

## **Evaluation of ureteral stents in the management of stone disease.**

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## INTRODUCTION

Ureteral stents are commonly-employed during routine stone procedures, including ureteroscopy, percutaneous nephrolithotomy, and shockwave lithotripsy. Their primary function is to preserve drainage and decompression of urine on the affected side. After stone procedures, they are commonly employed to counteract ureteral swelling which may otherwise temporarily impair drainage.

Though considered a staple of modern urology, ureteral stents are nonetheless the source of complaints from patients, who often report significant bother associated with the presence of a stent. Symptoms include urinary urgency and frequency from irritation of the bladder by the stent, pain in the back associated with reflux of urine along the stent, minor aches and cramping from the stent itself, blood in the urine, and discomfort during removal in the office. Over the past few decades, newer and smaller stents have become available; however, studies evaluating the impact of these newer stent technologies have been conflicting. Catheter/stent diameter is measured in French scale (Fr.). The french size is a measurement of external diameter of the catheter, not the internal drainage channel. (Fr. = D (mm) x 3) We plan to use 6Fr soft and hydrophobic, to prospectively evaluate the effect of stent composition upon patient comfort and satisfaction following stone surgery.

## RESEARCH QUESTIONS

Are hydrophobic stents more comfortable than standard soft stents?

## METHODS

### *Study design*

This is a single institution, randomized, single-blinded study to evaluate patient comfort and satisfaction following surgical stone management procedure with randomization allocation ratio of 1:1 (size 6Fr, soft; size 6Fr, hydrophobic;). Catheter diameter is measured in French scale (Fr.) the french size is a measurement of external diameter of the catheter, not the internal drainage channel. (Fr. = D (mm) x 3)

This study will be conducted at Washington University and will enroll 100 participants.

### *Subjects*

The study team will identify eligible patients from WU Urology patient population based on the following inclusion/exclusion criteria:

### *Inclusion Criteria*

The following patients will be eligible for participation in the study:

1. Over 18 years of age and willing and able to provide informed consent

2. Patients with current urinary stone disease, undergoing any procedure requiring a stent placement

### ***Exclusion Criteria***

The following patients will **not** be eligible for participation in the study:

1. Patients with compromised urinary tract due to cancer (e.g. bladder tumor, ureteral obstruction from non-GU malignancy)
2. Patients requiring bilateral surgical stone management procedure
3. Patients with any single stone exceeding 1.5 cm
4. Patients with severe concurrent disease, infection, or co-morbidity that, in the judgment of the investigator, would render the patient inappropriate for enrollment
5. Any patient who is on a genitourinary anticholinergic medication at baseline

### ***Study procedures***

#### **Screening and Informed Consent**

Subjects will be seen and counseled by their Urologist as part of the normal course of practice. Once a decision is made to proceed with a surgical procedure for stone management (cystoscopy with stent placement, ureteroscopy with intracorporeal lithotripsy), patients will be offered study participation and one of the members of the research team will discuss the study with them.

The discussion regarding study participation will take place in a private setting, such as in a private consult room, to maintain confidentiality. HRPO approved consent form will be used to guide the consent process and document participant's consent. During the consent process, the study team will explain that all stents used in this study are consistent with standard of care, but that an attempt is being made to determine features of the stent which may affect patient satisfaction. Patients will be asked to allow themselves to be randomized with respect to the stent they will receive. Patients will be encouraged to ask questions and discuss the study with family. They will be given ample time to review the consent. It is possible that some participants may be contacted by phone to assess their interest in this study. If the participant expresses interest in the study, informed consent form will be mailed/mailed to him/her. This will be done in an effort to allow the patient ample time to read the consent at home, consider the study and discuss it with friends and family. This will not replace the face to face consent discussion the research team will have with the patient prior to signing the consent form.

Patients may decline to participate without an impact on their care. They will not be pressured to participate. No study related procedures will take place prior to the completion of the informed consent process and participant signing the HRPO approved consent.

#### **Baseline**

Once informed consent for study participation is obtained, patients will be asked to complete:

- AUA Symptom Score Questionnaire
- Analog pain scale

#### Day 0 (Stent Insertion)

Randomization will take place prior to the procedure. Patients will be randomized in a 1:1 ratio for stent composition, soft vs. hydrophobic, for a total of 50 patients in each cohort. To minimize selection bias, a randomization table will be developed before initiation of enrollment. Envelopes containing randomization assignments will be created, sequentially numbered and sealed. Once enrollment is initiated, randomization envelopes will be opened for each subject after informed consent is granted and study eligibility is confirmed. Subjects will be blinded to the stent assignment so their reported pain level and satisfaction is not influenced by the knowledge of the inserted stent type.

The surgical procedure for stone management will be performed via an approach consistent with current standards-of-care.

Patients will be discharged on a standard regimen, consisting of Norco, or an equivalent narcotic, tamsulosin, and docusate. Patients will not be placed on anticholinergic or phenazopyridine medications at discharge.

When clinically indicated, exchange of stent is permitted. The patient data will be evaluable so long as adherence to initial randomization stratification is maintained.

#### At the Time of Stent Removal

The participants will be asked to complete the following questionnaires prior to stent removal:

- Ureteric Stent Symptoms Questionnaire 1 with Analog Pain Scale included (USSQ 1 stent in situ)
- AUA Symptom Score Questionnaire
- Satisfaction Questionnaire

In addition, the patients will be asked to share with us the number of days pain pills have been taken, and their compliance with tamsulosin and docusate. We will assess for any use of anticholinergics, other analgesics and antibiotics.

The participants will then undergo cystoscopic removal of the stent in clinic.

Results of any standard of care imaging obtained prior to stent removal will be collected.

## Day 7 Post-Stent Removal

On day 7 post stent removal, participants will be asked to complete:

- Ureteric Stent Symptoms Questionnaire 2 with Analog Pain Scale included (USSQ 2 post stent)
- AUA Symptom Score Questionnaire
- Satisfaction Questionnaire

Copies of the surveys along with addressed and stamped envelopes will be given to the participants at the time of office visit for stent removal. Surveys will be self-administered at home and mailed back to the research center. Reminder phone calls will be made to the participants to assure compliance.

## ***Outcome measures***

1. Stent
  - a. Type
  - b. Composition (soft or hydrophobic)
  - c. Length
2. Stent complications
  - a. Migration
  - b. Malposition
  - c. Dislodgement
  - d. Need for re-insertion
3. Time to stent removal
  - a. Clinically planned or required due to symptoms
4. Health Related Quality of Life
  - a. Ureteric Stent symptoms Questionnaire 1 and 2
  - b. AUA Symptom
5. Pain Score as reported by the participants on the self-administered assessment
6. Procedure Satisfaction Questionnaire
7. Use of analgesics for pain control
  - a. documented pain prescription at the time of discharge
  - b. self-reported duration of analgesics use after stent insertion (in days)
8. Residual stone burden
  - a. KUB, U/S, CT

## ***Covariate data***

1. Gender
2. Race

3. Height
4. Weight
5. Patient medical/surgical history
6. Type of procedure
7. Etiology of disease

### ***Sample size calculation and statistical analysis***

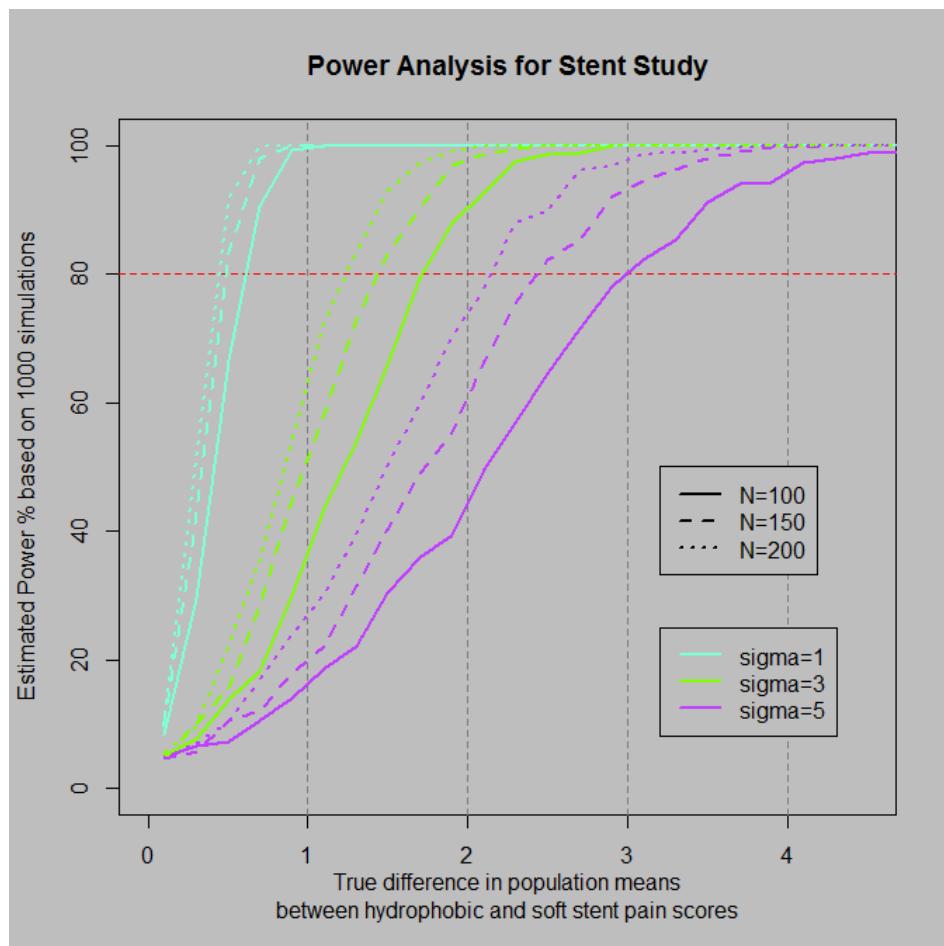
#### **Power Analyses**

Power is the probability to detect statistically significant results from a sample, if one actually exists in the population. In order to determine the sample size needed for adequate power, we are using an alpha (criterion of significance) of 0.05 in a two-tailed (non-directional) test (Figure) as our primary outcome is the pain index score.

Since there isn't a pilot study or previous work to base the assumptions of the power analysis, 216,000 simulations were performed varying sample size ( $n=100,150,200$ ), standard deviation of the population ( $\sigma=1,3,5$ ), and assumed true difference in population means of the pain index score (24 differences ranging from 0.1 to 4.7). For each combination of sample size, population standard deviation, and difference in population mean, 1000 simulations were tested. The results for these simulations are displayed graphically in Figure 1. The power analysis was calculated for soft versus hydrophobic stents.

Because of the uncertainty of the assumptions of the power analysis, it is recommended to perform an interim analysis at  $N=100$ . If there is low variability in the populations or if the true difference of the population is greater than 3 (or some combination of the two), 100 samples would potentially provide ample power to detect the differences in the populations.

Figure 1.



### Planned Statistical Analysis

We will evaluate parameters, including stent composition, and outcomes including complications, hematuria, pain medication requirements, return to work/normal activities, subjective assessments of pain, discomfort and satisfaction, and factors associated with stent removal, including periprocedural discomfort, and need for early/delayed removal of the stent. We will use t-test, U-test, ANOVA, chi-squared tests, and multivariate statistical methods to evaluate our outcomes.

After 100 patients are accrued, an interim analysis will be performed in order to determine if the research questions are statistically significant at the 0.05 level. If they are significant results, patient enrollment will end. If they are not significant, a second power analysis will be performed to determine if 100 more patients would provide reliable statistical power of achieving significant results. This power analysis will be much more informative as there would be actual estimates of the populations of interest. If it is determined that an additional 100 more patients would still be unlikely to yield statistically significant results, patient enrollment will end. If it is determined that an additional 100 patients would be likely to yield statistically significant results, an additional 100 patients will be enrolled into the study.

## **RISKS AND BENEFITS**

The results from this study will not directly benefit the patients who agree to participate, however, we hope they will help determine if composition of a stent impacts patient comfort, satisfaction, and outcomes following stone surgery. Knowledge gained from this study may help us improve our stone management practice.

Participation in this study will not affect the patient's risks associated with the standard of care stone management procedure. Risks associated with the surgical procedure for stone management will be discussed with all participants as part of their clinical care and clinical consent for the procedure will be obtained. Patients may feel uncomfortable or embarrassed answering some of the questions on the study questionnaires. They will be instructed to skip any questions that they are not comfortable answering.

## **DATA AND SAFETY MONITORING**

Participation in the proposed study will not pose any risks to the participants beyond what is expected from the standard of care surgical stone management procedure. Data will be reviewed bi-annually to ensure there are no significant outliers. If such are noted, they will be investigated by the research team.

The PI will monitor the study for any serious adverse events (SAEs) from the time of the initial stent placement through the completion of the 7 day post stent removal questionnaires. All HRPO guidelines for reporting SAEs will be followed. Should there be a serious adverse event that occurs related to the proposed protocol that increases the risks to the participants, the study will be stopped, an investigation will be conducted, and a findings report will be generated before the study is resumed.

## **REFERENCES**

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**Table 1: Schedule of Study Procedures and Assessments from Screening to Post-Stent Removal**

	<b>Screening Visit (Up to 28 days before surgery)</b>	<b>Day 0 (Stent Insertion)</b>	<b>Stent Removal</b>	<b>Day 7 (± 1 Day) Post Stent Removal</b>
<b>Informed Consent</b>	X			
<b>Demographics</b>	X			
<b>Medical &amp; Surgical History</b>	X			
<b>Height &amp; Weight</b>	X			
<b>Incl./Excl. Criteria Confirmation</b>	X	X		
<b>Randomization</b>		X		
<b>Procedure Data Collection</b>		X	X	
<b>Satisfaction Questionnaire</b>			X	X
<b>Analog Pain Scale</b>	X			
<b>AUA Symptom Score</b>	X		X	X
<b>Imaging Data</b>			X	
<b>USS Questionnaire 1 (stent in situ)</b>			X	
<b>USS Questionnaire 2 (post stent)</b>				X
<b>Adverse Events</b>		X	X	X