## ORIGINAL PAPER

#### UROLITHIASIS

# The effect of isothermic irrigation fluid on ureteroscopic lithotripsy outcomes

Yavuz Karaca<sup>1</sup>, Orhun Sinanoglu<sup>1</sup>, Fatih Ustun<sup>2</sup>, Emre Burak Sahinler<sup>1</sup>, Cahit Sahin<sup>1</sup>, Kemal Sarica<sup>1</sup>

<sup>1</sup>Department of Urology, Sancaktepe Sehit Prof. Dr. Ilhan Varank Research and Training Hospital, Istanbul, Turkey <sup>2</sup>Department of Urology, Sultanbeyli State Hospital, Istanbul, Turkey

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#### Article history

Submitted: Feb. 21, 2024 Accepted: Oct. 16, 2024 Published online: Dec. 27, 2024 **Introduction** Ureteroscopic lithotripsy is amongst the most performed surgeries in urology practice. To achieve better results and lower complications, several approaches have been proposed. Using isothermic irrigation fluid in ureteroscopy is a novel method.

The aim of this study was to show the advantages of body temperature irrigation fluid in ureteroscopy compared to room temperature fluid.

**Material and methods** A total of 94 patients with a single ureteral stone scheduled for semirigid ureteroscopy were enrolled into this study. Patients were randomised into 2 groups: group 1, ureteroscopy with room temperature (20–22°C) irrigation fluid and group 2, ureteroscopy with body temperature (37°C) irrigation fluid. Patient characteristics, stone characteristics (stone side, stone location, stone burden, Hounsfield unit), operation outcomes (operation time, ureteral JJ stenting, complications, stone free rate after 4 weeks, auxiliary intervention, Visual Analogue Scale) were analysed.

#### Corresponding author

Yavuz Karaca Sancaktepe Sehit Prof. Dr. Ilhan Varank Research and Training Hospital, Emek mah. Namık Kemal cad. No: 54 Sancaktepe 34785 Istanbul, Turkey mdyavuzkaraca@gmail.com **Results** There was no statistically significant difference between two groups regarding patient and stone characteristics. Operation time was found to be shorter in group 2 compared to group 1 (p = 0.02). Post-operative pain was also less common in group 2 compared to group 1 (p < 0.001). Complication rates were 17% in group 1 and 8% in group 2 but no statistically significant difference was found. **Conclusions** Isothermic irrigation fluid in ureteroscopy is beneficial because: it facilitates easier ureteral access by decreasing ureteral spasms, shortens operation times, lowers post-operative pain and lowers the complications rates. This method can be used in semirigid ureteroscopy because it is an easily ap-

Key Words: ureteroscopy  $\diamond$  warm irrigation  $\diamond$  ureteral calculi  $\diamond$  laser lithotripsy  $\diamond$  postoperative complications

plicable method with no known associated complications.

# INTRODUCTION

Urolithiasis is a common urological disease with prevalence rates ranging between 4% and 20% in developed countries [1]. Its prevalence is increasing due to diet, obesity, lifestyle changes and chronic diseases such as diabetes, gout [2]. Although some of the cases are asymptomatic, ureteral stones may lead to urinary obstruction, renal colic pain and requiring urgent medical care. Regarding the management of such stones, observation, medical expulsive therapy, extracorporeal shockwave lithotripsy (SWL) and semirigid ureteroscopic lithotripsy (URSL) are commonly applied treatment options. To make a rational decision treatment for such stones, patient related (presence of infection, renal failure, refractory pain, anticoagulant use) and stone related (stone size, location, Hounsfield unit) factors need to be evaluated in detail.

For ureteral calculi that are not likely to pass spontaneously, SWL and URSL are two definitive treatment modalities used commonly for stone removal. When compared to SWL, ureteroscopic lithotripsy gives the chance of immediate stone free status with higher success rates and less need for re-treatment [3, 4]. Despite its relatively invasive nature, complication rates in URSL have decreased substantially with the introduction of smaller ureteroscopes and more effective intracorporeal lithotripsy methods [5]. Semirigid ureteroscopic lithotripsy is a safe and minimally invasive technique which became the first treatment option in the removal of ureteral stones at any location [6].

Like in all endourological procedures, continuous irrigation fluid is used to dilate the mucosal spaces. remove blood clots, tissues and stone fragments during ureteroscopic stone removal [7]. In most cases, irrigation fluid at room temperature (20–22°C) is used with this aim. It is well-known that an irrigation fluid colder than the body temperature can cause a number of systemic complications such as shivering or late anaesthesia recovery by dropping the core body temperature [8]. Cold fluid irrigation can also trigger ureteral spasm which may cause failure to achieve ureteral access, lower stone free rates (SFRs), increased pain and certain complications [9, 10]. To our knowledge only one study has so far aimed to evaluate the possible effects of warm irrigation fluid (40°C) on the course and outcomes of ureteroscopy for stone removal [9].

In this present study, we aimed to evaluate the possible advantages of using body temperature  $(37^{\circ}C)$  irrigation fluid during ureteroscopy procedure compared to room temperature fluid  $(20-22^{\circ}C)$ .

# MATERIAL AND METHODS

## **Study population**

Between June 2022 and July 2023 a total of 100 patients with single radio-opaque ureteral stone scheduled for retrograde ureteroscopic lithotripsy were evaluated. Exclusion criteria were as follows: active urinary infection, age <18 years, pregnancy, indwelling ureteral stent, bilateral stones, multiple stones, previous urolithiasis procedure, solitary kidney and refusal to participate in the study. Multiple, bilateral and radio-lucent stones were excluded to prevent possible biases in measuring the stone volumes and for easier assessment of the stones with kidney-ureter-bladder radiography (KUB) pre/post-operatively. Written informed consent was obtained from all patients which included detailed information about the procedure and study protocol.

## **Study design**

This study was a single-center, prospective- randomised clinical trial. The sample size was calculated using G\*Power (version 3.1.9.6, Germany) considering Visual Analogue Scale (VAS) as primary outcome of interest. We conducted a test with a significance level of 0.05 and power of 0.80 and planned 2 groups with equal size, concluding that at least 15 patients were needed in each group.

A total of 100 consecutive ureteroscopies were performed and prospectively followed. Patients were randomly allocated into two groups using a computerised randomiser web-site (https://www.randomizer.org/) as follows: group 1 (n = 50) consisted of patients undergoing URSL by using irrigation fluids at room temperature (20–22°C) and group 2 (n = 50) comprised patients undergoing URSL by using irrigation fluids at body temperature (37°C). Patients were allocated for each ureteroscopy in a blinded randomisation manner by the resident which means the surgeon was unaware of the randomisation until the surgical procedure. In all patients, detailed medical history, physical examination, routine preoperative blood tests, urine culture and non-contrast computerized tomography (NCCT) were performed. The recorded data included patient and stone characteristics, perioperative and postoperative outcomes as well as VAS for pain and complications. Stone characteristics (side, location, burden) were derived by NCCT. Stone burden (mm<sup>2</sup>) was calculated by multiplying the largest stone diameters of the axial and the coronal NCCT images.

Three patients from each group were lost to followup and remaining 94 patients were enrolled into this study.

## **Surgical technique**

A single-dose 1 gram of intravenous (i.v.) ceftriaxone (in the case of an allergy, ciprofloxacin was used) was administered at the induction of anesthesia. Room temperature irrigation fluids were kept in the operation room while isothermic irrigation fluids were heated to 40°C in the incubator and cooled down to 37-38°C just before the surgery and wrapped the irrigation fluid with air bubble to prevent heat loss. Temperature of the irrigation fluids was measured by an infrared thermometer. All procedures were done under general anaesthesia using the same anaesthetic drugs. With the patient in the lithotomy position, a transurethral 6f catheter was placed for continuous bladder emptying. The ureter was accessed by a 6.5/8.5 semi-rigid ureteroscope (Richard Wolf, Germany). A safety guidewire was used in all cases. After the identification of the stone, holmium laser lithotripsy was performed (laser setting: 0.8 joule/ 10 hertz) with Litho Low Power Holmium Laser System, USA using 365  $\mu$ m diameter laser fiber. Stone fragments were removed by either forceps or nitinol basket. Ureteral stenting was decided considering perioperative parameters such as presence of mucosal oedema and/or injury and size of the stone fragments. Intravenous paracetamol was administered to all patients perioperatively.

#### **Outcome assessment**

Operation time (minutes), ureteral stenting (yes/ no), complications were recorded for each patient during the procedures performed. Complications were graded according to Modified Clavien classification System (MCCS) for ureteroscopy [11].

Patients were assessed for pain 4 hours after the operation using VAS (0 – no pain, 10 – worst pain ever experienced) by the resident (Figure 1). Four weeks after the operation, patients were re-evaluated by either kidney-ureter-bladder radiography (KUB) or NCCT. Residual fragments <4 mm were considered as stone free. Auxiliary interventions were recorded if present.

## **Statistical analysis**

Statistical analysis was performed with IBM SPSS software (version 26 for MacOS, IBM, New York, USA). The distribution of the variables was measured by Kolmogorov-Smirnov test. Mann-Whitney U test and  $\chi^2$  test were used for statistical analysis. A p-value <0.05 was considered as statistically significant.

#### **Bioethical standards**

The study was approved by the Institutional Reviewer Board (number of approval: May 2022. No. 58).

## RESULTS

Of 94 patients, 66 (71%) were male, 28 (29%) were female. The mean age of the patients was 35.79 years (SD = 7.8). Stones were located in: 12 (13%) upper, 17 (18%) middle and 65 (69%) lower ureteral portions.

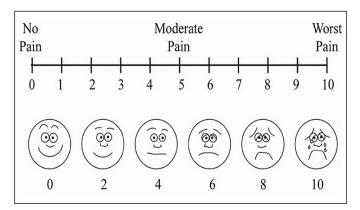


Figure 1. Visual Analogue Scale chart.

Forty-five (47%) cases had stones on the right side, 49 (53%) had stone on the left side. There was no statistically significant difference between two groups regarding patient related (age, sex) and stone-related (stone side, stone location, stone burden, Hounsfield unit) characteristics. Patient related and stone-related characteristics are summarised in Table 1.

#### Evaluation of our data revealed following findings

Procedural duration was significantly shorter in group 2 compared to group 1 (p = 0.02). Additionally, we were also able to demonstrate that, post-operative pain was less common in isothermic irrigation group than room temperature irrigation group (p <0.001). No statistically significant difference was found regarding ureteral stenting (p = 0.102), stone free rates at 4<sup>th</sup> week (p = 0.694) and auxiliary (p = 0.460) between group 1 and group 2. Although there was a difference in the complication rates between two groups (17% in group 1 and 8% in group 2 respectively), the difference was not statistically significant (p = 0.216). The results are summarised in Table 2.

All complications were minor (grade 1) according to MCCS (6 patients had mucosal injury, 2 had transient hematuria and 4 had post-operative fever; Table 3).

# DISCUSSION

With a nearly 3% rate of all urinary stones in general population, ureteral stones require a special attention in the majority of cases due to the risk

**Table 1.** Evaluation of the patient and stone-related charac-teristics

	Room temperature (group 1, n = 47)	Body temperature (group 2, n = 47)	p-value	
Age (years), mean ±SD	35.81 ±8.83	35.77 ±6.72	0.625ª	
Sex Male Female	34 13	32 15	0.652 <sup>b</sup>	
Stone side Right Left	23 24	22 25	0.836 <sup>b</sup>	
Stone location Upper Middle Lower	6 10 31	6 7 34	0.716 <sup>⊾</sup>	
Stone burden (mm²)	48.78 ±21.18	54.05 ±43.78	0.533ª	
Hounsfield unit	761.32 ±274.93	667.38 ±255.19	0.071ª	

<sup>a</sup> Mann-Whitney U test

<sup>b</sup> χ² test

	Room temperature (group 1, n = 47)	Body temperature (group 2, n = 47)	p-value 0.02ª	
Operation time (minutes, mean)	21.55 ±8.40	17.98 ±9.93		
Ureteral JJ stenting Yes No	38 9	31 16	0.102 <sup>b</sup>	
Complications Yes No	8 (17%) 39 (83%)	4 (8%) 43 (92%)	0.216 <sup>b</sup>	
Stone-free rate at 4 weeks Yes No	44 3	43 4	0.694 <sup>b</sup>	
Need for auxiliary intervention Yes No	3 44	5 42	0.460 <sup>b</sup>	
VAS values (0–10)	4.26 ±1.7	2.72 ±1.45	0.000ª	

**Table 2.** Comparative evaluation of procedure-related para-meters and outcomes in both groups

<sup>a</sup> Mann-Whitney U test

<sup>b</sup> χ<sup>2</sup> test

VAS – Visual Analogue Scale

#### Table 3. Post-operative complications

Complications	Group 1	Group 2	p-value	
Mucosal injury	4 (8%)	2 (4%)		
Transient macroscopic hematuria	1 (2%)	1 (2%)	0.216	
Post-operative fever	3 (6%)	1 (2%)		

of obstruction and severe colic pain. Regarding this issue, while small, asymptomatic ureteral stones (<5 mm) may pass spontaneously in most cases, larger stones causing obstruction, pain and/or infection may require an active treatment. Ureteroscopic lithotripsy is the most commonly performed procedure in the minimal invasive removal of such stones. Related with the ureteroscopic procedure, key to a successful operation is obtaining an easy ureteral access. Although this is possible in most cases in experienced hands, dimensions of the ureter may limit a successful access to upper urinary tract in some cases. Regarding this critical issue, in a prospective study from a tertiary stone unit showed that, 9% of all ureteroscopies were aborted due to a failed ureteral access [12]. Ji et al. [13] found a failed ureteral access rate of 11.5% in 512 ureteroscopic stone removal procedures. Based on the likelihood of this problem, endourologists introduced several approaches for facilitating easier ureteral access to improve the efficacy and safety of ureteroscopy. Currently most surgeons tend to prefer ureteral stenting after the initial failed ureteroscopy to achieve passive ureteral dilatation and perform the definitive procedure after a few weeks. Although this method has shown to be effective with minimal complications [13]. requirement of staged operation disturbing patients and increasing the costs were the main disadvantages noted [14]. As a second approach, balloon dilatation of the ureter can be applied in the same session but serious complications such as ureteral injury/stricture may have been reported in some cases after this maneuver [15, 16]. Last but not least, use of  $\alpha$ -blockers for ureteral relaxation (dilation) prior to ureteroscopic applications has been tried and Avdin et al. showed that  $\alpha$ -blockers applied 3 days before ureteroscopy may increase success rates and decrease the complication rates [17]. However possible side effects of these medications seem to be main concerns limiting the use in this purpose. As an alternative method, warmer irrigation fluid (40°C) has been used by Rezzai et al. [10] in ureteroscopy, in an effort to create acute ureteral dilatation for easier ureteral access and they found out that warmer irrigation  $(40^{\circ}C)$  creates an acceptable ureteral relaxation, decreases ureteral spasms compared to room temperature irrigation (22–24°C) thereby resulting in better surgical outcomes. On the other hand, Patel et al. [18] failed to show any difference regarding ureteral caliber and peristalsis between 37°C and 43°C irrigation ureteroscopy in a porcine model. Nevertheless, they stated that they continue using body temperature irrigation fluid in ureteroscopy [18]. At irrigation fluid temperature higher than 43°C, denaturation of urinary tract proteins start so care must be taken [19, 20]. Studies showed that continuous fluid irrigation through endoscope is the key factor maintaining ureteral lumen temperature between safe range in laser lithotripsy [21]. On the other hand in our study, we observed evident ureteral relaxation with significantly low spasms and peristalsis with isothermic fluid application compared to room temperature irrigation which provided easier access to the ureters and shortened the total procedural time in our cases.

Operation time is a highly crucial factor in ureteroscopy. Several reports stated that longer operation times may lead to certain complications during and after ureteroscopic procedures. In a retrospective analysis of 2,010 ureteroscopies, researchers found out that operation time was significantly higher in patients with complications compared to patients without complications [22]. Salciccia et al. showed that longer operation time is strongly associated with hospitalization need after ureteroscopy [23]. Additionally, longer operation times was found to be associated with higher grade complications (Clavien score ≥III) such as ureteral perforation, infectious complications and urosepsis after ureteroscopy [24-26]. Any new advances in endourology have the objective of shortening the operation time and reducing the complication rate [27]. In this study, we found out that warm irrigation shortens operation time  $(21.55 \pm 8.4)$  compared to room temperature irrigation  $(17.98 \pm 9.9)$ ; p < 0.05). Isothermic irrigation facilitates ureteral access, decreases ureteral spasms therefore shorter operation times can be anticipated in ureteroscopy. Although there was no statistically significant difference in complication rates between two groups in our study (p = 0.216), it is clear that warm irrigation is beneficial compared to room temperature irrigation to limit the risk of serious complications during these procedures.

Pain is amongst the most common complications of ureteroscopy. While increased pressure of the pelvicalyceal system due to continuous irrigation and the distention of renal capsule thought to be the primary cause, factors such as ureteral spasm, mucosal irritation can play role in pain after ureteroscopy [10]. In our study we found out that, warm irrigation significantly decreases post-operative pain after ureteroscopy compared to room temperature irrigation (p < 0.001). Lower integrated relaxation pressure (IRP) [10] and shorter operation times [24] are the main advantages of warm irrigation compared to room temperature irrigation in terms of decreased post-operative pain. Lower hospital re-admission rates, less need for narcotics, shorter hospitalization and better QOL may be achieved by less painful ureteroscopies [28, 29]. Low IRP is also associated with lower post-operative infectious complications [30].

Based on the reported data in the literature and our findings as well, we may claim that as practical and low-cost approach, use of isothermic irrigation fluid during ureteroscopic stone removal procedures may provide certain advantages to the endourologists. An easy and atraumatic access to the ureteral lumen without having any difficulty is the main expectation of surgeons and based on the useful effects mentioned above irrigation with warm fluid during the procedure will certainly shorten the procedural time. This advantage will in turn result in limited complications (mainly minor in nature) and more importantly limited pain after the procedure which affects the patient's quality of life to significant extent. Although not statistically significant the complication rate was also lower in cases being treated with isothermic irrigation and this could also constitute another important advantage for the use of isothermic irrigation fluid during ureteroscopic stone manipulations.

Our study has some limitations. First, our study consisted of a relatively small patient group. However, taking into account the highly limited data reported so far on this issue in the literature, we believe that our findings will contribute enough in this aspect. Secondly our follow-up time was limited to 4 weeks and we have no data on the long-term effects and complications of this method. Lastly, although we showed that application of warm irrigation significantly decreases post-operative pain compared to room temperature irrigation in ureteroscopy, the absence of quality-of-life assessment in our current study may constitute another limitation. We strongly believe that further studies with larger series of cases on the clinical use of this method may achieve more significant results.

# CONCLUSIONS

Our results and the limited data published so far indicate well that ureteroscopic procedures by using warm irrigation (37°C) fluid enables the surgeon to gain an easier ureteral access, shortens the operational duration and results in less pain compared to the use of room temperature irrigation (20–22°C) fluid during these interventions. Shorter operation time is the main finding of this study owing to the positive effects to post-operative pain and complication rate. As an easily applicable and practical method with above mentioned advantages as well as no associated complications use of isothermic irrigation fluid during ureteroscopy may be helpful for successful and safe procedures.

#### CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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#### ETHICS APPROVAL STATEMENT

The study was approved by the Institutional Reviewer Board (number of approval: May 2022. No. 58).

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