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Assessing the Effects of Using a Ureteral Access Sheath on Kidney Injury in Retrograde Intrarenal Surgery with KIM-1 and NGAL Biomarkers in Urine: A Prospective Cohort Study

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What's known on the subject? and What does the study add?

The pressure effect of the irrigation fluid used during retrograde intrarenal surgery (RIRS) and mechanical occlusion of the f-URS may have a negative effect on the kidney by increasing intrapelvic pressure. Even though its use is not mandatory in routine practices, ureteral access sheath (UAS) is generally preferred to be used by urologists considering its advantages. The use of UAS ensures removal of stones, ease of access of f-URS and low intra-renal pressure. Kidney injury molecule-1 (KIM-1) and neutrophil gelatinase associated lipocalin (NGAL) have been the leading tubule damage markers analysed in urine levels in recent years to show acute kidney injury. The use of UAS in RIRS applications was effective in preventing kidney damage and did not cause any complications. We demonstrated the development of kidney damage with KIM-1 and NGAL biomarkers measured in urine. It was revealed that more kidney damage developed in the group not using UAS compared to the group in which UAS was used, especially in the 24th postoperative hour.

Abstract

Objective: This study aimed to investigate the effects of ureteral access sheath (UAS) use in patients undergoing retrograde intrarenal surgery (RIRS) due to kidney stones on postoperative early kidney injury development using urine kidney injury molecule-1 (KIM-1) and neutrophil gelatinase-associated lipocalin (NGAL) measurements.

Materials and Methods: Thirty patients using UAS (UAS group) and 30 not using UAS (non-UAS group), for whom RIRS was planned, and 30 healthy controls (control group) were included between January and June. Blood urea nitrogen and creatinine in the blood and KIM-1 and NGAL in the urine at the pre-operative and postoperative 24th hours and KIM-1 and NGAL at the postoperative 4th and 24th hours were studied. The same biomarkers were analyzed once in the control group. During follow-up, KIM-1 and NGAL were measured using the enzyme-linked immunosorbent assay method within 6 months.

Results: There was no significant difference between the pre-operative KIM-1 and NGAL values and the postoperative 24-h KIM-1 and NGAL values in the UAS group ($p>0.05$), whereas there was a significant difference in the non-UAS group ($p<0.05$). The postoperative 24-h KIM-1 and NGAL values were significantly higher in the UAS group than in the non-UAS group ($p<0.05$).

Conclusion: It was determined that more kidney injury developed in the non-UAS group UAS than in the UAS group, especially at the postoperative 24th hour. The use of UAS in RIRS is effective in preventing the development of potential kidney injury.

Keywords: Kidney injury molecule-1, neutrophil gelatinase-associated lipocalin, retrograde intrarenal surgery, ureteral access sheath

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Introduction

Retrograde intrarenal surgery (RIRS) in kidney stone treatment is a minimally invasive surgical approach that is increasingly used with the development of laser technologies. Even though its use is not mandatory in routine practices, ureteral access sheath (UAS) is generally preferred by urologists because of its advantages.

Kidney injury molecule-1 (KIM-1) and neutrophil gelatinase-associated lipocalin (NGAL) are the leading biomarkers among tubular damage markers analyzed in urinary levels in recent years (1). These biomarkers are highly superior to blood urea nitrogen (BUN) and creatinine levels in revealing and detecting acute kidney injury early (2). KIM-1 and NGAL biomarkers have been shown to increase in proximal tubular cells in epithelial kidney injuries and after ischemia (3,4).

KIM-1 is a type-1 transmembrane glycoprotein that can adhere to the epithelium, has an immunoglobulin-like structure, and its ectodomain consists of mucin (3). It has been reported that most KIM-1-positive tubules (approximately 90%) are of proximal tubule origin in various renal diseases and were identified by double labeling with the proximal tubule marker aquaporin-1. In acute and chronic kidney injury, KIM-1 is located in the apical membrane of dilated tubules. In ischemic injury, *KIM-1* gene expression is most prominent in the S3 segment of the corticomedullary section, which is most sensitive to ischemia-induced damage. It has been reported that in acute kidney injury, the *KIM-1* gene and protein products are upregulated 3 h after experimental kidney injury, and the increase in urinary KIM-1 levels reaches a maximum at 24 h. The extracellular compartment of KIM-1 is widely used to measure urinary KIM-1 excretion. For this, 0.03 mL of urine sample is sufficient. Because the extracellular compartment of KIM-1 is stable at room temperature, KIM-1 can be measured in 24-h urine (5).

NGAL is a 25-kDa protein found in neutrophils and is easily detectable in urine. While NGAL was previously known to be found in neutrophil lysosomes, it has now been observed to be released at very low levels in tissues such as the renal tubular epithelium, colon, prostate, and breast. In addition to neutrophils, NGAL is released from epithelial cells in the thick ascending limb of the loop of Henle and collecting ducts (6). It may be affected by underlying kidney damage, systemic infection, or urinary tract infection. NGAL levels decrease when kidney damage improves. NGAL can be detected 24-48 h before the increase in serum creatinine values in acute renal failure. NGAL can identify low-level kidney damage to facilitate effective interventions. The *NGAL* gene is significantly upregulated in the kidney after ischemia (7).

Our objective in this study was to evaluate the effects of preferring UAS in patients undergoing RIRS on kidney injuries in the early postoperative period using KIM-1 and NGAL biomarkers.

Materials and Methods

The present study protocol was reviewed and approved by the Institutional Review Board of Ondokuz Mayıs University College of Medicine (approval number: 2018/21, date: 20.03.2018). It was planned as a prospective cohort study, and informed consent was obtained from all subjects when they were enrolled.

Sixty patients with a planned RIRS operation due to kidney stones between January and June 2018 and a control group consisting of 30 healthy individuals were included in the study. The number of patients and the control group were specified according to power analysis. The 60-patient study group was randomly divided into two groups, namely group 1 consisting of 30 patients using UAS and group 2 consisting of 30 patients not using UAS. The BUN and creatinine levels at the pre-operative and postoperative 24th hour, KIM-1 and NGAL values in preoperative urine, and KIM-1 and NGAL values at the postoperative 4th and 24th hours were analyzed for each patient. After the urinary samples were collected from the patient groups, a urinary sample was obtained once from the control group consisting of healthy individuals without any urinary system stone disease, and the same biomarkers were then evaluated. By including the control group in the study, we confirmed that the kits used for KIM-1 and NGAL biomarkers were standardized within the normal range.

The inclusion criteria of the study were that the patients should be above 18 years of age, have an RIRS operation indication based on a kidney stone smaller than 15 mm, approve for anesthesia so that they could tolerate the operation, sign the informed consent form regarding the study, and for the 30-person control group, not have a history of any kidney stone and chronic disease. Patients with disorders that cause chronic kidney injuries, such as hypertension, diabetes mellitus, and ischemic heart disease, and with one kidney, urological surgery undergone, and congenital renal anomaly history were not included in the study.

RIRS was performed for all patients under general anesthesia with the standard flexible ureterorenoscopy (f-URS) steps. For the patients included in group 1, a UAS (9.5-11.5 Fr 45 cm hydrophilic coated UAS, Cook Medical Bloomington, IN) was posited on the ureter via a guidewire without any force, accompanied by fluoroscopy. For the patients in group 2, the collecting duct system of the kidney was accessed via a guidewire with f-URS (7.5 Fr Storz Flex-X2 Tuttlingen, Germany). After accessing the collecting duct system, the stone was fragmented with a holmium: YAG laser (Dornier Medilas H Solvo, Dornier MedTech, Germany) by sending a 270 µm laser probe (Singleflex holmium laser fiber, Dornier MedTech, Germany) via the f-URS working channel. As the procedure of removing the stones was not implemented, the fragmentation process was continued until the stone was divided into fragments smaller than 2 mm. A JJ stent was then placed on the collecting duct system.

The urinary samples obtained from the sixty patients in the pre-operative period and postoperative 4th and 24th hours and from 30 healthy individuals from the control group were kept at -80°C until analysis. In the following six months, KIM-1 and NGAL measurements were performed using the enzyme-linked immunosorbent assay method.

For KIM-1, the standard at a concentration of 20.000 pg/mL included in the kit was diluted with standard dilution buffer. After dilution, the standards were adjusted to 5.000 pg/mL, 2.500 pg/mL, 1.250 pg/mL, 625 pg/mL, 312 pg/mL, 156 pg/mL, 78 pg/mL and 0 pg/mL concentration with the help of serial dilutions. Serum samples stored at -80°C were thawed at room temperature. KIM-1 Assay range: 78-5.000 pg/mL; sensitivity: 28 pg/mL. The measurement range is considered to be 78-5.000 pg/mL.

For NGAL, the standard included in the kit at a concentration of 20 ng/mL was diluted with standard dilution buffer. After dilution, the standards were adjusted to 10 ng/mL, 5 ng/mL, 2.5 ng/mL, 1.25 ng/mL, 0.625 ng/mL, 0.312 ng/mL, 0.156 ng/mL, and 0 ng/mL concentrations using serial dilutions. Serum samples stored at -80°C were thawed at room temperature. NGAL Assay range: 0.156-10 ng/mL; sensitivity: 0.065 ng/mL. The measurement range is considered to be 0.156-10 ng/mL.

These measurements were analyzed in accordance with the working procedures stated in the Cloud Clone Corp, Wuhan, China, SEB388Hu catalogs. The inner-test and intra-test variation coefficient values of the KIM-1 and NGAL kits were <10% and <12%, respectively.

Statistical Analysis

The IBM Statistical Package for the Social Sciences version 21 software package was used for statistical analysis. The Shapiro-Wilk test, Kolmogorov-Smirnov test, Paired Sample t-test, Wilcoxon test, Student's t-test, and Mann-Whitney U test were used to evaluate the data. The mean standard deviation or median minimum-maximum values were used to reveal the distribution ranges based on normal distribution fitness. Any p-value 0.05 was regarded as statistically significant in all statistical analyses of the study.

Results

The demographic data of all three groups are shown in detail in Table 1. A significant difference was observed between the pre-operative KIM-1 values and the postoperative 4th-hour KIM-1 values in both group 1 and group 2 ($p<0.05$). Preoperative

Table 1. Demographic data according to the groups

	UAS (+)	UAS (-)	Control group	p
Number of patients	30	30	30	
Sex (%)				
Male	16 (53.3%)	17 (56.7%)	21 (70.0%)	0.378
Female	14 (46.7%)	13 (43.3%)	9 (30.0%)	
Age (years)	42.5±12	43±12.4	36.7±15.6	0.118
BMI	28.6±3.9	27±3.8	25.8±4.8	**0.025**
Operational side				
Right	14 (46.7%)	16 (53.3%)		0.606
Left	16 (53.3%)	14 (46.7%)		
Localization				
Pelvis	18 (60.0%)	24 (80.0%)		**0.040**
UP junction	1 (3.3%)	3 (10.0%)		
Upper calyx	1 (3.3%)	1 (3.3%)		
Middle calyx	0	1 (3.3%)		
Lower calyx	10 (33.3%)	1 (3.3%)		
Stone volume (mm³)	14.4±1.7	11.1±2.8		**0.000**
HU	1082±341	1030±314		0.544
Hydronephrosis				
None	0	1 (3.3%)		**0.018**
G1	13 (43.3%)	21 (70.0%)		
G2-G4	17 (56.7%)	8 (26.7%)		

UAS: Ureteral access sheath, BMI: Body mass index, HU: Hounsfield unit

KIM-1 values in both groups were higher. While there was no statistically significant difference between the pre-operative KIM-1 values and the postoperative 24th hour KIM-1 values in group 1 ($p>0.05$), the postoperative 24th hour KIM-1 values were found to be higher with a statistical significance than the pre-operative KIM-1 values in group 2 ($p<0.05$) (Table 2).

As for the NGAL values, while no significant difference was found between the pre-operative NGAL values and the postoperative 4th-hour NGAL values in group 1 ($p>0.05$), the pre-operative NGAL values were detected to be higher with a statistical significance than the postoperative 4th-hour NGAL values in group 2 ($p<0.05$). Upon comparing the pre-operative NGAL values and the postoperative 24th-hour NGAL values in both groups, no significant difference was seen in group 1 ($p>0.05$), whereas the postoperative 24th-hour NGAL values were observed to be higher with a statistical significance than the pre-operative NGAL values in group 2 ($p<0.05$) (Table 3).

In the between-group evaluation, there was no difference between group 1 and group 2 regarding both the pre-operative and postoperative 4th hour KIM-1 values ($p>0.05$). However, a statistically significant difference was found between group 1 and group 2 regarding the pre-operative and postoperative 24th hour KIM-1 values ($p<0.05$), with group 1 having a significantly lower median KIM-1 value (Table 4).

The intergroup NGAL values were similar to those of KIM-1, and no difference was observed between the pre-operative NGAL values ($p>0.05$). While there was no significant difference between group 1 and group 2 regarding the postoperative 4th-hour NGAL values ($p>0.05$), a statistically significant difference was found between their postoperative 24th-hour NGAL values ($p<0.05$), with group 1 having a significantly lower median value (Table 4).

Table 2. The preoperative and postoperative KIM-1 values of both patient groups and the control group

Groups	Pre-op - control group KIM-1		p	Pre-op - Post-op 4th hour KIM-1		p	Pre-op - Post-op 24th hour KIM-1		p
UAS (+)	0.75 (0.25-1.25)	0.88 (0.36-5.00)	0.068	0.75 (0.25-1.25)	0.19 (0.09-0.85)	**0.000**	0.75 (0.25-1.25)	0.53 (0.16-2.25)	0.910
UAS (-)	0.96 (0.15-5.00)	0.88 (0.36-5.00)	0.976	0.96 (0.15-5.00)	0.21 (0.10-0.92)	**0.000**	0.96 (0.15-5.00)	1.05 (0.23-2.83)	**0.012**

KIM-1: Kidney injury molecule-1, UAS: Ureteral access sheath, Pre-op: Pre-operative, Post-op: Post-operative

Table 3. The preoperative and postoperative NGAL values of both patient groups and the control group NGAL values

Groups	Pre-op-control group NGAL		p	Pre-op-Post-op 4th hour NGAL		p	Pre-op-Post-op 24th hour NGAL		p
UAS (+)	4.16 (0.66-9.43)	3.49 (0.25-8.05)	0.236	4.16 (0.66-9.43)	3.42 (1.89-6.05)	0.210	4.16 (0.66-9.43)	3.18 (1-10)	0.773
UAS (-)	3.94 (0.27-8.17)	3.49 (0.25-8.05)	0.426	3.94 (0.27-8.17)	3.04 (0.97-6.33)	**0.039**	3.94 (0.27-8.17)	5.31 (1.29-10)	**0.000**

NGAL: Neutrophil gelatinase-associated lipocalin, UAS: Ureteral access sheath, Pre-op: Pre-operative, Post-op: Post-operative

Table 4. Comparison of KIM-1 and NGAL values between the group that used UAS and the group that did not use UAS

	UAS (+)	UAS (-)	p
Preoperative KIM-1 (pg/mL)	0.75 (0.25-1.25)	0.96 (0.15-5.00)	0.225
Postoperative 4th hour KIM-1 (pg/mL)	0.19 (0.09-0.85)	0.21 (0.10-0.92)	0.333
Postoperative 24th hour KIM-1 (pg/mL)	0.53 (0.16-2.25)	1.05 (0.23-2.83)	**0.004**
Preoperative NGAL (ng/mL)	4.16 (0.66-9.43)	3.94 (0.27-8.17)	0.709
Post-operative 4th hour NGAL (ng/mL)	3.42 (1.89-6.05)	3.04 (0.97-6.33)	0.123
Post-operative 24th hour NGAL (ng/mL)	3.18 (1-10)	5.31 (1.29-10)	**0.039**

UAS: Ureteral access sheath, KIM-1: Kidney injury molecule-1, NGAL: Neutrophil gelatinase-associated lipocalin

Discussion

The general search and preference for minimally invasive approaches in surgical treatments are increasing with the development of technology. We can see the effects of these approaches in RIRS implementations increasing in kidney stone treatment (8). UAS can be frequently preferred to increase the chances of treatment success and surgical comfort in RIRS implementations. The use of UAS is generally up to the surgeon's choice, and objective criteria have yet to be defined regarding the issue. In our study, it was revealed that more kidney damage developed in the group not using UAS than in the group in which UAS was used, especially in the 24th postoperative hour. We demonstrated the development of kidney damage using KIM-1 and NGAL biomarkers measured in urine. Considering our findings, the use of UAS in RIRS is effective in preventing possible kidney damage.

In a prospective study consisting of 248 patients conducted to predict efficient UAS use, Mogilevkin et al. (9) concluded that sex, body mass index (BMI), and operation side on the body do not have any effect on the placement of UAS in probable predictions, but advanced age is an important determinant. Because patient selection was randomly conducted in our study, we could not evaluate the factors affecting UAS preference, and there were no statistically significant differences in sex, age, BMI, and operation side on the body between the patients who used UAS and those who did not use UAS. Although the stone weight was calculated to be statistically higher in the UAS-using group, no difference was observed between the two groups regarding the rate of stonelessness.

The use of UAS has been stated to decrease general costs and minimize operational duration in various studies (10,11). In our study, the surgical duration, anesthesia duration, laser duration, laser power, laser hit number, and the amount of irrigation solution used were higher in the UAS-using group. We believe that this resulted from the fact that the stonelessness rate of the UAS-using group was not different from that of the group not using UAS, although the stone weight was statistically higher in the UAS-using group, as mentioned above. In addition, stone size and grade 2-4 hydronephrosis were found to be significantly higher in the UAS-using group than in the group not using UAS. However, these data also show that the UAS-using patient group has all the factors that increase kidney injury risks. Even though the UAS-using group had all the factors increasing renal injury risks, their KIM-1 and NGAL levels were found to be lower than those of the group not using UAS. Considering these results, we can say that the use of UAS in RIRS practices protects the kidney from injuries.

In their prospective controlled study conducted to investigate the effects of RIRS on kidney injury, Dede et al. (12) compared a patient group consisting of 30 patients with kidney stones smaller than 2 cm and undergoing RIRS with a control group consisting of 47 individuals applying to a urology clinic and not having any specific symptoms. The patients' preoperative, postoperative 2nd hour, and postoperative 1st-day urinary samples were obtained, and KIM-1, NGAL, N-acetyl-ß-D glucosaminidase (NAG), and liver-fatty acid binding protein (LFABP) molecules from these samples were analyzed. The postoperative 2nd hour KIM-1, NGAL, and serum creatinine levels increased significantly compared with the pre-operative levels, whereas they dropped in the postoperative 24th hour. No postoperative increases were observed in NAG and LFABP levels compared with pre-operative levels. The study concluded that RIRS is a safe method, and although the marker levels increased during the first 2 h, they dropped back to their initial levels within the postoperative 24 h (12). However, Dede et al. (12) excluded any information on whether they used UAS in their study. The harmful effects of high pressure, caused by the irrigation solution and laser energy used within the kidney in RIRS implementation, on the kidney with varying severity levels are known and expected. Even though Dede et al. (12) showed this kind of harm to be intentional and reversible, RIRS poses a risk for kidney health, and studies continue to be conducted to determine the conditions and methods to minimize these risks. As for our study, upon comparing the marker values of the two patient groups divided into those who used UAS and those who did not, the 24th hour KIM-1 and NGAL levels of the group that did not use UAS were detected to be higher than those of the group that used UAS. Besides, in the inner evaluations of both groups, while the 24th-hour marker levels of the UAS-using group did not bear any difference to the pre-operative levels, the KIM-1 and NGAL levels of the group not using UAS were found to increase with a statistical significance, rendering UAS use to be effective in preventing renal injury.

In their study in which they prospectively evaluated 30 patients undergoing f-URS for upper urinary system kidney disease treatment, Ertaş et al. (13) found that the NGAL and NGAL/creatinine ratio levels they analyzed in the spot urinary samples obtained from the UAS posited to the kidney undergoing an operation in the pre-operative period and the ureter catheter in the postoperative 1st and 24th hours increased 1 h after the operation and during the first postoperative day, but these differences were not seen to be significant. This study conducted by Ertaş et al. (13) has shown UAS-enhanced f-URS to be a safe procedure for treating kidney or upper ureter kidney disease with regard to renal injury and functional results. The postoperative urinary samples obtained in our study were mutual samples obtained from both healthy and operated kidneys. The superiority of the study conducted by Ertaş et al. (13) over our study stems from the fact that the obtained urinary samples exclusively came from the kidneys that were operated on. Therefore, Ertaş et al. (13) preferred to use a ureter catheter in all postoperative patients and did not use a JJ stent in any of their patients. We preferred to use a JJ stent in our study to avoid possible risks stemming from not using a JJ stent (14,15).

Mishra et al. (4) observed higher NGAL expression in renal tubulointerstitial lesions in *in vitro* renal ischemia-reperfusion injury. They showed that NGAL concentration in urine began to increase 3 h after kidney injury and that NGAL concentration peaked at 24 h, supporting our findings. In our study, no significant difference was observed in KIM-1 and NGAL values between the groups at the pre-operative and postoperative 4th hour. However, contrary to expectations, when the intra-group marker levels were compared, it was found that NGAL was lower in the group not using UAS, and KIM-1 was lower in both groups at the 4th postoperative hour, which was statistically significantly lower than the pre-operative levels. We think that this may be due to the intense hydration applied peroperatively, increased diuresis in the early postoperative period, inability to collect separate urine, and the markers beginning to increase in the 2-3nd hour, reaching the maximum level in the 24th hour. The fact that KIM-1 and NGAL values were lower in the group in which UAS was used at the 24th postoperative hour than in the group in which UAS was not used shows that these biomarkers can be used to indicate early kidney damage and the importance of using UAS.

In addition to the contributions and benefits it provides, UAS use may also cause undesired results (16-19). In particular, the undesired results during the period when its procedures were first defined led Kourambas et al. (10) to introduce a new and more reliable generation of UASs in 2001, which again increased UAS use during RIRS X. In a study they conducted to investigate the long-term ureter stricture or short-term ureter injury potential of UAS use, Delvecchio et al. (20) used a 10, 12, 14 Fr UAS and determined in their regular 3-month patient follow-ups throughout the following year that only one patient developed ureteral stricture. Various studies suggest based on analyses that UAS should be routinely used during f-URS as it is predicted to decrease the duration and costs of operation and decrease morbidity rates (11,12,20). No complications were encountered during the positioning of the UAS in our study. We believe that the most important factor for this is that the operation was performed under fluoroscopy and suspended for a second session by placing a JJ ureteral stent if any resistance was encountered during UAS placement. In addition, as Lallas et al. (17) put forth in the conclusion of their study, the use of a UAS with low Fr levels is known to decrease negative effects on ureter bleeding. In our study, the thinnest 9.5/11.5 Fr UAS was used. In this way, damage to the ureter was minimized, enabling the secretion of proinflammatory cytokines to decrease. Therefore, we decreased the possibility of urinary KIM-1 and NGAL values, which we used to evaluate kidney damage, being affected by the ureter, minimizing the risk of possible negative effects due to UAS use.

Among 256 patients on whom they performed ureterorenoscopy, L'esperance et al. (21) reported the stonelessness rates of 173 who used UAS and 83 who did not use UAS to be 79% and 67%, respectively. Conclusively, UAS use was stated to significantly decrease the stonelessness rates (21). Conversely, in their study in which they retrospectively evaluated data from 280 patients, Berquet et al. (22) compared the stonelessness rates of patients who used UAS and those who did not use UAS and did not find any significant differences between the two groups. Our study supports the findings of Berquet et al. (22) as there was no statistically significant difference between our patient groups regarding their stonelessness rates.

Study Limitations

If KIM-1 and NGAL could be measured in the urine at the postoperative 7th day and 1st month in our study, we might have obtained more valuable data and could have commented on late-stage kidney damage.

Conclusion

Our study was conducted on patients whose kidney function tests were normal. Although early diagnosed kidney injury can be treated in a later period, it should be noted that a reversible process may not be obtained in patients with limited kidney function reserves. If the KIM-1 and NGAL values in the urine had been analyzed during the postoperative 7th day and 1st month, then we could have obtained more valuable data and could be commenting on the late-period kidney injury. That said, the fact that our study is a prospective randomized study and that all RIRS implementations were carried out in a single center by the same surgical team comprises the advantages of our study.

Based on our study, it has been concluded that the use of UAS in RIRS practices is effective in preventing kidney injury and does not cause any complications. Multi-centered, prospective, and randomized controlled studies, in which more comprehensive and long-term follow-ups can be performed, are needed to be conducted on the use of UAS during RIRS.

Ethics

Ethics Committee Approval: The present study protocol was reviewed and approved by the Institutional Review Board of Ondokuz Mayıs University College of Medicine (approval number: 2018/21, date: 20.03.2018).

Informed Consent: Informed consent was obtained from all subjects when they were enrolled.

Authorship Contributions

Surgical and Medical Practices: E.K., M.A., A.B., S.G., L.İ., Concept: A.B., R.O., Design: M.A., S.G., L.İ., Data Collection or Processing: E.K., H.Y., R.O., Analysis or Interpretation: E.K., M.A., H.Y., Literature Search: R.O., L.İ., Writing: E.K., L.İ.

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References

1. D'Amico G, Bazzi C. Urinary protein and enzyme excretion as markers of tubular damage. Curr Opin Nephrol Hypertens 2003;12:639-643. [Crossref]
2. Lisowska-Myjak B. Serum and urinary biomarkers of acute kidney injury. Blood Purif 2010;29:357-365. [Crossref]
3. Han WK, Bailly V, Abichandani R, Thadhani R, Bonventre JV. Kidney Injury Molecule-1 (KIM-1): a novel biomarker for human renal proximal tubule injury. Kidney Int 2002;62:237-244. [Crossref]
4. Mishra J, Ma Q, Prada A, Mitsnefes M, Zahedi K, Yang J, Barasch J, Devarajan P. Identification of neutrophil gelatinase-associated lipocalin as a novel early urinary biomarker for ischemic renal injury. J Am Soc Nephrol 2003;14:2534-2543. [Crossref]
5. Waanders F, van Timmeren MM, Stegeman CA, Bakker SJ, van Goor H. Kidney injury molecule-1 in renal disease. J Pathol 2010;220:7-16. [Crossref]
6. Schmidt-Ott KM, Mori K, Li JY, Kalandadze A, Cohen DJ, Devarajan P, Barasch J. Dual action of neutrophil gelatinase-associated lipocalin. J Am Soc Nephrol 2007;18:407-413. [Crossref]
7. Soni SS, Cruz D, Bobek I, Chionh CY, Nalesso F, Lentini P, de Cal M, Corradi V, Virzi G, Ronco C. NGAL: a biomarker of acute kidney injury and other systemic conditions. Int Urol Nephrol 2010;42:141-150. [Crossref]
8. Matlaga BR, Assimos DG. Changing indications of open stone surgery. Urology 2002;59:490-493; discussion 493-494. [Crossref]
9. Mogilevkin Y, Sofer M, Margel D, Greenstein A, Lifshitz D. Predicting an effective ureteral access sheath insertion: a bicenter prospective study. J Endourol 2014;28:1414-1417. [Crossref]
10. Kourambas J, Byrne RR, Preminger GM. Does a ureteral access sheath facilitate ureteroscopy? J Urol 2001;165:789-793. [Crossref]
11. Vanlangendonck R, Landman J. Ureteral access strategies: pro-access sheath. Urol Clin North Am 2004;31:71-81. [Crossref]
12. Dede O, Dağguli M, Utangaç M, Yuksel H, Bodakcı MN, Hatipoğlu NK, Sancaktutar AA, Penbegül N. Urinary expression of acute kidney injury biomarkers in patients after RIRS: it is a prospective, controlled study. Int J Clin Exp Med 2015;8:8147-8152. [Crossref]
13. Ertaş K, Temiz MZ, Çolakerol A, Küçük SH, Şahan A, Yürük E. Effects of flexible ureteroscopy on kidney: A prospective clinical trial. Turk J Urol 2020;46:297-302. [Crossref]
14. Chen YT, Chen J, Wong WY, Yang SS, Hsieh CH, Wang CC. Is ureteral stenting necessary after uncomplicated ureteroscopic lithotripsy? A prospective, randomized controlled trial. J Urol 2002;167:1977-1980. [Crossref]
15. Torricelli FC, De S, Hinck B, Noble M, Monga M. Flexible ureteroscopy with a ureteral access sheath: when to stent? Urology 2014;83:278-281. [Crossref]
16. Rizkala ER, Monga M. Controversies in ureteroscopy: Wire, basket, and sheath. Indian J Urol 2013;29:244-248. [Crossref]
17. Lallas CD, Auge BK, Raj GV, Santa-Cruz R, Madden JF, Preminger GM. Laser Doppler flowmetric determination of ureteral blood flow after ureteral access sheath placement. J Endourol 2002;16:583-590. [Crossref]
18. Tokas T, Herrmann TRW, Skolarikos A, Nagele U; Training and Research in Urological Surgery and Technology (T.R.U.S.T.)-Group. Pressure matters: intrarenal pressures during normal and pathological conditions, and impact of increased values to renal physiology. World J Urol 2019;37:125-131. [Crossref]
19. O'Keeffe NK, Mortimer AJ, Sambrook PA, Rao PN. Severe sepsis following percutaneous or endoscopic procedures for urinary tract stones. Br J Urol 1993;72:277-283. [Crossref]
20. Delvecchio FC, Auge BK, Brizuela RM, Weizer AZ, Silverstein AD, Lallas CD, Pietrow PK, Albala DM, Preminger GM. Assessment of stricture formation with the ureteral access sheath. Urology 2003;61:518-522; discussion 522. [Crossref]
21. L'esperance JO, Ekeruo WO, Scales CD Jr, Marguet CG, Springhart WP, Maloney ME, Albala DM, Preminger GM. Effect of ureteral access sheath on stone-free rates in patients undergoing ureteroscopic management of renal calculi. Urology 2005;66:252-255. [Crossref]
22. Berquet G, Prunel P, Verhoest G, Mathieu R, Bensalah K. The use of a ureteral access sheath does not improve stone-free rate after ureteroscopy for upper urinary tract stones. World J Urol 2014;32:229-232. [Crossref]