

PROSPECTIVE RANDOMIZED COMPARISON OF 2 URETERAL ACCESS SHEATHS DURING FLEXIBLE RETROGRADE URETEROSCOPY

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Introduction

Ureteral access sheaths provide effective and reliable access during flexible ureteroscopy, and have demonstrated numerous advantages. Access sheaths have been shown to optimize success of flexible ureteroscopy, decrease operative time and cost, and minimize morbidity [1]. Technological advancements in ureteral access sheath design have significantly improved physical properties that have led to reduced failure rates and complications, however, the general design of access sheaths has remained similar for some time until recently. New designs, though commercially available, have a paucity of data comparing different models.

Background and Significance

After gaining initial ureteral access with a guidewire, access sheaths are typically back-loaded onto the safety guidewire through the inner lumen of the dilator, allowing for gradual ureteral dilation and smooth access to the upper collecting system. Until the recent development of Re-Trace™ (Coloplast) and Flexor Parallel™ (Cook Urological), guidewires would remain within the inner lumen of the access sheath after removal of the dilator, requiring additional instruments to pass directly alongside the guidewire as they are advanced through the sheath. These devices have now been designed with a slit on the dilator that guides the wire outside of the sheath, leaving the guidewire to remain parallel but exterior to the sheath as the dilator is removed. This design limits the need to place an additional working wire, and provides a clear working channel through the lumen of the sheath. A clear working channel is likely to increase irrigation flow for improved visibility, reduce intrarenal pressures, and help minimize interference between delicate ureteroscopes, baskets, and guidewires.

A recent prospective study by Doizi et al [2] evaluating the ability of the Re-Trace™ to gain ureteral access with the use of a single safety guidewire demonstrated good insertion rates and validated the effectiveness of the design, however, no study to date has systematically evaluated the impact of the design on ureteral trauma or provided a comparative analysis between commercially available devices incorporating this design.

We propose this randomized study to evaluate the effectiveness and safety of current commercially approved devices integrating this design (Re-Trace™ and Parallel™).

Purpose and Objectives

The primary objective of this study will be to evaluate the ability for 2 different ureteral access sheaths to obtain and maintain access to the upper collecting system, as well as evaluate ureteral injury using standardized 5-point classification system.

Secondary endpoints will include evaluating ease of instrument passage, stone extraction, device placement, and radiopacity.

Hypothesis

We hypothesize that the modified designs of Re-Trace and Parallel devices will demonstrate similar safety profiles.

Research method

The proposed study is a prospective randomized controlled trial comparing the safety and efficacy of ureteral access sheaths used in flexible ureteroscopy.

Patients scheduled for flexible ureteroscopy will be identified by the investigator at clinic visits or hospital admission at Cleveland Clinic. The research coordinator will approach patients to determine the patient's initial interest in research, and if interested, the consent process will be initiated prior to surgery.

In order to be eligible the patient must be a suitable operative candidate for flexible ureteroscopy and have an abdominopelvic computed tomography (CT) to delineate pre-operative stone size, with measurements captured in greatest axial and coronal dimensions. Patients who have had prior ipsilateral upper urinary tract reconstructive procedures, ureteral stricture, ureteral malignancy, or impacted ureteral stones will be excluded. Pregnant subjects will also be excluded.

Ureteroscopic treatment of renal calculi is a standard of care treatment approach, and participating in this study will not deviate from standard of care ureteroscopy procedures, however, procedures specific to the research will involve being randomized to the use of one of two ureteral access sheaths:

1. Coloplast Re-Trace
2. Cook Flexor Parallel

Choice of sheath length will be left to the discretion of the surgeon based on body habitus and site of pathology, while sheath diameter will be standardized to 12/14F. Smaller diameter sheaths (11/13F, 10/12F) will be used if significant resistance occurs during advancement, otherwise patients will be excluded from the study if unable to gain ureteral access, or if ureteral balloon dilation or semi-rigid ureteroscopy is required to gain ureteral access.

If unable to obtain access with the initial sheath the patient is randomized to, the patient will be randomized to a backup sheath. If unable to obtain access with backup sheath, then a second backup sheath will be used. If unable to obtain access with any of the three sheaths with diameter 12/14F, an attempt will be made with up to three additional sheaths of a similar smaller diameter (11/13F or 10/12F), in a random order. If access has not been obtained after randomization to 6 sheaths, the patient will be considered a failure and it will be the surgeon's discretion to either place a stent and do a staged second look at a later time, proceed with ureteroscopy without a sheath, or balloon dilate.

Pre-operative data collection will include age, race, gender, ASA (American Society of Anesthesiologists) score (for comorbidity assessment), body mass index (BMI), and disease history, including stone disease, prior ureteroscopic procedures, vascular disease, and pelvic radiation. Disease fields that will be obtained include stone size (maximal axial and coronal dimensions), degree of hydronephrosis (mild/moderate/severe), and duration of prior ureteral stenting (if applicable).

Intra-operative data will include recording any buckling, kinking, or difficulty in instrument passage that occurs. Surgeons will be asked to subjectively rate the ease of sheath placement, stone extraction through sheath (if applicable), and ease of instrument passage on a scale 1 to 4, with 1 being poor and 4 being excellent. Ureteroscopic video will be taken for all procedures, and ureteral wall injuries will be evaluated after removal of the UAS by a urologist (Olivier Traxer, MD) blinded to the treatment device using the classification methodology previously described by Traxer and Thomas [3].

UAS related injuries determined by ureteroscopic video will be categorized into five (or 4 per PULS) grades, ranging from 0-4, defined by the following characteristics:

- Grade 0: No ureteral lesion or only mucosal petechiae
- Grade 1: Mucosal erosion or a mucosal flap without smooth muscle injury
- Grade 2: Damage to the mucosa and smooth muscle but no adventitia, with no retroperitoneal tissue visible
- Grade 3: Injury indicating ureteral perforation involving the full thickness of the ureteral wall, including the adventitia
- Grade 4: Total ureteral avulsion

Location of the primary injury site(s) (lumbar, iliac, pelvic ureter) will also be noted to determine impact on development of future pathology including stenosis, fistula or ureteral stone formation.

Perioperative fields will include OR (surgical) time, type of anesthesia, laser fiber size, guidewire specifications, need for dual lumen catheter or introducer catheter, settings of lithotripsy (if applicable - rate/energy), use of active extraction for fragments (include basket/grasper specifications), any device breakage or damage, and intraoperative complications.

All other procedures associated with standard of care for ureteroscopic treatment of stones, including stent placement, will be left to the discretion of the investigator. Postoperative fields will include postoperative complications, need for ancillary procedures, development or persistence of hydronephrosis/obstruction, and stone-free status at 4 to 6 week postoperative imaging as determined by ultrasound of kidneys, ureters and bladder.

Sample Size

A recent prospective study evaluating ureteral damage in 359 patients undergoing ureteroscopy with a 12/14F diameter sheath found that when using the same 5-point ureteral damage classification system, low grade ureteral injury (score of 0-1) occurred in 86.6% (311/359) of patients, and high grade (score of 2-4) occurred in 13.3% (48/359) of patients.

Based on this preliminary data, the study is powered to detect whether there is a difference between device designs to cause low (0-1) vs. high grade (2-4) ureteral injury. Using an alpha of 0.05 and beta of 0.80, and assuming a difference greater than 20% between groups is considered significant, approximately 49 patients will be required per arm, for a total of approximately 98 patients.

We are requesting the IRB allow for a total enrollment of 117 patients to account for screen failures (inability to gain access, rigid ureteroscopy required, strictures, etc).

Recruitment and Consent

Based on current volumes of ureteroscopic procedures, we anticipate approximately 2-3 patients per week will be randomized requiring a total of approximately 9-12 months of active enrollment between to reach a total of 100 randomized subjects. Patients will be recruited from either office visits or inpatient hospitalizations. The study coordinator will consent patients using the uploaded consent form accompanying this document. All procedures, devices and protocols are standard of care. There is no additional cost to the patient outside of standard care. The patient's insurance company will be billed for medical costs.

Data Analysis Plan

Data analysis will involve comparisons of ureteral damage between groups related to device design, gender, age, BMI, preoperative stenting, prior stone disease, and prior stone procedures. Differences in operative time, ease of placement, ability to maintain access, and ease of instrument passage will also be evaluated between devices, as well as post-operative complications, success rates, and device failure rates. The analysis will be completed by the approved researchers in coordination with a CCF biostatistician Jesse Schold. Study data will be stored on the RedCap database. Data may also be stored on encrypted CCF issued IronKey and encrypted CCF issued computers. Signed consent forms will be stored in a compartment with a lock for the duration of the trial. Approved researchers on this IRB will have access to these data.

Adverse Events and Data Monitoring Committee

The investigator will report any adverse events to the IRB within 10 days of awareness. A data monitoring committee will not be used. The primary risk to participants will be the loss of confidentiality, which will

be maintained by physical and electronic locks. Any unexpected findings of concern will be communicated face-to-face to the patient by the investigator in a clinic visit. A Data Monitoring Committee will not be used for this study as the devices and procedures used are standard care.

Study Costs

REFERENCES

1. Kourambas, J., Byrne R, Preminger G: Does a ureteral access sheath facilitate ureteroscopy? *J Uro* 165:789, 2001.
2. Doizi S, Knoll T, Scuffone CM: First clinical evaluation of a new innovative ureteral access sheath (Re-Trace): A European Study. *World J Urol*. May 3, 2013.
3. Traxer O, Thomas A: Prospective evaluation and classification of ureteral wall injuries resulting from insertion of a ureteral accesss sheath during retrograde intrarenal surgery. *J Urol*. 189: 580-584.