Controversies associated with ureteral access sheath placement during ureteroscopy

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The use of ureteral access sheaths (UAS) is common practice during routine flexible ureteroscopy procedures. However, debates and concerns continue amongst endourologists on routine UAS placement. UAS placement allows for multiple passages of the ureteroscope, decreases intrarenal pressure, and may improve stone-free rates. However, concerns for the UAS’s effectiveness in these claimed benefits and complications related to UAS placement has been documented and investigated by many. In this review, we will discuss the controversies surrounding the placement of UAS during ureteroscopy.

Keywords: Kidney calculi; Nephrolithiasis; Ureteroscopy; Urolithiasis

INTRODUCTION

In the past decades of urologic surgery, technological development in flexible ureteroscopy has greatly expanded in its role for the treatment of kidney stone disease. With this rapid development, supporting instruments were created to ease and facilitate this treatment modality, including the introduction of the ureteral access sheath (UAS) in 1974 as a means of passing a flexible ureteroscope into the ureter [1]. Although UAS placement performance was poor during its initial introduction (19% of 43 cases resulted in ureter perforation) [2], UAS placement during ureteroscopy has now become an often standard practice amongst endourologists since the introduction of modern UASs that are hydrophilically coated with hub-locking mechanisms [3]. With such modifications, the safety and wide use of UAS was established, and is now commonly seen in every endourologist’s armamentarium.

The use of a UAS during ureteroscopy allows for the access and investigation of the urinary collecting system in rapid repeated succession, lower intrarenal pressures, improved visibility as well as improved drainage around the ureteroscope. Despite these benefits of UAS placement, current guidelines of the European Association of Urology have no clear recommendations for UAS usage during typical ureteroscopy procedures, whereas the American Urological Association guidelines recommend the use of a UAS when performing retrograde intrarenal surgery for complex, high-volume renal stones [4,5]. In a survey of 216 endourologists worldwide, respondents routinely use UAS for the treatment of ureteral stones and kidney stones 46% and 76% of the time, respectively [6]. Despite widespread adoption of the UAS, concerns and controversies remain surrounding the use of UAS. This review will identify the controversies surrounding UAS use, and address concerns that endourologists may have regarding UAS placement during ureteroscopy.
Table 1 summarizes the articles relating to controversies associated with UAS placement in this review.

Due to this manuscript being a review in nature, ethics application was not required as per the University of British Columbia Clinical Research Ethics Board (CREB) guidelines.

DOES UAS PLACEMENT ALWAYS IMPROVE STONE-FREE RATES?

One of the principle goals in any form of urologic treatment of kidney stones is the stone-free rate (SFR). As UAS use allows the urologist to enter and exit the urinary collecting system in rapid succession, there have been studies that looked into whether UAS placement facilitates greater SFRs during ureteroscopy. Reported results have been mixed, as some authors have reported increased SFRs associated with UAS use [7], while others did not find any significant difference whether UAS was used or not [8].

In a multi-institutional prospective study conducted by Traxer et al. [9], patients who underwent ureteroscopy with and without UAS placement were followed for a period of one year. Out of the 2,239 patients included in the study, 1,494 (67%) patients were treated with the use of a UAS and 745 (33%) without. Laser fragmentation was the most common method for stone comminution. It was found that SFRs were significantly higher SFRs in all portions of the kidney in a cohort of 256 ureteroscopy procedures (173 UAS vs. 83 no UAS). In contrast, L’esperance et al. [7] concluded in their retrospective study that UAS placement leads to significantly higher SFRs in all portions of the kidney in a cohort of 256 ureteroscopy procedures (173 UAS vs. 83 no UAS). However, subgroup analysis on stones per location in the renal pelvis and calices showed no significance. Various limitations in this study should be considered: non-UAS cases were performed at an earlier time period compared to UAS cases. As such, developments in more modern ureteroscopes (inferior deflection may have affected stone clearance in lower pole of the kidney) and surgeon experience may have affected results. Moreover, all procedures were performed by a single urologist and may have reflected their ureteroscopy learning curve. Lastly, SFRs in this study should be interpreted cautiously due to the lack of computed tomography (CT) performed to assess SFRs, as well as a greater number of patients within the UAS arm. Despite these results, the authors mention that it is currently their practice to use a UAS routinely during ureteroscopy [7].

An important patient factor in case-planning is the body mass index of patients. Obese patients undergoing ureteroscopy can pose as a challenge due to difficulties in patient positioning, and can potentially restrict the endourologist’s dexterity within the urinary collecting system. Hypothetically, the placement of a UAS during ureteroscopy can circumvent issues of visibility related to body habitus. However, Chew et al. [11] concluded that ureteroscopy for obese patients are equally efficacious when compared to non-obese patients, and their data showed that UAS placement in obese patients did not affect SFRs. Their study results are consistent in the notion that external obesity does not necessarily correlate with an aberrant internal anatomy; factors such as increased retroperitoneal fat in obese patients do not influence the ability of the urologist in gaining access with a flexible ureteroscopy, with or without an UAS. In essence, obesity does not affect the internal diameter of a patient’s ureter.

Ultimately, the indication of UAS placement for the improvement of SFRs remains controversial and should not be solely used for this reason but rather may improve surgical efficacy. In a study by Miernik et al. [12] calling for the standardization of ureteroscopy procedures to improve SFRs, the ureteroscopy procedural model advocated by the authors includes the use of an UAS for patients presenting with multiple renal calculi or calculi >5 mm. These studies on UAS placement and SFRs suggest that the decision on UAS placement should be made on a case-dependent basis by the urologist, and not solely to improve SFRs.

COMPLICATIONS ASSOCIATED WITH UAS PLACEMENT

As the role of retrograde intrarenal surgery for treatment of stone disease expands, the use of UAS has become more widespread but the complications associated with UAS have come into the foreground. It is important to understand the potential complications in order to recognize and prevent their occurrence. These complications can range from intraoperative, immediately post-operative, and into the long term.

Intraoperative complications associated with the use of UAS include bleeding, perforation and avulsion. The trend has been to underreport the damage caused by UAS inser-
Table 1. Summary of articles relating to controversies associated with UAS placement

| Reference                   | Number of subjects | UAS-related topic       | Results                                                                                                                                                                                                 |
|-----------------------------|--------------------|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| L’esperance et al. [7] (2005) | 256                | SFR                     | UAS placement leads to significantly higher SFRs in all portions of the kidney in a cohort of 256 ureteroscopy procedures (173 UAS vs. 83 no UAS).                                                        |
| Kourambas et al. [8] (2001)  | 59                 | SFR                     | No significant difference in SFRs with and without UAS placement (79% UAS vs. 86% no UAS).                                                                                                                   |
| Traxer et al. [9] (2015)     | 2,239              | SFR                     | Multi-institutional study with 1,494 (67%) patients treated with the use of a UAS and 745 (33%) without. SFRs were overall lower with the use of a UAS (73.9 vs. 82.8%).                                      |
| Berquet et al. [10] (2014)   | 280                | SFR                     | SFRs at one and three months were comparable between UAS vs. No UAS. Stone size was the only predictive factor for SFR.                                                                                     |
| Chew et al. [11] (2013)      | 292                | SFR                     | No difference in SFRs found for obese patients undergoing ureteroscopy with and without an UAS.                                                                                                           |
| Traxer and Thomas [13] (2013)| 359                | Complications           | Superficial mucosal ureteral wall lesions in nearly half of the patients following the insertion of a 12/14 Fr UAS. No complete avulsions. Pre-operative stenting decreased the risk of severe injury associated with UAS placement by seven-fold. |
| Delvecchio et al. [14] (2003)| 130                | Complications           | Incidence rate for stricture formation with UAS placement during ureteroscopy was 0.8% (1/130).                                                                                                          |
| Lildal et al. [17] (2017)    | 22 (porcine)       | Complications           | UAS placement significantly increased the expression of pro-inflammatory markers TNF-a and COX-2 in the in-vivo porcine model.                                                                        |
| Oguz et al. [22] (2019)      | 250                | Complications           | Duration of UAS placement was the only intraoperative factor significantly affecting immediate post-operative pain.                                                                                     |
| Lallas et al. [23] (2002)    | 2 (porcine)        | Complications           | Ureteral blood flow measured during 12, 14, 16 Fr UAS placement. Transient decrease in ureteral blood flow detected.                                                                                     |
| Rehman et al. [25] (2003)    | 7 (cadaveric kidneys)| Pressure reduction      | Progressive reductions in intrarenal pressure associated with increasing the diameter of UAS.                                                                                                             |
| Noureldin et al. [31] (2019)| 3 (porcine)        | Pressure reduction       | Only the largest diameter UAS (14/16 Fr) may sufficiently decrease intrarenal pressure to safe physiological levels.                                                                                     |
| Kaler et al. [34] (2019)     | 6 (porcine)        | UAS size                | Significant ureteral injury can routinely be avoided if the applied force is <4.84 N; PULS ≥3 routinely occurred when forces exceeded 8.1 N.                                                           |
| Tefik et al. [35] (2018)     | 7                  | UAS size                | Highest insertion force was found associated with 12/14 Fr UAS (5.9 N) UAS placement without prior stenting may cause low-grade ureteral trauma for sizes.                                              |
| Kawahara et al. [39] (2013)  | 93                 | Stenting and UAS        | UAS placement can result in prolonged hydronephrosis, higher pain scores, stent migration, encrustation and discomfort.                                                                                 |
| Rapoport et al. [40] (2007)  | 161                | Stenting and UAS        | Non-stenting reduces operative costs by CAD$140 per patient in ureteroscopy cases with UAS, but costs increase dramatically for unstented patients if they need to return to the ER due to readmission. |
| Astroza et al. [41] (2017)   | 70                 | Stenting and UAS        | Postoperative stenting is not always necessary after UAS placement if the patient was pre-stented. No significant differences in postoperative events, ER visits or need of hospital readmission. |
| Zilberman et al. [6] (2019)  | 216                | Stenting and UAS        | Amongst members of the Endourologic Society, 90% of 216 international endourologists believed that a double-J stent insertion is not mandatory prior to UAS insertion.                                           |
| Mogilevkin et al. [42] (2014)| 248                | Stenting and UAS        | Pre-operative Double-J stenting is a predictive factor for more successful UAS insertions.                                                                                                           |
| Breda et al. [43] (2016)     | 134                | Stenting and UAS        | 99% of the pre-stented patients had a successful UAS placements vs. 82% of non-pre-stented. Pre-stenting status was the only independent factor for a successful access sheath insertion. |
| Lildal et al. [33] (2016)    | 22 (porcine)       | Pharmacologic Management and UAS | β-agonist isoproterenol-infused irrigation resulted in significantly higher successful UAS insertions when compared the saline group (63 vs. 27%). No serious lesions (<PULS grade 2) were observed in the experimental group. |
| Koo et al. [44] (2018)       | 135                | Pharmacologic Management and UAS | Non-stented patients who received tamsulosin for seven days (0.4 mg PO) pre-operatively had a significant reduction in UAS insertion forces and were comparable to that of pre-stented patients who did not receive tamsulosin. |

UAS, ureteral access sheath; SFR, stone-free rate; PULS, Post-Ureteroscopic Lesion Scale; ER, emergency room; PO, per os.
tion over the years due to lack of a reliable classification system. This issue was addressed in 2013 by Traxer and Thomas [13] in a prospective study where they endoscopically evaluated 359 patients following the removal of a UAS. They found superficial mucosal ureteral wall lesions in nearly half of the patients following the insertion of a 12/14 Fr UAS with 15% extending beyond the mucosa into the smooth muscle layer [13]. Luckily, no complete avulsions were found.

Ureteral stricture post intrarenal surgery with the use of UAS is a concern which Delvecchio et al. (2003) [14] addressed in a series of 130 patients who underwent ureteroscopy for treatment of stones. On follow-up imaging, one patient was found to have developed a stricture after multiple ureteroscopies for treatment of recurrent struvite stones for an incident rate of 1.4% [14]. These findings suggest that access sheath use during ureteroscopy is safe. Interestingly, in an in vivo porcine model, Lildal et al. [15] compared the histopathologic and visual grading of ureteric lesions using a Post-Ureteroscopic Lesion Scale (PULTS). They found the mean endoscopic score of 1.49 is significantly less than the mean histopathologic finding of 2.51, thereby concluding that endoscopy underestimated the histopathological extent of the lesion in the majority of cases [15]. It can be argued that immediate changes in tissue do not correlate with long term damage and dysfunction, and there is a distinct need for studies with long term follow-up in patients to better elucidate the effects of UAS on healthy ureters. Conversely, immediate changes do not represent the reparative process that goes on after UAS use and the reason for placing a ureteral stent is to allow this process to occur while promoting urinary drainage.

A number of animal studies have demonstrated decreased blood flow and subsequent ischemia and necrosis of the ureter causing thickening and stricture within the ureter following compression of the ureter using UAS [15,16]. Lildal et al. [17] demonstrated, using an in vivo porcine model that the duration of use of UAS significantly increased the expression of pro-inflammatory markers TNF-a and COX-2. This is believed to be caused by UAS insertion increasing the outer diameter of the ureter from approximately 6 to 9 Fr in the native tissue to 11.5 to 18 Fr, which results in severe overstretching of the ureteral tissue [18]. Similar overstretching is seen in obstructed ureters, where TNF-a production was shown to last upwards of 3 days post-ureteral obstruction and may lead to renal tissue injury [19]. Similarly, COX-2 has been shown to be expressed in bladder smooth muscle in response to stretch causing smooth muscle proliferation and pathological bladder wall thickening in response to bladder obstruction [20]. UAS use may also result in stricture formation and edema of the ureteral smooth muscle that can lead to ureteral obstruction and eventually upregulation of Cox-2. Nørregaard et al. [21] showed that ureteral obstruction induced higher levels of Cox-2 expression in comparison to unobstructed ureters in both rats and humans at the protein level by immunohistochemistry in obstructed ureteral smooth muscle and urothelium. Given that UAS insertion triggers a physical ureteral response similar to that observed with obstruction involving the production of TNF-a and COX-2 known to result in potential negative effects on ureteral function, whether UAS placement has similar longer-term consequences warrants further investigation. While the relatively short duration of UAS placement may suggest that any changes are short-lived, the fact that TNF-a and COX-2 are increased suggests that the insult on the ureter, albeit short, still results in significant tissue changes.

Interestingly, a prospective study which included 250 patients undergoing ureteroscopy for stone treatment, demonstrated that the only intraoperative factor which significantly affected immediate post-operative pain was the duration of use of UAS [22].

In a porcine model, Lallas et al. [23] measured ureteral blood flow using a laser Doppler flowmeter every 5 minutes for 70 minutes following the insertion of 12, 14, and 16 Fr UAS. Using this model, they were able to demonstrate that the use of an access sheath does cause a transient decrease in ureteral blood flow, and although the flow is restored to near baseline levels by 70 minutes, the long-term effects of the transient ischemia may be long-lasting. Similarly, when a UAS is placed within the ureter, a temporary obstruction occurs over the duration of the procedure, and can lead to a decrease in ureteral blood flow. In the setting of 18 hours of complete unilateral ureteral occlusion, ipsilateral renal blood flow and ureteral pressure were recorded in five awake dogs. During the first 90 minutes, increase of both renal blood flow and ureteral pressure was noted followed by decrease blood flow and continued rising of ureteral pressure from 90 minutes to 5 hours of obstruction, at which point both renal blood flow and ureteral pressure decreased and fell together [24].

Although the guidelines between the American Urological Association (AUA), Canadian Urological Association, and European Association of Urology (EAU) vary in their recommendations for the use of UAS, it is important to keep in mind the individual patient’s risk of complications and target stone(s) characteristics when opting to use a UAS.
INTRARENAL PRESSURE REDUCTION AND UAS PLACEMENT

During a typical ureteroscopy procedure, pressurized irrigation systems are important for visualization and lead to more successful procedures and patient outcomes. However, an increase in intrarenal pressure is associated with the use of such systems. During flexible ureteroscopy without UAS placement, intrapelvic pressure is highest when the ureteroscope is located in the renal pelvis and lowest when located in the distal ureter (59 vs. 52 cm H$_2$O, or 44 and 39 mmHg, respectively, when instrument inflow pressure is 200 cm H$_2$O) [25]. Normal intrarenal pressures range from zero to a few cm H$_2$O [26] and should be maintained at a low pressure throughout the procedure to prevent damage to the kidney and post-operative complications such as bleeding, sepsis, and post-operative pain.

In laboratory studies using porcine kidneys, increases in intrarenal pressures greater than normal physiological values result in renal tissue damage [27]. Clinical complications related to increased intrarenal pressure have been investigated as well. High intrarenal pressures during ureteroscopy may lead to calyceal rupture and/or intravasation of bacteria, and is a risk factor for the development of post-operative fever, sepsis, bleeding, hemATOMA, urinoma, and postoperative pain [25,27-29].

One of the potential benefits warranting UAS placement during ureteroscopy (URS) is the reduction in intrarenal pressure through facilitating flow and irrigant out of the collecting system, thus reducing intrarenal pressure [30]. In laboratory studies on cadaveric human and porcine models, it was demonstrated that UAS placement is capable of reducing intrarenal pressure compared with no UAS at various irrigation pressures [25]. Progressive reductions in intrarenal pressure was shown to be associated with increasing the diameter of UAS [23]. Although studies have shown that UAS placement is promising in decreasing intrarenal pressures in ex-vivo models, the results from an in-vivo porcine study by Noureldin et al. [31] showed such intrarenal pressure reduction from UAS placement may not translate. Although it was found that normal physiological intrarenal pressures were achievable by UAS sizes 12/14 Fr and greater under gravity irrigation, only the 14/16 Fr UAS was able to achieve similar results under pressure irrigation with a manual pump. These results in the in-vivo porcine model may raise some concern since only the largest diameter UAS (14/16 Fr) may sufficiently decrease intrarenal pressure to safe physiological levels. The most commonly utilized UAS diameters are smaller than 14/16 Fr. Although the described studies conclude that UAS placement during flexible ureteroscopy does decrease intrarenal pressures compared to without, the degree of pressure reduction may not reach sufficient levels to prevent complications associated with high intrarenal pressures during surgery, especially under pressure irrigation.

Pathology studies have shown that even at moderately elevated intrarenal pressures, kidney injury, arterial blood flow reduction, and cellular damage is evident at one hour post intrarenal pressure increase; an increase in incidence of post-operative fever and sepsis have also been documented [28,31]. From these studies, sub-20 cm H$_2$O intrarenal pressures can be achieved only with the larger diameter UASs (>12/14 Fr). The use of such larger diameters may be concerning to endourologists, as studies have shown that increasing the diameter of UAS used also increases the percentage of associated injury and complications, though not to statistically significant degrees (10.5% 12/14 Fr vs. 11.4% 14/16 Fr) [32].

It is also worth mentioning that increased COX-2 expression in response to UAS placement as discussed above, may influence the regulation of ureteral pelvic pressure [21]. If a UAS is not used during ureteroscopy, intrarenal pressures may also be decreased pharmacologically rather than mechanically. The COX-2 inhibitor parecoxib at a dosage of 5 mg/kg/day has been shown to significantly reduce intrarenal pressures in ureteral obstructed rats and also reduces the physiological intrarenal pressure after the obstruction has been removed [21]. Furthermore, intraluminal administration of isoproterenol (ISO) (a $\beta$-agonist) has been shown to decrease pressures without systemic side effects [33].

The indication for UAS placement to intrarenal pressure decrease should be proceeded with caution, and endurologists should consider whether the benefit of intrarenal pressure reduction outweighs the risk of UAS placement injuries. Controlling the irrigation pressures during ureteroscopy is the principle factor in preventing related complications, and UAS placement should not be used as compensating measure as evident from the studies described.

DOES UAS SIZE MATTER

As discussed previously, UAS placement during ureteroscopy can decrease intrarenal pressures to safe levels if larger sizes are used. In such instances, this may decrease complications related to high intrarenal pressures during ureteroscopy; however, this raises the question whether the benefit of
using a larger diameter UAS outweighs the risk of ureteral injury? In a survey conducted amongst 216 endourologists worldwide, the most common use of UAS used was the 12/14 Fr [6]. Traxer and Thomas [13] showed in their study of 359 patients that severe ureteral wall injury involving ureteral smooth muscle layers is not uncommon after insertion of a 12/14F UAS, and the incidence of postoperative pyelonephritis is higher with higher grade UAS-related injury. Moreover, the increase in UAS diameter also results in increases in force applied to the urothelium [34]. In a UAS insertion force study of seven patients, the highest force observed was 5.9 Newtons (N) with a 12/14 Fr UAS, and 0.91N with a 9.5/11.5 Fr UAS [35]. Such forces associated with larger UAS sizes is concerning, as applied forces greater than 4.84 N results in ureteral injury to porcine kidneys, with forces >8.1 N routinely resulting in a PULS score >3 injury (perforation with less than 50% partial transection) [34]. One patient from the UAS insertion force study did develop a PULS score of 1 post-operatively due to the UAS placement (superficial mucosal lesion and/or significant mucosal edema/hematoma) [35].

Speaking strictly on UAS sizing, technological development in flexible ureteroscopy can allow for smaller diameter UAS to be pre-dominantly used and is hypothesized to reduce UAS-related complications [36]. However, although the use of smaller sized UAS is warranted in preventing ureteral wall injury, insertion studies have shown that increasing the diameter of a UAS results in decreased UAS insertion success rates due to kinking and buckling [32].

This leads to a possible dilemma when deciding between UAS diameters. Smaller diameter UASs (<12/14 Fr) decreases the chances of ureteral wall injury due to lower applied forces but are unable to lower intrarenal pressures to appreciable amounts and also limit the size of fragments that can be basket extracted. Larger diameter UASs (>12/14 Fr) are observed to improve surgical efficiency, greater intrarenal pressure reduction at a cost of greater risks of injury and placement failures. If a >12/14 Fr UAS is used, ureteral integrity should be assessed at the end of each procedure to prevent stricture formation.

TO STENT OR NOT TO STENT

Following ureteroscopy, ureteral stenting is considered routine practice by many urologists to prevent obstruction, renal colic, deterioration of renal function and post-operative complications [37]. If ureteral wall injury occurs during ureteroscopy due to a UAS placement, stenting post-operatively has been shown to play a reparatory role in the prevention of ureteral edema and directly minimizes pain secondary to residual stone fragments and blood clots [9]. Levine et al. [38] state that in many cases, mucosal edema is seen in most patients with indwelling stents and that after stent removal, some of the patients develop a transient obstruction. Furthermore, stenting following UAS placement can also result in prolonged hydronephrosis, higher pain scores, stent migration, encrustation and discomfort [39].

From cost-analysis perspectives, non-stenting reduces operative costs by CAD$140 per patient in ureteroscopy cases with UAS, but costs increase dramatically for unstented patients if they need to return to the emergency room (ER) due to readmission, CT imaging or the need for upper-tract decompression [40]. Not stenting following ureteroscopy with UAS placement results in higher rates of ER return (17 vs. 22%), emergency CT scans for returning patients (28% vs. 75%), hospital readmission (22% vs. 58%) and the need for urgent decompression (0% vs. 25%) [40]. As such, stenting post-operatively is warranted to prevent post-operative complications associated with UAS placement. However, is this always the case? Astroza et al. [41] investigated whether stenting is required following URS and a UAS, and their retrospective data showed that postoperative stenting is not always necessary after UAS placement in a pre-stented patient.

Although stenting post-operatively is routine, stenting pre-operatively is not routine and typically occurs in the presentation of infection, compromised renal function or a tight ureter to facilitate introduction of a ureteroscope. AUA and EAU guidelines states that routine preoperative stenting before URS for ureteric or renal stones is not necessary and should not be performed routinely [43,45]. Amongst members of the Endourologic Society, 90% of 216 international endourologists who responded to a UAS practice pattern survey believed that a double-J stent insertion is not mandatory prior to UAS insertion [6]. Despite this consensus, various studies have shown that pre-operative stenting allows for more successful UAS insertions, and acts as a preventative measure in preventing associated ureteral wall injuries [13,35,41,42]. In a prospective evaluation of ureteral wall injuries by Traxer and Thomas [13], the most significant predictor for severe injury associated with UAS placement was the absence of pre-operative stenting. In their study, pre-operative stenting decreased the risk of severe injury associated with UAS placement by sevenfold. Furthermore, stenting with double-J stents has been shown to protect the ureter from injuries associated with UAS insertion, even with larger diameter UASs (>12/14 Fr), and its absence may result in low-grade ureteral trauma during retrograde intrarenal surgery [35]. In regards to pre-operative stenting in UAS insertion suc-
cess, a prospective evaluation of the showed that 98.5% of the pre-stented patients had a successful UAS placements vs. 82% of non-pre-stented, and pre-stenting status was the only independent factor for a successful access sheath insertion [43].

Pre-operative stenting protects the ureter from injuries associated with UAS insertion and usage, and should be considered by the endourologist especially if larger diameter UASs are to be used as they may predispose patients to greater chances of ureteral wall injury [34].

**PHARMACOLOGICAL MANAGEMENT IN THE PREVENTION OF UAS-ASSOCIATED INJURY**

As surgical efficiency has been described to increase with larger UAS diameters, as does the concerns of ureteral damage which may subsequently result in stricture formation and potential loss of kidney function. However, it has been reported that the tissue dynamics (e.g., resistance, elasticity, etc.) is related to potential injury rather than the physical narrowness of the ureter [13,42]. The relaxation of ureteral tissue can be managed pharmacologically, and may be beneficial in preventing UAS-related complications. Lildal et al. [33] showed that the β-agonist ISO can inhibit the ureteral muscle tone and lower the pressure in the upper urinary tract during ureteroscopy without causing systemic adverse effects. In their randomized feasibility trial on the effects of adding ISO to the irrigation fluid, ISO-infused irrigation resulted in significantly higher successful UAS insertions when compared the saline group (63% vs. 27%). No serious lesions (<PULS grade 2) were observed in the ISO group. This suggests that irrigation fluid with ISO may facilitate higher success rates in UAS insertion and potentially decrease UAS related ureteral lesions.

Pre-operative α-adrenergic antagonists may reduce maximal UAS insertion forces, as well as a reduction in intrarenal pressure by inhibiting peristalsis [44]. In a study by Koo et al. [44] non-stented patients who received tamsulosin for 7 days at a dose of 0.4 mg per os pre-operatively had a significant reduction in UAS insertion forces and were comparable to that of pre-stented patients who did not receive tamsulosin. Given these results, considerations into prescribing pre-operative α-adrenergic antagonists may be taken for patients who are not pre-stented prior to their ureteroscopy procedure to prevent UAS-associated injuries. Further studies into varying pre-operative doses of α-adrenergic antagonists is warranted to elucidate whether UAS insertion force reductions are dose-dependent.

**CONCLUSIONS**

The UAS is an important tool in the armamentarium of the endourologist and facilitates multiple and rapid passages of the ureteroscope during ureteroscopy. There is little evidence that UAS improves SFR so this should not be the main reason to use a UAS UASs vary in size which produces unique advantages and disadvantages. Larger diameter UASs (>12/14 Fr) allows for greater surgical efficacy and intrarenal pressure reduction to safe physiological levels at the cost of increased insertion forces, greater risk for ureteral wall injury, and lower insertion success rates. Pre-operative stenting and pharmacological management has been shown to be a protective factor in preventing UAS associated complications. Post-operative stenting has been shown to reduce post ureteroscopy and potential complications. These factors associated with UAS placement suggests that endourologists can contemplate UAS placement on a patient-to-patient basis to prevent associated complications and maximize surgical efficiency.

**CONFLICTS OF INTEREST**

The authors have nothing to disclose.

**AUTHORS’ CONTRIBUTIONS**

Conception and design, data acquisition, data analysis and interpretation, drafting the manuscript, critical revision of the manuscript for scientific and factual content, approval of final manuscript: Victor K.F. Wong. Data acquisition, data analysis and interpretation, drafting the manuscript, critical revision of the manuscript for scientific and factual content: Khatereh Aminoltejari. Data acquisition, data analysis and interpretation, drafting the manuscript, critical revision of the manuscript for scientific and factual content: Khaled Almutairi. Data acquisition, data analysis and interpretation, drafting the manuscript, critical revision of the manuscript for scientific and factual content: Dirk Lange. Conception and design, data acquisition, data analysis and interpretation, drafting the manuscript, critical revision of the manuscript for scientific and factual content, supervision: Ben H. Chew.

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