



# Can alpha blockers facilitate the placement of ureteral access sheaths in retrograde intrarenal surgery?

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## ABSTRACT

**Objective:** To investigate the effects of alpha blocker treatment on the placement of ureteral access sheaths (UAS) during retrograde intrarenal surgery (RIRS).

**Material and methods:** This study was a retrospective analysis of prospectively collected data. Patients who underwent RIRS due to renal stones between November 2015 and December 2017 were separated into two groups. Age, gender, body mass index (BMI), stone size, laterality, hydronephrosis degree, and renal stone density were recorded. Tamsulosin (0.4 mg/day) was prescribed to the study group (n=25) 2 weeks before the operation. The control group (n=25) underwent the operation without any additional treatment. All the operations were performed using a 7.5 Fr flexible ureteroscope and 9.5/11.5 Fr (Cook, Blooming, USA) UAS.

**Results:** Two patients in the study group were excluded from the study as they suffered from dizziness and retrograde ejaculation. No statistically significant difference was found between the patients in the study group (n=23) and control group (n=25) in terms of age, gender, BMI, stone size, laterality, hydronephrosis, and renal stone density (p=0.470, p=0.536, p=0.456, p=0.102, p=0.555, p=0.732, and p=0.317, respectively). The UAS could be successfully placed on the first attempt in 15 (65.2%) patients in the study group and 11 (44%) patients in the control group during the first attempt itself. Even though the successful UAS placement rate was higher in the study group, no statistically significant values were observed (p=0.141).

**Conclusion:** The data obtained from the present study showed that the use of alpha blockers prior to RIRS did not improve the UAS placement rates. It is considered that studies conducted on more patients might be able to achieve significant values.

**Keywords:** Alpha blocker; retrograde intrarenal surgery; ureteral access sheath.

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## Introduction

The upper urinary system was first accessed using a flexible ureteroscope by Marshall in 1964.<sup>[1]</sup> After initial diagnostic interventions, along with advances in laser technology, attempts have been made to tackle upper urinary system stones. Since 2000, laser applications combined with flexible ureteroscopy and retrograde intrarenal surgery (RIRS) applications have gained popularity. Today, it is possible to successfully perform RIRS operations on upper urinary system stones by using devices that yield high-quality images due to

advancements in digital technology as well as increased deflection ability.<sup>[2]</sup> Initially, according to the literature data, RIRS was recommended for <2 cm stones. However, today, it is reported that RIRS can also be successfully used on >2 cm stones in parallel with increased experience and technological developments.<sup>[3]</sup>

The ureteral access sheaths (UAS) used during RIRS were produced for easy access to the upper urinary tract. The main advantages of UAS are providing repetitive access to the ureteral and collecting duct system, decreasing intrarenal pressure, preventing bleeding-

related distortion of vision by acceleration of liquid flow, and eventually contributing toward the protection of the flexible device.<sup>[4]</sup> Nevertheless, there might be certain challenges during UAS placement. There are also risks, such as ureteral injury and the occurrence of ureteral stricture in the long term.<sup>[4,5]</sup> However, considering the benefit/risk balance, RIRS is routinely performed in many clinics because of the ease provided by UAS.

Some problems might occur during the placement of UAS whose diameters vary between 9.5 and 14 Fr. In cases where UAS cannot be placed, manipulations can be used, such as ureteral balloon dilatation, providing access through a rigid ureteroscope with a guide wire, or dilatation with the inner sheath of the UAS, which may vary depending on the amount of personal experience. Despite such manipulations, if UAS placement is still unsuccessful, it is always more logical to place a double-J stent, enable passive dilatation, and postpone RIRS until the second operation.<sup>[4-6]</sup>

In our study, we attempted to discover if the use of alpha blockers might be beneficial in facilitating UAS placement. According to the literature, alpha blockers increase the spontaneous passage of ureteral stones and enable a reduction in the severity and frequency of pain, which is more evident in distal ureteral stones.<sup>[6,7]</sup> The critical point in the increase in the spontaneous passage of ureteral stones led by alpha blockers is to enable relaxation and to reduce intramural ureteral resistance in ureteral smooth muscles. This study examined whether intramural ureteral resistance can be reduced or not and whether UAS placement can be facilitated using alpha blockers or not.

## Material and methods

This study was a retrospective analysis of prospectively collected data. The study protocol was approved by the Local Ethics Committee (University of Gaziantep, 2018/10: January 18, 2018). Patients who underwent RIRS between November 2015 and December 2017 were included in the study. Informed consent forms were signed by the patients before the operation. Prior to the operations, routine hematologic and biochemical examinations, urine analyses, and urine culture were performed. Patients were not involved in the operation before the urine culture became sterile. Kidney-ureter-bladder (KUB) graphs and unenhanced abdominal computed tomography were performed on the patients before the operation.

Age, gender, body mass index (BMI), stone size, laterality, hydronephrosis degree, and renal stone density (HU) were determined. Patients who had double-J stents, had ureteral stones, had a history of lower urinary system surgery, were less than 18 or more than 65 years old, had high urea-creatinine

levels, had a distinctly large prostate, had defined drug-related adverse effects, or refused medication were excluded from the study. These patients were separated into two groups. Two weeks before the operation, a tamsulosin treatment of 0.4 mg/day was prescribed to the patients in the study group (n=25). No treatment was performed in the control group (n=25). Patients in the study group were called for a follow-up on the fifth day of medication and queried in terms of medication use and its adverse effects.

## Operative procedure

All the operations were performed by a single surgeon (SE). A 7.5 Fr fiber-optic flexible ureteroscope (Storz Flex-X2, Tuttlingen, Germany), 9.5/11.5 Fr (Cook, Blooming, USA) UAS, and a 0.038 inch hydrophilic guide wire were used in all the operations. RIRS was performed on both the groups guided by C-arm fluoroscopy. Firstly, the bladder was accessed using a 20 Fr rigid cystoscope at the lithotomy position under general anesthesia. Diagnostic cystourethroscopy was performed, and a guide wire was advanced toward the renal pelvis under the guidance of fluoroscopy. If there was a suspicion of abnormality about the anatomy of the renal collecting system in the unenhanced abdominal computed tomography, retrograde pyelography was performed before the RIRS.

The UAS was pushed forward in the ureter guided by the fluoroscopy data. In patients who had unsuccessful UAS placement, a 2-min ureteral balloon dilatation procedure using a guide wire, advancement of the inner sheath of the UAS, and ureteral access using a rigid ureteroscope were sequentially tried, and the UAS was attempted to be placed again. For patients in whom the UAS advancement failed, the process of UAS placement was considered to be unsuccessful, and 4.8 Fr 26 cm double-J stents were placed for passive dilatation; they were retained in the waiting period for at least 2 weeks. At the end of this period, the above-explained procedure was repeated on the patients, and RIRS was performed. In cases with successful UAS placement, the stones were fragmented (200 mm holmium:YAG laser fiber; dusting setting: 0.4-0.6 J/35-40 Hz; fragmentation setting: 0.6-0.8 J/10-15 Hz).

Pre- and postoperative complications in patients were classified under five grades in accordance with the modified Clavien system. KUB and sonographic evaluations were performed on all the patients at the postoperative 24<sup>th</sup> hour and 2<sup>nd</sup> week for residual stone-steinstrasse detection. In addition, in the case of any suspicions, the patients were postoperatively analyzed with unenhanced abdominal computed tomography.

## Statistical analysis

The Statistical Package for the Social Sciences version 11 (SPSS Inc.; Chicago, IL, USA) for Windows statistical pack-

age was used for the statistical calculations, and the data were expressed as arithmetic mean and standard deviation. The chi-squared test was performed for calculating the categorical variables, and the Mann-Whitney U test was used to compare the mean values. Here 95% confidence interval ( $p < 0.05$ ) was considered to be statistically significant.

**Table 1. Demographic data**

	Study group (n=23)	Control group (n=25)	p
Age, year	40.47±12.28	38.48±9.46	0.470
<b>Gender</b>			0.536
Male	14	13	
Female	9	12	
BMI (kg/m <sup>2</sup> )	27.47±3.01	28.28±3.39	0.456
Stone size (mm)	15.13±4.94	15.32±4.58	0.102
<b>Laterality</b>			0.555
Left	13	12	
Right	10	13	
<b>Hydronephrosis, n (%)</b>			
None or mild	14 (60.8)	14 (56)	0.732
Moderate or severe	9 (39.2)	11 (44)	
Renal stone density (HU)	1057.17±139.04	1013±140.55	0.317

BMI: body mass index; mm: millimeter; n: number of patients; HU: Hounsfield unit

## Results

Two patients in the study group were excluded from the study due to complaints of dizziness and retrograde ejaculation. No statistically significant difference was found between the patients in the study group (n=23) and control group (n=25) in terms of age, gender, BMI, stone size, laterality, hydronephrosis, and renal stone density ( $p=0.470$ ,  $p=0.536$ ,  $p=0.456$ ,  $p=0.102$ ,  $p=0.555$ ,  $p=0.732$ , and  $p=0.317$ , respectively) (Table 1).

Ureteral access sheaths could be successfully placed on the first attempt in 15 (65.2%) patients in the study group and 11 (44%) patients in the control group during the operative procedures. Even though the successful UAS placement rate was higher in the study group, no statistically significant differences were observed ( $p=0.141$ ). In addition, no significant difference was observed between the groups in terms of operation duration, fluoroscopy duration, stone-free rates, and postoperative double-J stent placement ( $p=0.134$ ,  $p=0.683$ ,  $p=0.819$ , and  $p=0.738$ , respectively) (Table 2).

According to the Clavien classification, there was no difference between the patients in the study and control groups in terms of complications [fever (GI) ( $p=0.819$ ), urinary tract infection requiring additional antibiotics (GII) ( $p=0.738$ ), and sepsis (GIV) ( $p=0.819$ )]. Steinstrasse (GIII) was observed in two patients in the control group with stone sizes of 20 mm and 19 mm (study group: 0% vs. control group: 18.18%;  $p=0.086$ ) at the postoperative 2<sup>nd</sup> week follow-up (Table 2).

**Table 2. Data for first operations**

	Study group (n:23)	Control group (n:25)	p
UAS placement in the first attempt, n (%)	15 (65.2%)	11 (44%)	0.141
Duration of operation (mean) (s)	54.4±6.03	58.36±6.54	0.134
Duration of fluoroscopy (mean) (s)	23.8±1.93	24.09±1.86	0.683
Stone-free rate (%)	93.3	90.9	0.819
Double-J catheter placement (postoperatively), n (%)	13 (86.66%)	10 (90.90%)	0.738
<b>Complications (Clavien classification), n (%)</b>			
-Fever (GI)	1 (6.6)	1 (9.09)	0.819
-Urinary tract infection requiring additional antibiotics (GII)	2 (13.2)	1 (9.09)	0.738
-Steinstrasse (GIII)	0 (0)	2 (18.18)	0.086
-Sepsis (GIV)	1	1	0.819

n: number of patients; G: grade; UAS: ureteral access sheaths

## Discussion

Ureteral access sheaths are currently produced by various companies with diameters ranging between 9.5 and 14 Fr and lengths between 13 and 55 cm.<sup>[4]</sup> The main advantages of UAS are fast, repeatable, and safe access to the upper urinary tract with improved visibility. However, their uncontrolled use, forceful attempts in patients that experience difficulty in the ureter, or attempts to advance through the ureter without any inner sheath may lead to ureteral injury. Such injury may have severity varying from ureteral mucosal erosion to ureteral avulsion. In a study by Traxer et al.<sup>[5]</sup> comprising 359 patients, an overall ureteral complication of 46.5% and severe ureteral damage of 13.5% in patients were reported. In the same study, severe damage risk was higher in old age and male patients ( $p=0.018$  and  $p=0.024$ , respectively). As another speculative issue, UAS may lead to ureteral stricture in the long term. It is claimed that UAS might cause a reduction in blood flow due to compression on the ureter wall, as well as a stricture secondary to ischemia in the long term. In the animal model proposed by Lallas et al.,<sup>[8]</sup> ureteral blood flow was measured with UAS under different calibrations, and they showed that there was a reduction in the blood flow at the same rate as that of the increase in the UAS thickness. However, no histologically ischemic finding was observed in any subject.

The risk of ureteral mural damage is higher in patients with UAS placement. Therefore, treatment involving alpha blocker medication was used before the operation in the present study to overcome this challenge. The fact that alpha blockers accelerate the spontaneous passage of ureteral stones has been recently demonstrated in publications with strong methodologies.<sup>[9,10]</sup> Alpha blockers create such an effect by enabling relaxation in the ureteral smooth muscles, as well as a reduction in the intramural ureter resistance. The most critical point in the placement of UAS is the passage through the ureter orifice and the intramural ureter section, which is the narrowest part of the ureter. Therefore, in our study, it was aimed to relax this area and facilitate the placement of UAS by using alpha blockers before the operation. Hence, in the current study, we were able to successfully place a higher rate of UAS on the first attempt in the study group during surgery, even though significant values were not obtained (65.2% vs. 44%;  $p=0.141$ ).

In a recent study by Koo et al.,<sup>[11]</sup> the effect of preoperative  $\alpha$ -adrenergic antagonists on the UAS insertion force was evaluated with a homemade device. Here, 41 patients and 42 patients were randomized as the control and study groups, respectively, who underwent RIRS for ureteropelvic junction or renal pelvis stones. Alpha blockers were prescribed to the patients in the study group. Here, 21 patients with double-J stents were separately examined. Maximal insertion force in the alpha blocker

group was reported to be significantly lower than that in the control group at the ureterovesical junction ( $p=0.008$ ) and proximal ureter ( $p=0.036$ ). Maximal insertion force in the alpha blocker group was comparable with patients who preoperatively had double-J stents. In addition, the authors reported that the rate of grade 2 or greater ureteral injury was lower in the study group than that in the control group ( $p=0.038$ ). In the current study, there was no difference between the patients in the study and control groups in terms of complications [fever (GI) ( $p=0.819$ ), urinary tract infection requiring antibiotics (GII) ( $p=0.738$ ), and sepsis (GIV) ( $p=0.819$ )].

In addition to the several advantages, the challenges experienced in the placement of UAS gave rise to the following questions: "Are UAS mandatory during RIRS?" or "can RIRS be performed without UAS?" Baseskioglu et al.<sup>[12]</sup> reported a stone-free rate of 81.4% with sheathless RIRS in 43 patients with renal stones <2 cm. However, it should be noted that 60% of these patients had preoperative double-J stents in their study. In a trial by Ozyuvali and Damar,<sup>[13]</sup> no difference was observed in the stone-free rates for UAS-supported or sheathless RIRS in 504 cases. On the contrary, in a multicenter retrospective study, Traxer et al.<sup>[14]</sup> investigated the prevention of septic events with UAS, and a lower rate of sepsis was observed in patients in whom UAS were used (4.3% with UAS vs. 15.2% without UAS). In addition, there are many publications that have reported that flexible ureteroscopy lasts longer in subjects with UAS as compared to sheathless interventions.<sup>[15,16]</sup> In brief, there are no strong data that support sheathless RIRS management.

The small sample size is the main limitation of the present study. The current findings should be supported by prospective, randomized trials that include a larger patient series. It is considered that studies conducted on more patients might achieve significant values.

In conclusion, UAS not only provide advantages to the surgeon during RIRS, but also reduce operation-related complications and risks and prolong the life of flexible ureteroscopes. However, the fact that UAS placement is not always successful might lead to problems such as postponing of the procedure to a second operation following the placement of a double-J stent, exposure of the patient to anesthesia twice, and increase in operation costs. Our main aim in this study was to investigate if it was possible to resolve such problems by the use of alpha blockers before RIRS and to facilitate the placement of UAS without the need of conducting a second operative procedure. The obtained data have revealed that UAS placement rates were higher when alpha blockers were used for at least 2 weeks before the operation. However, such difference has not led to statistical significance.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of University of Gaziantep (2018/10: January 18, 2018).

**Informed Consent:** Written informed consent was obtained from patient who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – S.E., Ö.B.; Design – S.E.; Supervision – İ.S.; Resources – S.E., H.Ş.; Materials – A.E.Y.; Data Collection and/or Processing – S.E., A.E.Y.; Analysis and/or Interpretation – S.E., Ö.B., H.Ş.; Literature Search – S.E., Ö.B.; Writing Manuscript – S.E., Ö.B.; Critical Review – S.E., İ.S.; Other – H.Ş.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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