PROTOCOL TITLE: *Prospective, single arm study to assess duration of ureteral rest prior to ureteral reconstruction surgery*

PRINCIPAL INVESTIGATOR:
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VERSION DATE:
1.1

STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	
IND / IDE / HDE #	
Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	20-25
Funding Source	None
Indicate the type of consent to be obtained	☒ Written ☐ Verbal/Waiver of Documentation of Informed Consent ☐ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process
Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☒ Yes ☐ No
DSMB / DMC / IDMC	☐ Yes ☐ No

OBJECTIVES:

Our objective is to assess the effect of duration of ureteral rest, defined as time from conversion of ureteral stent to percutaneous nephrostomy, on stricture length prior to ureteral reconstruction surgery. The null hypothesis is that we will observe no difference in ureteral stricture length when evaluated at two weeks of rest compared to six weeks of ureteral rest.

BACKGROUND:

In the setting of ureteral strictures, it is well accepted that ureteral rest, defined as the absence of a ureteral stent or percutaneous nephroureteral tube, improves outcomes for ureteral reconstruction surgery.[1] Ureteral rest allows for stricture maturation and decreases inflammation allowing for easier dissection and improved intraoperative discernment of stricture margins. However, the optimal duration of rest has not been established and varies by surgeon preference and experience, ranging from 1-6 weeks. Percutaneous nephrostomy tubes, the alternative for drainage that allows for ureteral rest in the setting of a ureteral stricture, require patients to have an external hardware device and can be quite cumbersome. A shorter period of rest would be preferred if possible, however not if this were to compromise surgical outcomes. Shorter periods of rest may not allow for full stricture maturation, however this process has never been formally evaluated overtime.

All patients at our institution undergo an endoscopic evaluation in the operating room to evaluate stricture location, length, caliber, and quality prior to definitive ureteral reconstruction. The exact timing of this prior to definitive ureteral reconstruction is variable based on surgeon and patient availability, but generally all patients undergo at least six weeks of ureteral rest.

Endoscopic instruments are routinely used during all ureteral reconstruction cases, however a formal endoscopic evaluation with antegrade and or retrograde pyelograms to reassess stricture length are not always routinely performed. We propose a prospective, single arm study where patients will undergo endoscopic evaluation in the operating room after two weeks of ureteral rest, and then again on the day of ureteral reconstruction surgery (approximately 6 weeks of ureteral rest). Participation in this study would only expose patients to approximately 5 minutes of additional anesthetic time, however, would expose patients to a small amount of additional radiation during their definitive ureteral reconstruction surgery, estimated at 1-4mSv, approximately 1-2 additional x-rays.

STUDY ENDPOINTS:

The primary study endpoint is determination of ureteral stricture length measured by antegrade or retrograde pyelogram at two and six weeks of ureteral rest.

The secondary endpoint is ureteral stricture quality at two and six weeks of ureteral rest (example, transformation from narrowing to complete obliteration).

STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S):
No investigational agents will be used.

PROCEDURES INVOLVED:
Prior to surgery: Patients who have been identified and meet inclusion criteria for this study will be approached by a study team member either in the clinic or the pre-op area prior to the initial endoscopic evaluation surgery.

Day of endoscopic evaluation: After consent is obtained, all patients will undergo routine endoscopic evaluation of their stricture as determined by the surgeon. This usually includes cystoscopy, antegrade and retrograde pyelogram, and ureteroscopy. The fluoroscopy images will be saved in the EMR. This is all standard of care procedure that would occur regardless if the decides to be a part of the study.

Day of definitive ureteral repair: After consent is obtained, all patients will undergo repeat endoscopic evaluation with antegrade and or retrograde pyelogram prior to definitive ureteral repair**. This is the only research related procedure that is outside the standard of care.** Patients routinely undergo endoscopic evaluation the day of surgery already however do not always have a formal antegrade and retrograde pyelogram obtained. Participation in the study will guarantee that they will undergo this evaluation, although many patients undergo this repeat evaluation already as determined by the surgeon.

After surgery: All patients undergoing ureteral reconstruction surgery will have a preoperative CT scan. Using this, we will measure the height of the L5 vertebrae. We will extrapolate stricture length on retrograde pyelogram by using this measurement for scale. All stricture length measurements will be done by the same researcher and they will be blinded to timing of when the images were obtained. Ureteral stricture quality will also be graded as either a narrowed segment or obliterated segment, with obliteration defined as inability of any contrast to pass through the segment on retrograde or antegrade pyelogram. Luminal diameter will also be measured.

Post-surgery: All patients will return to clinic for standard of care follow up. All patients will be included regardless of their follow up postoperatively as the purpose of the study is to determine stricture maturation preoperatively.

SHARING RESULTS WITH PARTICIPANTS
Results will not be shared with participants.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria:

- >18 years of age

- Undergoing ureteral reconstruction surgery for ureteral stricture with conversion of an indwelling stent to a percutaneous nephrostomy tube for ureteral rest
- Willing to sign informed consent form
- Able to read and understand informed consent form

Exclusion criteria:

- <18 years of age
- Inability to provide informed consent
- Members of vulnerable patient populations

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Local	Adults	80	20-25
Study-wide			
Total:		80	20-25

RECRUITMENT METHODS

Potential subjects will be identified during their pre-operative clinic visit. Physician-investigators will review the medical chart to ensure the patient meets inclusion and exclusion criteria. Potential subjects will then meet with a member of the study team to read the consent in detail and discuss the study in full.

WITHDRAWAL OF PARTICIPANTS

Decision to participate is completely voluntary, and patients will be notified at the start of the study that if they choose not to participate, then they will continue with our standard care. If a subject wishes to withdraw from the study, they may do so verbally or written request to the research team. A subject may be withdrawn from the study by the physician investigator if determined to be in the subject's best interest for medical reasons.

RISKS TO PARTICIPANTS

The risks of this study are a potential very minimal increase in anesthetic time, predicted to be no more than five minutes. The anesthetic agent is completely determined by the anesthesiologist and is the same agent that is used for the definitive repair. We have no

way of knowing the agent and dose that will be used as this is determined by the attending anesthesiologist and is dictated by the larger ureteral reconstruction surgery. There is no significant increased risk to less than five minutes of additional anesthesia beyond the general risks of anesthesia that are discussed with the patient by the anesthesiologist. We believe this is not a significant increase as the overall length of theses surgeries ranges 3-4 hours, sometimes longer depending on the repair and individual patient factors. We do not anticipate any increase in equipment costs to the hospital as all the equipment required for the antegrade and retrograde pyelogram is currently already pulled for all ureteral reconstruction cases. There is a nominal increase in radiation risk to the patient, estimated to be ~1-4 mSv (expected radiation dose would be less than what would be associated with a ureteral stent which is ~4.7 mSv).

Additional risks include breach of privacy and confidentiality.

POTENTIAL BENEFITS TO PARTICIPANTS
Repeat endoscopic evaluation of the stricture length may allow for better intraoperative surgical planning and efficiency as we will better delineate stricture length and location prior to deciding on the surgical repair.

DATA MANAGEMENT AND CONFIDENTIALITY
All information obtained from the medical record will be kept secured in a password-secured REDCap database and only accessed by study personnel. Manual entry will be performed, and double entry verification will occur between research staff and study personnel. Data will undergo regular backups during data entry. All data will be de-identified from the patient, and the key for the de-identification process will be maintained in a secure location. The presentation of the results of this study will maintain patient confidentiality.

Enrollment for this study is expected to be completed within 24 months of initiation. Identifiable data will be kept until data analysis is complete. A limited data set will be kept for a minimum of 7 years.

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS
Data will be collected and stored electronically in REDCap and will only be accessible to members of the study team.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS
Data resulting from this study will not be linked to subjects. Subjects will not be referred to by name of initial in any publications.

ECONOMIC BURDEN TO PARTICIPANTS
Participants will not be responsible for any cost related to participation in this research study.

CONSENT PROCESS
Enrollment into the study will be performed by a qualified research coordinator. After the patient completes their pre-surgical enrollment paperwork in the clinic, they will then be met in a private room away from the treating physicians by a qualified research coordinator who will discuss their potential enrollment and complete any research paperwork. Some patients may be approached via telephone with virtual consent.

NON-ENGLISH SPEAKING PARTICIPANTS
This study will provide access to participants with limited to no English proficiency and we will follow the IRB to effectively communicate the study to the participants during recruitment, consent, and the duration of the study. This study will utilize the short form consenting process as described by the IRB. This short form consent will attest to the information in the informed consent and will be presented orally or by the participant's legal authorized representative. We will provide the short form to the participant or legal authorized representative. The short form will be signed and confirmation that the participant was consented in the language that is understandable by the participant, the person will be authorized by the IRB, there will be a witness to the presentation, the short form will be signed by the witness, the written summary will be signed by the witness and person obtaining consenting and finally a copy of the oral summary and short form will be given to the participant.

Once the participant is enrolled, we will adhere to the IRB standard requirements for non-English speaking participants and obtain certified translations of the documents related to the study.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)
This research study will involve the collection of Protected Health Information (PHI) from the patient's electronic medical record (EMR). PHI will also be created in this study: the questionnaires participants will be asked to complete will collect health information which may otherwise not be captured in the EMR.

HIPAA Authorization will be obtained from all participants. The following information may be collected for each participant:

- Name
- Medical Record Number
- Telephone number
- Email address

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE

Persons involved in this study have experience with patient care and the handling of sensitive information. Dr. Lee is an assistant professor of urology here at Northwestern who specializes in reconstructive urology. Other staff, including residents, research coordinators, medical students, and nursing will have appropriate oversight by the PI. Staff are familiar with study sites at Northwestern Memorial Hospital / Northwestern Medical Group and Northwestern University culture. Facilities for conducting this

research are adequate, including clinic space, secure computer workstations, and availability of access to other Northwestern University resources including the EDW. All persons assisting with research will be adequately informed regarding the protocol and research procedures and will have access to both text of the protocol and an “open-door policy” to promote a culture of questions, transparency, and communication.

Reference

1. Lee Z, Lee M, Lee R, et al. Ureteral Rest is Associated With Improved Outcomes in Patients Undergoing Robotic Ureteral Reconstruction of Proximal and Middle Ureteral Strictures. *Urology*. 2021;152:160-166. doi:10.1016/j.urology.2021.01.058