid extravasation on NCCT (Clavien grade 1)	3 (2.1)
Perinephric stranding on NCCT (Clavien grade 1)	7 (4.9)
Low grade Fever 37- 37.5 C (Clavien grade 1)	10 (7.0)
Sepsis	0
Persistent haematuria needing intervention	0
Mean VAS score for loin/abdominal pain	2 [1-2]
Length of hospital stay	1 [1-2]
Planned for reintervention by RIRS	4 (2.8)
SFR	
Intraoperative 100% SFR	66 (46.5)
Grade A+B	137 (96.5)
Grade A (100% SFR)	75 (52.8)
Garde B	62 (43.7)
Grades C and D	5 (3.5)

Table note: Data are expressed as median [IQR] for continuous variables and n (%) for categorical variables. **NCCT:** non-contrast computed tomography. **RIRS:** retrograde intrarenal surgery. **SFR:** stone-free rate. **VAS:** visual analogue score

Table 4. Multivariable logistic regression analysis of factors affecting Grade A stone-free status.

	OR	95% CI	p
Stone volume	0.999	0.999-1.000	**0.007**
Hounsfield units	1.001	0.999-1.002	0.296
Sheath size (reference 12-14 Fr)			
11-13 Fr	0.563	0.206-1.497	0.253
10-12 Fr	0.622	0.214-1.770	0.375
Stone location (reference Upper pole)			
Interpolar/pelvis	0.621	0.225-1.661	0.347
Lower pole	0.768	0.262-2.215	0.626
Thulium fiber laser (reference Holmium Laser)	0.776	0.297-1.994	0.599
Reusable scope (vs disposable scope)	1.84	0.620-5.739	0.279
Bone window used	3.156	1.177-9.130	**0.027**

Manuscript Title: Operative outcomes 24 hours after Retrograde Intrarenal Surgery for solitary renal calculi using a Flexible and Navigable Suction Ureteral Access Sheath. A prospective global multicentre study by the European Association of Urology Section on Urolithiasis.

Running Title: 24-hour outcome of RIRS using FANS-UAS

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ABSTRACT

Background: Suction techniques showed potential to improve outcomes of retrograde intra-renal surgery (RIRS). We assessed the 24-hour stone-free rate (SFR) and complications after RIRS using flexible and navigable suction ureteral access sheaths (FANS-UAS).

Methods: Sixteen centers prospectively contributed to data (August 2023-October 2023). Inclusion criteria: age ≥18 years, single renal stone, pre and 24-hour post-RIRS CT scan. Exclusion criteria: ureteral stone, anomalous kidney, multiple stones. SFR: *Grade A*: no fragments; *Grade B*: fragments ≤2 mm; *Grade C*: fragments 2.1-4 mm; *Grade D*: fragments >4 mm. A multivariable logistic regression analysis model was performed to assess factors associated with the odds of having Grade A stone-free status. Data are expressed as median (interquartile range), absolute numbers and frequencies, odds ratio (OR), and 95% confidence interval (CI).

Results: 142 patients with a median age of 52 years (40-61) were enrolled. 61.3% were males. Median stone volume was 1165 mm^3 (656-1936). Median operative time was 48.5 (36.25-71.75) min. Transient fever (37°C-37.5°C) occurred in 10 (7%) patients. No sepsis case occurred. 96.5% of patients were stone-free (Grade A+B). Grade A SFR was 52.8%. All patients were discharged within 48 hours. Bone window (OR 3.156 95% CI 1.177-9.130,p=0.027) was the only factor significantly associated with higher odds of 100% SFR, while stone volume (OR 0.999, 95% CI 0.999-1.000,p=0.007) was significantly associated with lower odds.

Conclusions: Imaging and clinical evidence demonstrate excellent perioperative outcomes just 24 hours post RIRS with FANS-UAS. The technique demonstrates a good safety profile, ability for immediate high SFR, and a low rate of infective complications.

Key words: Kidney Calculi; Flexible Ureteroscopy; Lithotripsy, Laser; Retrograde Intrarenal Surgery; Vacuum assisted surgery.

TEXT

1. INTRODUCTION

Vacuum-assisted techniques are revolutionizing the endourological management of urolithiasis by flexible ureteroscopy[1] and percutaneous nephrolithotripsy[2,3]. The main aim of a successful retrograde intra-renal surgery (RIRS) as a minimally invasive approach is to render the patient stone-free with the least morbidity[4]. However, as has been reported by the FLEXOR study, despite best efforts in real-world practice, residual fragments (RFs) remain in 21.7% of patients and 51.5% of these patients have a second intervention[5].

To improve RIRS outcomes apart from more powerful lasers, dust, and fragment removal devices like the flexible and navigable suction ureteral access sheath (FANS-UAS)[6], direct in scope suction technique[7], and steerable post lithotripsy aspiration catheters[8] are some of the novel proposals. Of these, in a retrospective single-center study, FANS-UAS has shown a higher SFR when compared to a standard ureteral access sheath (UAS) with lower incidences of infectious and overall complications[9]. A few studies are reporting the outcomes of RIRS using FANS-UAS[9–11]. However, most of these are single-center and retrospective studies with a low number of cases and there is concern that sheath placement across the ureteropelvic junction and its movement within the collecting system may cause more injuries whilst attempting aspiration.

In this prospective study, we aimed to assess by using imaging and clinical outcomes within 24 hours of the procedure if FANS-UAS is safe, feasible, and helps to improve stone-free rate (SFR) in a multicenter real-world practice. The secondary outcome was to assess the utility of the sheath as an effective device for improving visibility, and the ability to navigate the sheath in different parts of the pelvic caliceal system (PCS), especially the lower pole, and document any specific or unique challenges encountered.

2. MATERIAL AND METHODS

2.1 Study design

This study was conducted under the auspices of the European Association of Urology Section of urolithiasis (EULIS). Twenty surgeons from 16 centers from 15 countries prospectively contributed to the data as per protocol designed by the primary site, the Asian Institute of Nephrology and Urology after obtaining institutional review board approval (#AINU 12/2022) and has been conducted in accordance with the principles set forth in the

Helsinki Declaration. Each participating center also obtained its own ethics board approval. Patients have given their informed consent for participation in the research study.

All contributing surgeons had prior experience of performing at least 250 RIRS cases, however, only 3 of the 20 surgeons had any prior experience of using a FANS-UAS. Hence a training video was provided[6], and all surgeons were asked to use the sheath in at least one trial case before starting the study. Study period was between 1st August 2023 and 31st December 2023. We report here an interim analysis assessing the 24-hour outcomes of the 142 patients enrolled until October 20th. Inclusion criteria were symptomatic and asymptomatic patients aged ≥18 years, single renal stone of any size and location in the pelvicalyceal system deemed suitable for RIRS under fluoroscopy guidance by the treating surgeon and pre and post-RIRS non-contrast computed tomography (NCCT) scan. Exclusion criteria were children, multiple stones, isolated or concomitant ureteral stone, endoscopic combined intra-renal surgery, same-sitting bilateral procedure, staged surgery for residual fragments, previous ureteric injury or known ureteric anomalies or past ureteric reconstruction, patients who had incidental on table renal or ureteric pathology and concomitant intervention for same, and patients mentally unable to provide a written informed consent or unfit for general or spinal anaesthesia.

2.2 FANS-UAS and Surgical Procedure

NCCT scan with 2.5 mm slice thickness was performed in each case before RIRS to calculate the stone volume as per EAU urolithiasis guidelines[12]. Any positive urine culture was treated preoperatively as per the center's own antibiogram/protocol. Any antiplatelet or anticoagulation was stopped for 5 days before surgery and 5 days after surgery if deemed feasible and to be documented likewise. Baseline and operative characteristics were collected.

The following FANS-UAS were employed according to local practice provided by any company depending on the region of practice: Clearpetra (Welllead Medical, Panyu, Guangzhou, China), Negative Pressure Ureteral Access Sheath (Innovex Medical, Shanghai, China), Elephant second generation (Zhejiang YiGao Medical Technology, Hangzhou, China), Suction UAS (SEPLOU, Beijing, China), Disposable Ureteral Guide Sheath (ZSR Biomedical Technology, Dongguan, Guangdong China China). Size and type of scope and laser were as per surgeons’ own choice and available resources. Irrigation was performed using gravity assisted with either intermittent manual syringe irrigation or the

TRAXERFLOW Dual Port Gravity Line (Rocamed, Southborough, Massachusetts) as per availability of each center. Pressure bags were not used in any of the cases.

All surgeons were asked to follow the steps for the procedure as per the step-by-step video published[6]. One-dose antibiotic prophylaxis was given in all cases at induction according to local protocols.

RIRS was to be performed under any anesthesia and fluoroscopy guidance. This included positioning the patient in the lithotomy position, followed by a retrograde pyelogram and diagnostic semi-rigid ureteroscopy to ascertain that there were no ureteric abnormalities and delineating the pelvicalyceal system before placement of the FANS-UAS.

Lithotripsy was performed using either Thulium fiber laser (Fibre dust, Quanta System, Varese, Italy or Soltive, Olympus, Hamburg, Germany or Urolase SP 60W, IPG Photonics, Oxford, MA) or Holmium laser (Lumenis Pulse™ 100H, Boston Scientific, Marlborough, MA or Medilas H Solvo, Dornier, Weßling, Germany or Cyber Ho 60 Quanta System, Varese, Italy).

The operative parameters were defined as follows: i) Operative time: Time from start of Cystoscopy to exit (stent or ureteric catheter or nil drainage); ii) Ureteroscopy time: Time from placement of UAS to removal of UAS for exit; iii) Lasing time: actual time recorded during laser lithotripsy as per that indicated on the machine; iv) Radiation time: Total time from the start of retrograde pyelogram to exit (as seen on radiation monitor screen).

On table decision to use accessories like baskets for stone extraction, the need to abandon the procedure, change to another UAS, or any malfunction was recorded. The choice of energy source for RIRS and perioperative decisions such as pre-stenting and postoperative exit strategy and stent dwelling time ~~was~~ were at the respective surgeon's own discretion. Intraoperative visual inspection of all calyces and stone-free assessment by the surgeon were recorded to correlate how these measures fare vis a vis post-operative imaging assessment. Surgeons were also asked to grade their experience of using the FANS-UAS at the end of each case using a 5-point LIKERT-type scale (1 excellent; 2: very good; 3: good 4: average; 5: difficult)[13]. As an objective evaluation, surgeons were asked to document if RIRS with FANS-UAS had contributed to a change or deviation in their exit strategy concerning stent placement after each case.

Patients were assessed postoperatively according to the study protocol using an NCCT scan with 2.5 mm slice thickness 24 hours after the surgery and RFs categorized into one of the following categories using the bone window[14]: i) *Grade A*: there were no visible fragments (100% SFR); ii) *Grade B*: fragments up to 2 mm; iii) *Grade C*: fragments 2.1-4 mm; iv) *Grade D*: fragments >4 mm. For our study purposes patients with Grade A and B were considered “stone-free” and would not need any further imaging or re-intervention unless mandated by the surgeon for other reasons. Only Grades C and D would require follow-up with imaging between 4 weeks and 3 months to plan subsequent intervention if needed. Other 24-hour outcomes included immediate peri and postoperative complications, such as bleeding, need for transfusion, ureteric or PCS injury, infective complications, persistent haematuria prolonging hospital stay, and loin pain. Loin pain was scored using the standard 10-point visual analogue scale (VAS)[15]. All patients with RF(s) were counseled for either observation or re-intervention based on surgeons’ assessment and if planned for a late (>6 weeks within 3 months) surgical intervention. A repeat NCCT scan would be done to confirm the need for re-intervention. Outcomes for these would be followed up subsequently.

2.3 Statistical analysis

Continuous variables are expressed as medians and interquartile ranges while categorical variables are reported as absolute numbers and percentages. Variables were selected a priori and entered into a multivariable logistic regression model to assess their significance as independent of 100% SFR. Data are expressed as odds ratio (OR) and 95% confidence interval (CI) with a double-sided p-value <0.05 indicating statistical significance. All statistical tests were performed using R Statistical language, version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

2.4 Data availability

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

3. RESULTS

During the study period, 142 patients with loin pain as the most common reason for intervention were enrolled with a median age of 52 years (40-61) (Table 1). There were 87 (61.3%) males. 71.1% were first-time stone formers. Median stone volume was 1165 (656-1936) mm^3. Median stone size was 1-2 cm in 66.9% of the cases with interpolar/renal pelvis as the most common location in 41.5% of cases followed by the lower pole as the next most common location in 34.6% of cases. Median Hounsfield unit was 1070 (890-1212). 49.3% of patients were pre-stented. 76.8% of patients received prophylactic antibiotics but only 21.8% of cases had a positive urine culture.

Preferentially, 11/13 Fr sheath in 44.4% of patients and a disposable scope in 77.5% was used under general anesthesia in 80.3% of cases (Table 2). Thulium fiber laser was used in 44.4% of cases, whereas Holmium laser was employed in the other ones. A basket was used in 15.5% of cases only to reposition stone fragments and nil was used for stone extraction. Pure dusting technique for lithotripsy was deployed in 45.8% but 52.1% of surgeons reported using a combination of dusting and fragmentation and none used popcorning. Median lasing, ureteroscopy, and overall operative times were 16.5 (10.31-26.82) min, 35.5 (25.00-59.75), and 48.5 (36.25-71.75) min, respectively. In 86.6% of the cases, the sheath was successfully navigated into all parts of the kidney and suction could be deployed successfully without any issues in 97.2 % of cases. In only 2 cases the FANS-UAS needed to be downsized from 12-14 Fr to a 10-12 Fr sheath. As part of the exit strategy, in 84.5% of cases a double J stent and in 9.2% and 6.3% of patients an overnight ureteric catheter was placed, or no drainage was deployed, respectively. For the latter 2, a change from their routine exit strategy was reported by the surgeon in 12.7% of cases. No case was abandoned intra-operatively due to non-technical reasons and no patient was lost at follow-up so far. For 46.5% of cases, surgeons reported intraoperative visual complete clearance which correlated when confirmed by the 24-hour NCCT. Perioperative complications and outcomes within the first 24 hours are reported in Table 3. Intra-operatively by virtue of sheath manipulation mild PCS oozing was reported in 11 cases (7.7%) and transient fever (37°C -37.5°C, Clavien grade 1) was reported overnight in 10 (7%) patients. There were no cases of sepsis. All 5 patients with ureteric access sheath injury Traxer grade 1 (n=4), grade 2 (n=1) needed only a double J stent placement[16]. As the NCCT was done 24 hours after surgery, we were able to document the presence of some perinephric stranding and perinephric fluid in 4.9% and 2.1% cases respectively. Median VAS score for loin pain was 2 (1-2). Median LIKERT score was 2 (1-3) points for ease of using suction with the navigation sheath, manipulating the sheath and scope together, and improving visibility during the procedure by minimizing the snow globe effect.

Overall, 96.5% of cases were stone-free (Grade A+B). 100% SFR (Grade A) was seen in 52.8% of cases. Grade B SFR was 43.7%. Grades C and D SFR was 3.5% and these patients were planned for re-intervention by RIRS (Table 3). All 142 cases were discharged within 48 hours and may be followed up to 3 months post-operatively and intervention outcomes will be documented in those planned for re-intervention. The surgeons reported an estimated 100% SFR in 66 cases (46.5%) by visual examination of all calyces which had a 100% correlation with post-operative 24-hour NCCT imaging. At multivariable analysis (Table 4), using bone window (OR 3.156 95% CI 1.177-9.130, p=0.027) was the only factor significantly associated with higher odds of 100% SFR, while stone volume (OR 0.999, 95% CI 0.999-1.000, p=0.007) was significantly associated with lower odds.

4. DISCUSSION

4.1 The rationale and information gained using a 24-hour NCCT scan and bone window

Since it is not a routine practice, we decided to use a 24-hour NCCT with the bone window to discuss the rationale and objectives, as well as its impact on primary outcome assessment compared to the traditional method of reporting SFR at one month. We chose this approach for the following reasons:

1) A CT scan is the only true road map to determine the presence of RF, allows for accurate calculation of the size of RF, and must be advocated especially if a surgical re-intervention is planned as part of follow-up[17].
2) There is no definite consensus on the timing of the CT scan and guidelines advocate imaging anytime within 3 months of RIRS intervention[12,18]. Whilst this is acceptable, the only proof of correlating intraoperative findings like complete stone clearance, missed injury to the ureter and PCS along with post-operative outcomes such as the presence of the type of RFs (dust or pieces), evidence of PCS injury, manifestations of high intrarenal pressure due to pyelovenous and pyelolymphatic and retrorenal backflow seen as perinephric stranding or perinephric fluid extravasation[19] is possible only with visual imaging done within first 24 hours. These manifest clinically as loin pain, fever, and sepsis. All three were significantly and evidently low or negligible in our study. In future, perhaps our limitation of not being able to assess intrarenal is a an important consideration to further improve outcomes when using FANS-UAS.
3) A bone window was used as it is superior to abdomen window for measuring stone size, stone volume, and even RF size as well as for identifying stone dust[14]. In fact, Bhojani et al. observed that in comparison to endoscopic evaluation, an NCCT scan in the abdominal window underreports the number and size of residual stones as it is unable to detect multiple small stones lying close to one another[20]. Hence, we abide that

stone volume and bone window are the better assessment tools in any lithotripsy. Indeed, the fact that our regression analysis also shows stone volume to be a significant predictor of lower odds of being stone-free SFR re-iterates predictions of Ito et al[21].

By virtue of having an evidence-based imaging correlation, we are emphatically able to say that indeed as a device designed to improve RIRS, FANS-UAS clearly showed that a high immediate single-stage SFR (96.5%) is achievable with negligible minor and nil significant morbidity in the first 24 hours. The low incidence of loin pain, absence of sepsis, and ability to discharge patients stone-free with imaging evidence elevates surgeons' confidence and patients' trust factor that indeed the procedure is safe and the possibility of re-intervention is less likely.

4.2 The rationale of using FANS-UAS in RIRS

The Trifecta for any surgery in managing urolithiasis patients including RIRS is to obtain complete stone clearance with minimal morbidity and improve the patient's quality of life. Well established as a first-line intervention in guidelines for stones up to 2 cm[12], the challenge in RIRS lies in achieving a complete clearance in a single stage, and if RFs persist, then deciding on what is the best management strategy for the same[22,23].

With a better understanding that apart from patient, stone, and technological factors[24], other physiological parameters contribute to intra-operative morbidity such as intra-renal pressure[25] and temperature[26], suction devices and techniques are advocated as possible game changers in RIRS management of kidney stone disease. Chen et al. showed in a porcine model that with FANS-UAS surgeons can actively regulate the intrarenal pressure that can be reduced to the desired range by adjusting the negative value under any irrigation fluid velocity[10]. By keeping the sheath across the pelvic-ureteral junction and close to the stone, one can achieve a complete stone-free status in RIRS. In a feasibility audit study using two different sheath and scope combinations, it was noted that using a 10 Fr sheath a 97.4% SFR could be achieved in 3 months with zero infectious complications[11]. Similarly, Zhang et al also reported a 24-hour SFR of 86.3% vs. 75.0% (p= 0.038) when using ultrasonography and/or KUB and a 91.2% vs. 81.3% (p=0.037) 30-day SFR using a FANS-UAS vis a vis a traditional UAS confirmed by ultrasonography and/or KUB and/or NCCT examination[9]. In our study, we achieved an overall 96.5% SFR which is multifactorial. Firstly, in terms of technique by applying a controlled suction, the snow globe effect was minimized during dusting which allowed for better stone lithotripsy and simultaneous removal of all dust not allowing it to sediment in calyces. This enables better visualization of larger hidden fragments if generated and when feasible they were successfully aspirated by navigating the sheath to the desired calyx. Laser was mainly needed to chip the remnant stones to make them fit into the sheath. This was feasible irrespective of stone composition and location including the lower pole. This obviated the need for unnecessary popcorning and hence was reportedly not used by any surgeon. Perhaps because of this higher frequency laser lithotripsy would have been avoided which further negated any inadvertent PCS injury or bleeding as is seen by our low intraoperative bleeding and peri-operative complications. In our series, within the first 24 hours, we have very few overall low-grade complications irrespective of the type of scope, laser, lasing technique, and size of the FANS-UAS sheath used. As reported, experienced surgeons were asked to participate but the majority were using FANS-UAS for the first time and yet reported a highly satisfactory operator experience. This indicates that in experienced hands the technique of performing FANS-UAS can be easily learned and safely deployed for stones in any location. We are limited by the fact that they are all solitary stones, and we do not have data of any less experienced surgeon using the same. Yet, our patients will be followed up and any readmissions within 30 days or late complications will be documented subsequently but the early intra and perioperative outcomes are very encouraging. Importantly as has been proposed by other single-centre retrospective studies[9–11], zero sepsis was indeed achievable. This is because suction prevents the intra renal intravasation, negates bacteriemia due to pyelovenous or pyelolymphatic reflux, and reduces the absorption of endotoxic substrates as debris and dust are immediately suctioned[9,19].

A clearer operative view of the PCS, allowing larger irrigation flow with effective aspiration, facilitates the aspiration of stone fragments and dust by selective calyceal targeting of the atraumatic flexible tip of FANS-UAS, especially for the lower renal pole, and deep and dilated calyces permitting surgeons to systematically perform a detailed visual inspection and they aspirate and remove any missed fragment or residue when needed. This contributes to the excellent stone-free results documented within the first 24 hours. Our 24-hour SFR is higher than the other single series, 86.3% by Zhang et al[9]. Despite the movement of the sheaths inside the PCS, the good hydrophilic coating and soft tip collapsible design of the sheaths do not cause any friction trauma, are safe, and do not precipitate intraoperative bleeding[6]. In summary, a clear field, good irrigation, actively controlled suction, and aspiration are the key essentials to operative success when using the FANS-UAS both for stone-free and infective complications. This is why we had a zero-sepsis rate.

4.3 Study limitations and future directions

As alluded to before, a longer follow-up, higher volume of enrolment, and use in multiple stones will be needed to determine the real operative sequelae of using FANS-UAS in all ages and by surgeons of different levels of experience. We do not at this stage advocate the use of this without adequate training and expertise. Notably, from a technical standpoint and encouraged by a visual assessment of all calyces devoid of any dust and fragments few surgeons were prompted to alter their exit strategy by abstaining from stent placement or placing a temporary ureteric catheter overnight. Perhaps, this is a variable to investigate in depth in future studies, whilst not directly evaluated in our study, this could improve a patient's experience of RIRS, avoid stent-related pain and haematuria, and minimize ancillary procedures like stent removals. Our findings provide us an opportunity to design a patient-reported outcome measures study to better identify the nuances of FANS-UAS treatment outcomes. Yet, experienced surgeons (>250 cases) were asked to participate and this would definitely influence the good early outcomes we see but the majority were using FANS-UAS for the first time and yet reported a highly satisfactory operator experience. It is indeed possible expertise is in itself a very important variable to ensure good intra and immediate post-operative outcomes.

Further, how FANS-UAS is performed needs fluoroscopy assistance albeit the radiation and surgical times are short and within acceptable practices. We need more data to better evaluate radiation exposure and how to better adopt ALARA practices when using FANS, also considering that RIRS can be done safely without fluoroscopy guidance[27,28]. Our preliminary image-guided assessment in 24 hours of using FANS-UAS as an adjunct for RIRS indicates that it is safe and effective. Urologists could use this information to pre-operatively better counsel patients about what to realistically expect in the first 24 hours after RIRS. Yet, we have employed in our study five different FANS-UAS which are probably not equivalent in terms of physical features (i.e. friction, elasticity, and bendability) but we do not have the experimental information on this. Lastly, this study lacks a comparative group either against traditional UAS or non-flexible tip suction UAS but our results can be considered a landmark for planning future comparative studies.

Our study comprehensively supports the conclusion by Schoenthaler et al that technical and technological developments like FANS-UAS when used effectively are much needed to achieve a zero RF following RIRS without compromising safety[29]. Further, this paper challenges many conventional practices of RIRS such as how to place a UAS, the need for high power lasing or popcorning, the timing of SFR assessment, the need for accessories like baskets for repositioning and the role of post-operative stenting, re-assessment of factors that contribute to SFR and infective complications thus opening several avenues for future research.

5. CONCLUSIONS

Our results indicate that in the hands of experienced urologists, even as early as the first 24 hours of surgery, FANS-UAS showed significant promise both to improve SFR and minimize infective complications. Measuring stone volume and bone window in NCCT helps improve intra and immediate post-operative SFR assessment.

Indeed, comparing FANS-UAS with traditional UAS may further enhance key features of this new technology. However, our findings provide a platform for future studies to improve RIRS outcomes

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Table 1. Patient baseline characteristics.

	Overall (N=142)
Age	52 [40-61]
Male gender	87 (61.3)

ASA score 1 2 3	 80 (56.3) 55 (38.8) 7 (4.9)
Body Mass Index, kg/m^2	26 [24-29]
Anticoagulants/antiplatelets	15 (10.6)
First-time stone former	101 (71.1)
Presentation Hematuria Pain Fever Incidental	 6 (4.2) 114 (80.3) 4 (2.8) 18 (12.7)
Urine culture positive	31 (21.8)
Preoperative antibiotics	109 (76.8)
Pre-stented patients	70 (49.3)
Right-sided kidney	59 (41.5)
Stone diameter <1cm 1-2cm >2cm	 24 (16.9) 95 (66.9) 23 (16.2)
Hounsfield units	1070 [890-1212]
Stone volume, mm^3	1165 [656-1936]
Stone location Upper pole Interpolar/pelvis Lower pole	 34 (23.9) 59 (41.5) 49 (34.6)

Table note: Data are expressed as median [IQR] for continuous variables and n (%) for categorical variables. **ASA:** American Society of Anesthesiologists

Table 2: Intraoperative characteristics.

	Overall (N=142)
General anesthesia	114 (80.3)
Sheath size, French 12-14 11-13 10-12	 37 (26.1) 63 (44.4) 42 (29.5)

Type of Sheath	
Clearpetra	78 (54.9)
Negative Pressure Ureteral Access Sheath	9 (6.3)
Elephant	40 (28.2)
Others	15 (10.6)
Disposable scope	110 (77.5)
Scope size	
≥8 French	64 (48.1)
<8 French	78 (51.9)
Type of laser	
Holmium:YAG laser	79 (55.6)
Thulium fiber laser	63 (44.4)
Laser time, min	16.50 [10.31-26.82]
Ureteroscopy time, min	35.50 [25.00-59.75]
Total operation time, min	48.50 [36.25-71.75]
Radiation time, min	0.60 [0.34-1.50]
Radiation dose, mSv	7.40 [3.00-12.18]
Lithotripsy mode	
Dusting only	65 (45.8)
Popcorning only	0
Fragmentation only	3 (2.1)
Combination of techniques	74 (52.1)
Stone basketing	22 (15.5)
Need for sheath change	2 (1.4)
Sheath able to access all parts of the kidney	123 (86.6)
Working suction	138 (97.2)
Postoperative exit strategy	
Double J stent	120 (84.5)
Overnight ureteric catheter	13 (9.2)
No stent or ureteric catheter	9 (6.3)
Change of surgeon's routine practice (sheath/not stenting)	18 (12.7)
Likert scale rating for sheath performance	
Ease of suction	2 [1, 3]
Manipulation	2 [2, 3]
Visibility	2 [1, 3]

Table note: Data are expressed as median [IQR] for continuous variables and n (%) for categorical variables.

Table 3: Peri-operative complications and outcomes within the first 24 hours

	Overall (N=142)
Mild pelvic-caliceal system oozing due to sheath manipulation	11 (7.7)
Case abandoned	0

Transfusion	0
Ureteric injury Traxer grade 1 Traxer grade 2	5 (3.5) 4 (2.8) 1 (0.7)
Pelvic-caliceal system injury	2 (1.4)
Fluid extravasation on NCCT (Clavien grade 1)	3 (2.1)
Perinephric stranding on NCCT (Clavien grade 1)	7 (4.9)
Low grade Fever 37- 37.5 C (Clavien grade 1)	10 (7.0)
Sepsis	0
Persistent haematuria needing intervention	0
Mean VAS score for loin/abdominal pain	2 [1-2]
Length of hospital stay	1 [1-2]
Planned for reintervention by RIRS	4 (2.8)
SFR Intraoperative 100% SFR Grade A+B Grade A (100% SFR) Garde B Grades C and D	 66 (46.5) 137 (96.5) 75 (52.8) 62 (43.7) 5 (3.5)

Table note: Data are expressed as median [IQR] for continuous variables and n (%) for categorical variables. **NCCT:** non-contrast computed tomography. **RIRS:** retrograde intrarenal surgery. **SFR:** stone-free rate. **VAS:** visual analogue score

Table 4. Multivariable logistic regression analysis of factors affecting Grade A stone-free status.

	OR	95% CI	p
Stone volume	0.999	0.999-1.000	**0.007**
Hounsfield units	1.001	0.999-1.002	0.296

Sheath size (reference 12-14 Fr)			
11-13 Fr	0.563	0.206-1.497	0.253
10-12 Fr	0.622	0.214-1.770	0.375
Stone location (reference Upper pole)			
Interpolar/pelvis	0.621	0.225-1.661	0.347
Lower pole	0.768	0.262-2.215	0.626
Thulium fiber laser (reference Holmium Laser)	0.776	0.297-1.994	0.599
Reusable scope (vs disposable scope)	1.84	0.620-5.739	0.279
Bone window used	3.156	1.177-9.130	**0.027**