PROSPECTIVE STUDY INVESTIGATING THE OPTIMAL DURATION OF INDWELLING URINARY CATHETER FOLLOWING INFRAPERITONEAL COLORECTAL SURGERY AND ROLE OF POSTOPERATIVE ALPHA-BLOCKADE

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PROTOCOL

Protocol No./ Title:	Prospective study investigating the optimal duration of indwelling urinary catheter following infraperitoneal colorectal surgery and role of postoperative alpha-blockade
Study Rationale	The purpose of this study is to evaluate whether a postoperative pelvic colorectal patient can safely have an indwelling catheter removed on postoperative day one with the addition of a study medication, without a statistically significant difference in the incidence of urinary retention compared to the standard, accepted approach of delayed removal.
Study Population:	Determine the incidence of retention of two groups. A control group of 72 hours catheterization (Group 1) to 24 hours catheterization plus medication (Group 2) to potentially reduce retention. ***Data Description***: Non-inferiority study p_A=0.15, p_B=0.15, d=0.15 (tolerance). We would like to test 1) If Group 2 is non-inferior to Group 1 (2 is not worse than 1). ***Power Analysis and Sample Size Calculation:*** A sample size for 80% power is 71 per group. This would be a total of 142. Two group test of equivalence in proportions Test significance level, a (one-sided): 0.050 Standard proportion, p_S: 0.150 Equivalence limit difference, p_T - p_S, D_0: 0.150 Test expected proportion, p_T: 0.150 Expected difference, p_T - p_S, D_1: 0.000 Power (%): 80 n per group: 71
Hypothesis	Early removal of a urinary catheter in postoperative infraperitoneal colorectal surgery patients will experience a similar incidence of acute urinary retention than delayed removal, will likely have a lower incidence of clinically important urinary tract infections, and experience improvement in quality of life measures.
Study Design:	Single-center, randomized, prospective study. Patients in the 24-hour catheter removal group will be given 1 mg prazosin orally (per os). The pharmacy will be responsible for the distribution of the medication when indicated. The study drug will be given 6 hours prior to catheter removal in Group 2 patients.

Primary Efficacy Endpoint:	Acute urinary retention (Re-catheterization)
Secondary Endpoints:	1. Urinary tract infection (>10^5 CFU/mL **with** symptoms) 2. Cardiopulmonary complications 3. Surgical site infections 4. Anastomotic leaks 5. Quality of life 6. Length of postoperative stay 7. Volume of retained urine if re-catheterized (Bladder Scan) 8. Adverse side effects from treatment drug
Safety Endpoints:	Receiving care patient would have otherwise received.
Sample size:	With a sample size of 71 patients per group for a total of 142 patients, this study will have 80% power to detect a statistically significant difference between acute urinary retention in patients with urinary catheter removal 24 hours postoperatively compared to 72 hours postoperatively.
Interim Analysis	There will be an interim analysis after 71 patients enrolled (half the study group)
Key Inclusion Criteria:	1. Able to freely give written informed consent to participate in the study and have signed the Informed Consent Form; 2. Males or females, >18 years of age inclusive at the time of study screening; 3. American Society of Anesthesiologists (ASA) Class I-III; 4. Infraperitoneal colorectal surgery (open and/or laparoscopic); 5. Elective Surgery
Key Exclusion Criteria	1. Mentally incompetent or unable or unwilling to provide informed consent or comply with study procedures; 2. Children <18; 3. No perioperative antibiotics; 4. Past or current urinary tract malignancy; 5. Urinary catheter inserted before surgery; 6. Chronic kidney insufficiency with Creatinine> 2 7. Diagnosis of benign prostatic hyperplasia

	8. Chronic urinary infections 9. Neurogenic bladder 10. History of enter vesicle fistula 11. Pregnancy 12. Prior surgery of the lower urinary tract 13. Epidural 14. Perioperative ureteral stents After randomization: 1. Catheter pulled out inadvertently; 2. Postoperative complications requiring prolonged monitoring of urine output 3. Postoperative complications requiring early reoperation
Treatment Regimen/ Duration:	Patients will be assigned into one of three groups: Group 1- removal of urinary catheter 72 hours postoperatively (Control) Group 2 – randomized to receive prazosin **6 hours prior to catheter removal** and removal of urinary catheter 24 hours postoperatively
Treatment Failure/ Discontinuation Criteria:	Patients will be discontinued from the trial at any time as a result of any other event that in the opinion of the investigator warrants discontinuation from the trial. Additionally, patients will be excluded after randomization if: 1. Catheter pulled out inadvertently; 2. Postoperative complications requiring prolonged monitoring of urine output; 3. Postoperative complications requiring early reoperation

2. SCHEDULE OF EVENTS

	Group 1: Delayed Catheter removal
Visit Number	Admission
Informed Consent	□
Demographics	□
Height	□
Medical History[1]	□
Inclusion/ Exclusion Criteria Review	□
Previous /Concomitant Medications	□
Physical Exam[2]	□
Vital Signs[3]	□
Body Weight	□
Adverse Events[4]	□
Quality of Life Assessment[5]	✓
Hospital Discharge or Early Termination Visit[6]	✓

1. Medical History obtained at index admission including: Hypertension, Lung Disease, Diabetes
2. Comprehensive physical exam performed at index admission
3. Vital Signs (systolic and diastolic blood pressure, heart rate, respiration rate, and temperature) at index admission.
4. Adverse events (AEs) will be recorded at every visit post screening. AEs will be followed until resolution.
5. Quality of Life assessment will be performed on last hospital day prior to discharge (Appendix A)
6. Early Termination visits are used when a patient withdraws from the study (i.e., prior to hospital discharge).

	Group 2: Prazosin and early catheter removal
Visit Number	Admission
Informed Consent	□
Demographics	□
Height	□
Medical History[1]	□
Inclusion/ Exclusion Criteria Review	□
Previous /Concomitant Medications	□
Physical Exam[2]	□
Vital Signs[3]	□
Body Weight	□
Adverse Events[4]	□
Quality of Life Assessment[5]	✓
Hospital Discharge or Early Termination Visit[6]	✓

1. Medical History obtained at index admission including: Hypertension, Lung Disease, Diabetes
2. Comprehensive physical exam performed at index admission
3. Vital Signs (systolic and diastolic blood pressure, heart rate, respiration rate, and temperature) at index admission.
4. Adverse events (AEs) will be recorded at every visit post screening. AEs will be followed until resolution.
5. Quality of Life assessment will be performed on last hospital day prior to discharge (Appendix A)
6. Early Termination visits are used when a patient withdraws from the study (i.e., prior to hospital discharge).

Postoperative Data	
Open or Laparoscopic	
Reason for surgery (benign or cancer)	
Type of Surgery (LAR, APR, IPAA, etc)	
ASA Score	
TMN stage	
Metastatic Lymph Nodes	
Total Mesorectal Excision	
Level of anastomosis (<5 cm from anal verge)	
Neoadjuvant chemotherapy	
Neoadjuvant radiation therapy	
Intraoperative Fluid Volume (mL)	
Intraoperative Blood Loss (mL)	
Intraoperative/Postoperative Blood Transfusion	
Bowel preparation	
Diverting stoma	
Antibiotic therapy >24 hours postoperatively	
Morphine equivalent (mg)[1]	
Quality of Life[2]	

1. Morphine equivalent: 7 mg ≈ 1 mg hydromorphone
2. Quality of Life: obtained on last day of hospitalization

	Group 1	Group 2
Endpoints		
Acute urinary retention[1] (re-catheterization)		
Bladder scan volume (mL)		
Symptomatic urinary tract infection[2]		
Cardiopulmonary complications		
Surgical site infection		
Anastomotic Leak		
Adverse side effects		
Overall complication rate		
Post-void residual (mL)		

1. Acute urinary retention defined as the inability to void despite urge and attempt, and/or the inability to void within 8 hours post-removal of the catheter.
2. Dysuria and $>10^5$ CFU/mL on urine culture