Randomized Study of Ultralow versus Standard Pneumoperitoneum Pressure during Robotic Prostatectomy using the AirSeal® Insufflation System

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1.0 – INTRODUCTION

1.1 – Background

Technological improvements are ongoing in minimally invasive surgery. Laparoscopic surgery has allowed for enhanced patient comfort and recovery in numerous procedures including cholecystectomies, gastric bypasses, and laparoscopic renal procedures. Laparoscopic surgeries must insufflate the abdomen in order to perform the necessary procedures of the surgery. In order to maintain space and vision, carbon dioxide (CO_2) must be used to inflate the abdomen with trocars being used as the entry points to the abdomen. These trocars are then connected to insufflation systems to increase intraabdominal volume. Many different trocars have been used historically to accomplish this task at OhioHealth, with recent focus on valve-less trocars. Since its FDA clearance, the AirSeal system has been used routinely in centers throughout the United States, including OhioHealth Dublin Methodist Hospital. The AirSeal system has been observed by surgeons and anesthesia teams to provide a more gentle, stable, and consistent pneumoperitoneum.[1]

The AirSeal System consists of an insufflation, filtration, and recirculation system (AirSeal iFS), a triple lumen filtered tube set, and a valve free trocar (AirSeal Access Port). The device enables peritoneal access with a novel mechanism to maintain pneumoperitoneum without a mechanical seal. Specifically, the AirSeal System creates a pressure barrier within the proximal housing of the cannula which acts as an invisible seal to maintain pneumoperitoneum during the course of surgery. It utilizes a re-circulation and filtration control unit (AirSeal iFS) designed specifically for the AirSeal Access Port to create and maintain the pressure barrier. The AirSeal iFS is reusable and the AirSeal Access Port and triple lumen filtered tube set are designed as single patient use devices. The AirSeal System has applications in minimally invasive abdominal surgical procedures to establish a path of entry for laparoscopic instruments. The lack of a physical valve allows the AirSeal port to vent immediately in the event of any pressure spikes, as the port has a constant opening where the pneumoperitoneal gas may escape to keep pressures down.

Since first described in 2001, robotic assisted laparoscopic prostatectomy (RALP) has been traditionally performed at a pneumoperitoneal insufflation pressure of 12-15 mmHg, derived from standard practice used during laparoscopic surgeries.[2] Abdominal insufflation with carbon dioxide causes a multitude of known physiologic changes including increased peak airway pressures, depressed cardiac output, oliguria, and systemic acidosis,[3-7] many of which show dose-dependent improvement with the reduction of intraoperative pressures.[8,9]

Reducing intraperitoneal stretch with lower intra-abdominal pressures may also improve postoperative pain and facilitate earlier hospital discharge as evidenced by studies in general surgery comparing outcomes following laparoscopic cholecystectomy.[10-11] Despite these results, few surgeons perform RALP at reduced pressure likely due to habit or the perceived concern for poorer visibility, compromised hemostasis, and/or technical difficulty. Furthermore, some have even proposed performing RALP at an increased pressure of 20 mmHg in an effort to achieve better hemostasis despite other physiologic consequences.[12] There remains a paucity of data exploring the feasibility and potential benefits of performing RALP at low insufflation pressures, and no studies have explored how high the pneumoperitoneal pressure must be to perform RALP or, in other words, the minimum pressure that is adequate.

We plan to examine the impact of low pressure during RALP with the intention of identifying whether lower pressures might benefit patients. We hypothesize that a low insufflation pressure may provide an improvement in postoperative pain and abdominal distension in addition to potential physiologic benefits, and that these factors might then allow a shorter hospital stay. We previously initiated a protocol in September of 2016 (IRB# 1066864) to perform RALPs at an insufflation pressure of 6 mmHg with the intention of increasing the pressure as needed on an individual patient level. In order to determine whether this might allow earlier discharge when successful, we began allowing for same-day discharge in patients meeting appropriate criteria. Having now demonstrated feasibility in over 300 consecutive patients using this ultralow pneumoperitoneum protocol, we now plan to conduct a randomized trial to compare a pressure of 6 mmHg with patients having RALP at a standard pressure of 15mmHg to determine whether there is a true benefit.

1.2 – Specific Aims/Rationale

We propose a study comparing insufflation pressures during RALP. Standard pressure is typically 15 mmHg, while in our previous study we determined that 6 mmHg is possible routinely. Therefore, we plan to compare the clinical outcomes of patients at a pneumoperitoneal pressure of 15 versus 6 mmHg.

Aim #1) Compare average postoperative pain medication use between groups, as measured in total morphine equivalents (MME) over time at pre-specified time intervals through follow-up at 1 week.

Aim #2) Compare average and maximum postoperative pain scores between groups, as measured using the self-reported 11-point numerical rating scale (NRS), over time at pre-specified time intervals through discharge.

Time intervals for Aims #1 & 2 are as follows: during the post-anesthesia care unit (PACU) stay, the first 4 hours on the floor, next 8 hours, and the following 8 hours; as well as the final score immediately prior to discharge.

Aim #3) Compare operative ventilation as measured by average tidal volume (ml) between groups.

Tidal volume is the lung volume representing the normal volume of air displaced between normal inspiration and expiration when extra effort is not applied (i.e., normal/resting breathing), and is measured continuously throughout the procedure by Anesthesia. Potential patient benefits to a lower pneumoperitoneal insufflation pressure include decreased postoperative pain and improved intraoperative ventilation.

Aim #4) Compare average length of stay (typically 0-1 days) between groups.

2.0 – METHODS

2.1 – Study Population

The study population will include males age 18 or older with prostate cancer who are eligible and electing to undergo robotic assisted laparoscopic prostatectomy (RALP) at OhioHealth Dublin Methodist Hospital (DMH) Robotic Urology with the Principal Investigator (PI). We anticipate that enrollment of 192 patients (96 in each group) will take a minimum of 1 year to complete. See section 2.4 (Statistical Analysis) for the details of the sample size calculation.

Exclusion criteria for RALP include:

1. Cirrhosis or liver failure (Child-Pugh class A, B, or C) or clinical suspicion of liver failure
2. Ascites
3. Uncontrolled diabetes [as reported by the pre-anesthesia testing (PAT) physician]
4. Renal insufficiency (serum creatinine level > 3.0 mg/dl)

Exclusion criteria to participation in this study include:

1. Age < 18
2. Emergency surgery
3. Patients with a significant preoperative dependence on narcotic medications
4. Unable to give informed consent
5. Dementia, history of dementia, or other significant mental impairment that would, in the opinion of the investigator, impede patient self-reporting
6. Persons participating in any other research study involving an investigational drug or device or investigational surgical procedure that could interfere with the physiologic parameters being collected (for example, a study evaluating different anesthesia regimens that could confound study results)
7. Non-English-speaking or reading

2.2 – Study Variables & Outcomes of Interest

The following data points will be collected for patients who choose to receive treatment and consent to this study at OhioHealth Dublin Methodist Hospital (see Table 1). Patient data will be collected via Epic/CareConnect, as well as by means of study specific Data Collection Forms (DCFs; see Appendices A-D). Only the designated study staff will have access to the REDCap database and paper DCFs created solely for use in this study. Patient data will be de-identified upon study completion, prior to statistical analysis.

Table 1. ***Study Variables.***

Category	Data points
Enrollment Log	1. MRN 2. Name 3. DOB 4. Date of consent 5. DOS/randomization 6. Enrolled (y/n) 7. Randomized (y/n)

	8. Randomization envelope (#) 9. Withdrawn (y/n) 10. Reason withdrawn (if applicable)
Demographics	1. Phone number 2. BMI (kg/m^2) 3. Weight (lbs) 4. Medical history (free text) 5. Surgical history (major only; free text) 6. Serum creatinine (most recent prior to surgery) (mg/dl; date) 7. Hemoglobin (most recent prior to surgery) (g/dl; date)
Intraoperative	1. Details of the surgical procedure (free text) 2. Port number/size(s)/locations (standard protocol -or- deviation from standard protocol) – if deviation, explain 3. Continuously recorded values *(only means/standard deviations recorded in REDCap) – as measured by Anesthesia* a. End tidal CO_2 (mmHg) b. O_2 saturation (%) c. Respiratory rate (bpm) d. Blood pressure (mmHg) e. Heart rate (bpm) f. Tidal volume (ml) g. PIP (peak inspiratory pressure) (mmHg) h. PEEP (positive end-expiratory pressure) (mmHg) 4. Core body temperatures (F) – *as measured by Anesthesia* a. After trocar placement (baseline) b. 30 minutes c. 60 minutes d. End of procedure 5. Insufflation time (minutes) 6. Insufflation pressure (6 or 15 mmHg) 7. Increased pressure episodes necessary to successfully complete the procedure (# times) a. Time of each adjustment (hh:mm) b. Level of each adjustment (mmHg) 8. Significant loss of pneumoperitoneum (# times) a. Time of each adjustment (hh:mm) b. Level of each adjustment (mmHg) 9. Pressure range (lowest and highest; mmHg) 10. Smoke evacuation quality (below average, average, above average) 11. Total amount of gas used during the procedure (l) 12. Scope cleanings (#) 13. Malfunctions of the AirSeal iFS or control devices (# times)

	14. Estimated blood loss (EBL; ml) 15. Obturator artery manipulation (no, left, right, bilateral) – *only on Case Sheet (Appendix F)* 16. Console time (minutes from initial incision to closure) 17. Use of intraoperative pain medication a. Fentanyl (y/n) i. Dose (mg) ii. Morphine equivalents (MME) b. Toradol (y/n) i. Dose (mg) 18. Pathology report a. Pathological Stage b. Clinical Stage (T1a-c, T2a-c, T3a-c) c. Gleason Score (ranging from 6-10: 3+3=6, 3+4=7, 4+3=7, 3+5=8, 5+3=8, 4+4=8, 4+5=9, 5+4=9, 5+5=10) d. Margins (positive/negative) e. Extra prostatic extension (EPE; y/n) f. Tumor quantification (%)
<u>Postoperative</u> *(PACU & Floor)*	1. Recorded in PACU a. Vital signs recorded in PACU setting i. Time ii. Respiratory rate (bpm) iii. Blood pressure (mmHg) iv. Heart rate (bpm) v. Temperature (F) b. Other PACU assessments i. O_2 saturation (%) (first recorded) ii. Post-operative nausea and vomiting (y/n for each) iii. Wound infection (y/n) c. Time in PACU (hours) i. Arrival & discharge times (hh:mm) 2. Recorded on Floor a. Vital signs first recorded in non-PACU setting (i.e., on the floor) i. Respiratory rate (bpm) ii. Blood pressure (mmHg) iii. Heart rate (bpm) iv. Temperature (F) b. Other non-PACU / Floor assessments i. Labs drawn (y/n) 1. Serum creatinine (mg/dl; date) 2. Hemoglobin (g/dl; date)

	ii. Wound infection (y/n) c. Length of stay (days; typically 0 to 1) i. Discharge date/time (m-d-y; hh:mm) 3. Use of postoperative pain medication a. Opioids (y/n for each: fentanyl, Dilaudid, oxycodone, Norco, tramadol, Percocet, Demerol) i. Morphine equivalents (MME) b. Non-opioids (y/n for each: Toradol, Tylenol, oxybutynin) 4. Postoperative pain scores (0-10; asleep, missed, or discharged) a. Average and maximum scores during each interval (during the PACU stay, the first 4 hours on the floor, next 8 hours, and the following 8 hours; as well as the final score immediately prior to discharge) b. At each location (abdomen, legs, groin, scrotum, shoulder, other/specify) 5. Timing of ability to pass gas (day 0, day 1, day 2, >day 2) 6. Clinically-significant ileus (i.e., requiring treatment; y/n)
<u>Follow-Up</u> *(1 week, 1 month, & 3 months)*	1. QoR-15 (0-150) – *only asked at week 1* a. Collected (y/n) b. Score (0-150) 2. Prescription(s) given (y/n) – *only asked at week 1* a. Prescription(s) filled (y/n) b. Opioids (y/n for each: fentanyl, Dilaudid, oxycodone, Norco, tramadol, Percocet) i. Number of pills taken for each (#) ii. Morphine equivalents (MME) c. Non-opioids (y/n for each: Toradol, Tylenol, oxybutynin) 3. Scrotal swelling (y/n) – *only asked at week 1* 4. Leg weakness (y/n) a. Left, right, bilateral b. Degree of weakness (each leg; mild, moderate, severe) c. Impaired ability to walk d. Impaired ability to drive

We will collect information on pertinent surgical outcomes that occur through discharge. The average amount of time spent in the PACU is roughly 1-2 hours, and the average hospital length of stay is 0-1 days. For Intraoperative Item #2, a deviation from the standard port number/size(s)/locations would be due to body habitus, and will not have an effect on clinical outcomes. For Intraoperative Item #3, continuous values will be exported into individual patient-specific Excel spreadsheets with the assistance of the CareConnect Systems Analysts. This is due to the fact that there are far too many data points (8 different variables every 1 minute for 120 minutes) to be manually extracted and subsequently manually entered. The PI will perform individual analyses on these data sets in conjunction with Analysts, and

calculate means and standard deviations to be entered into REDCap. For Intraoperative Item #15, we are collecting whether the obturator artery was affected for each leg, as this could potentially be a confounder to postoperative leg pain (i.e., increased pain in the affected leg). Finally, the presence of wound infection (in the PACU and on the Floor; Postoperative Items #1b-iii and #2b-iii, respectively), as well as clinically-significant ileus (on the Floor; Postoperative Item #6) will be evaluated and assessed by nursing staff per routine care and entered into the medical record.

The Quality of Recovery (QoR)-15 questionnaire (Appendix E) is used to evaluate recovery from anesthesia. The tool consists of 15 questions that assess patient-reported quality of postoperative recovery using an 11-point (i.e., 0-10) numerical rating scale, where "0" refers to "all of the time [poor]" and "10" refers to "none of the time [excellent]." Therefore, a higher score refers to better quality of recovery. The questionnaire assesses basic and essential activities of daily life (ADLs), pain, emotions, and personal/overall well-being, among others. The survey will be administered at the 1-week follow-up visit only, and takes approximately 2-3 minutes to complete.

The Physician Case Sheet (Appendix F) is a routine form used in the operative suite by the PI. In the case of research-related data that is not otherwise recorded intraoperatively, certain data points are added for research purposes so the surgeon/PI is reminded to document. For the purposes of this study, we have added "obturator artery affected (no/left/right/bilateral)," as this is not collected consistently, and could be a confounder to our secondary outcome of pain scores (specifically for the affected leg/s, as applicable).

2.3 – Study Design

We propose a prospective, randomized, controlled trial comparing insufflation pressures during RALP. Standard pressure is typically 15 mmHg, while in our previous study we determined that 6 mmHg is possible routinely; therefore, we plan to compare the clinical outcomes of patients between pneumoperitoneal pressures. Potential study subjects will be identified by reviewing clinic schedules at the PI's Robotic Urology practice at Dublin Methodist Hospital. As part of the new patient paperwork, patients will be mailed an informational letter (see Appendix G) highlighting active research studies for review prior to the index routine visit with the PI.

All patients that are candidates for RALP will be screened by the Clinical Research Coordinator (CRC) prior to their surgery planning visit. Once a patient is identified as meeting all study criteria, they will be approached by the CRC at their visit and the study will be thoroughly explained. After the patient has had all their questions answered and has agreed to participate in the study, informed consent will be obtained, followed by randomization in a 1:1 single-blinded fashion to either a pneumoperitoneal insufflation pressure of 15 mmHg (control group) or 6 mmHg (study group). The randomization allocation schedule will be developed by staff from the OhioHealth Research & Innovation Institute (OHRI), and will be hidden from the investigators until directly prior to surgery to prevent bias. Specifically, the CRC will open the randomization envelope in the operating room (OR) immediately prior to surgery. Randomization will be blocked to prevent selection and accidental bias.

Patients will be prepared for surgery per standard institutional policy and routine practice; the only difference in surgical technique will be the insufflation pressure applied. All ports will be placed

according to routine care using the AirSeal iFS, and all clinical decisions will be made per standard practice and policy. Dr. Abaza (the PI) will be the only surgeon performing these procedures, eliminating any variation in technique between surgeons. Participants in this study are not exposed to any additional or different risks associated with the surgery, as all patients will undergo insufflation. Following trocar placement, initial insufflation will be performed at 6 mmHg for patients in the study group and 15 mmHg for patients in the control group. If required, insufflation pressures for the study group will be increased up to 15mmHg per standard surgeon protocol. Increased insufflation pressure will be maintained either transiently (≤5 minutes to control bleeding or to improve access/visualization) or for the duration of the procedure as per surgeon need. The amount of time at each insufflation pressure will be recorded.

Table 2. *Post-operative pain monitoring schedule.*[1]

Timeframe	Description	Time-Points	Pain Locations
During PACU stay	Upon admission to the PACU (typical stay of 1-2 hours)	PACU	Abdomen Legs Groin Scrotum Shoulder Other/specify
1st 4 hours on the floor	Every 2 hours during the first 4 hours on the floor	Floor-0, 2, & 4 *(hours 0 through 4)*	
Next 8 hours on the floor	Every 2 hours during the next 8 hours on the floor	Floor-6, 8, 10, & 12 *(hours 5 through 12)*	
Following 8 hours on the floor	Every 2 hours during the following 8 hours on the floor	Floor-14, 16, 18, & 20 *(hours 13 through 20)*	
Final score immediately prior to discharge	Recorded on the floor prior to discharge; *OR* via phone call by CRC for those discharged same-day	Discharge, *or* Post-discharge	

1-Scores measured only while inpatient (or post-discharge for those discharged same-day) and awake; measures not taken in <1 hour from planned time will be marked as "missed."

Pain scores are measured using an 11-point numerical rating scale (NRS), in which a rating of 0 corresponds to no pain, 1-3 indicates mild pain, 4-6 indicates moderate pain, and 7-10 corresponds to severe pain. Scores are recorded by nursing staff as part of routine care in the PACU and on the postoperative recovery floor during the inpatient stay, however these measures are often not recorded in a consistent fashion with respect to timing. Therefore, we will record scores every 2 hours during the inpatient stay while the patient is awake (with the exception of the PACU, which occurs only at admission), and determine the average and maximum scores reported over sequential timeframes: during the PACU stay (typical stay of 1-2 hours), the first 4 hours on the floor, next 8 hours, and the following 8 hours; as well as the final score immediately prior to discharge (see Table 2). There will be no strict time window due to the variability of sleep schedules and discharge timing during the short inpatient stay, however, scores will be marked as "missed" if not recorded in <1 hour of the planned time. Pain will be measured with respect to the abdomen, legs, groin, scrotum, shoulder (due to insufflation), and "other" location. Pain medication morphine equivalents (MME) will also be measured over the same sequential timeframes during the inpatient stay through 1 week postoperatively. Patients

will be educated on the importance of bringing all medications to follow-up visits, which will lead to more accurate pain medication counts and calculations.

Patients are typically discharged on Day 0-1, and for those discharged on Day 0 (i.e., same-day), the CRC will call the following morning to evaluate pain (see Appendix C). Because we are targeting same-day or next-day discharge, there is the potential for missing data in the first 24-hour period. Therefore, there will be no restrictions or protocol deviations for pain scores, as we are collecting scores only while inpatient/awake and via phone call for those discharged same-day. Follow-up visits per routine care occur at approximately 1 week postoperatively for catheter removal, as well as at 1 month and 3 months. Appointments will follow routine scheduling practices for the office, which may include variance in exact visit timing. Generally, patients will have 1 week postoperative visit around 5-7 days after surgery, but may be delayed further by approximately 1 week depending on scheduling availability and/or clinical indication (e.g. need for cystogram). Follow-up visits are generally 1 month and 3 months post-surgery, but may occur approximately a couple weeks before or after as per physician standard of care scheduling to accommodate patient and physician availability. There will be no strict visit windows to allow for visit scheduling flexibility. Because the majority of RALP patients will be eligible for participation, schedulers will be educated on the importance of return visit timing accuracy. There will be no extended or long-term follow-up via direct patient contact or EMR review.

Patients that are unable to pass gas while inpatient will be called on postoperative day 1 (if discharged same-day only) and day 2. The post-operative day 1 phone call will also be utilized to assess pain for those who were discharged same-day, as explained above. If a patient confirms that they have passed gas on day 1, they will not be called again on day 2. For Thursday/Friday procedures where days 1 and/or 2 (as applicable) fall on the weekend, patients will be called on Monday morning and asked to recall when they were able to pass gas (i.e., whether it occurred on Saturday or Sunday). If patients are not discharged same-day, they will only receive a single phone call on day 2 if they did not pass gas prior to discharge. Patients who are not discharged same-day and are able to pass gas prior to discharge will not receive any phone calls. In the case that a patient is still unable to pass gas on day 2, we will repeat phone calls daily until they are able to do so, although we do not anticipate many patients will need to be called past day 2. We are collecting this data due to recent anecdotal evidence in Robotic Urology that patients who receive Percocet were able to pass gas on average in 1.6 days versus 1.4 days for those that did not receive Percocet.

Table 3. *Study Calendar.*

	Baseline	**Surgery & Post-Op Stay**	**Days 1 & 2** *(post-discharge)*	**1-Week Follow-up**	**1-Month Follow-up**	**3-Month Follow-up**
Informed Consent	x					
Randomization		x				
Office Visit	x			x	x	x
Intra- & Post-Op DCF		x				

(Appendices A&B)						
Post-Discharge DCF *(Appendix C)*			x*			
Follow-Up DCF *(Appendix D)*				x	x	x
QoR-15 *(Appendix E)*				x		
Phone Calls			x			

* Patients will be called for pain scores on day 1 if discharged same day; patients will be called on days 1 & 2 to assess the ability to pass gas.

We do not expect any treatment-related adverse events (AEs) or excess risk associated with randomization to the study group, as all surgical procedures are considered routine care. Therefore, we will not be tracking treatment-related AEs, only treatment-related serious adverse events (SAEs), which will be reported to the OhioHealth IRB via IRBNet reporting using the Adverse Event Template Form, per institutional and national guidelines, within 10 business days of discovery or notification of the event. SAEs will be tracked for 90 days following discharge via chart review. Patients will be removed from the study only if they revoke their informed consent prior to surgery. There are no intraoperative events that would warrant study removal, and changes in insufflation pressure will be recorded intraoperatively as mentioned above. Further, patients who do not return for follow-up visits (which is not anticipated in this population) will still be analyzed in the final dataset.

Only de-identified or non-identifiable data will be reported in the study. Only the IRB-approved study staff will have access to patient information. All resulting data will be stored in electronic format; electronic files will be stored on a password-protected computer and paper files will be stored in a secure facility with limited access (the offices of the OhioHealth Research Institute). Participants will not be excluded on sexual orientation, socioeconomic, racial, or religious identity. The data collection and storage processes will follow HIPAA guidelines in accordance with 21 CFR 46.115 (b): to protect both confidentiality and privacy of each participant. All PHI data will be released or destroyed per institution protocol.

The only potential risk associated with this study is loss of confidentiality, which will be minimized by limiting access to data and de-identifying data at study completion. The information from this study will be used to identify opportunities to improve the care of our patients by potentially encouraging surgeons performing all types of laparoscopy or robotic surgery to use lower pressures, in compliance with current recommended evidence-based practice guidelines for our patients at OhioHealth. Potential patient benefits to a lower pneumoperitoneal insufflation pressure include decreased postoperative pain and improved intraoperative ventilation. As this study meets the FDAAA 801 definition of an “Applicable Clinical Trial”, it is required that the study be registered on ClinicalTrials.gov. The PI will register and activate the study account prior to enrollment, and all results will be entered upon study completion, following statistical analysis, per the Results Database Guidelines.

2.4 – Statistical Analysis

The demographic and clinical characteristics of male patients age 18 or older with prostate cancer who are eligible and electing to undergo robotic assisted laparoscopic prostatectomy (RALP) at OhioHealth Dublin Methodist Hospital (DMH) Robotic Urology with the Principal Investigator will be reported using means and standard deviations or medians and interquartile ranges for continuous variables, or frequencies and percentages for categorical variables. We plan to compare the clinical outcomes of patients between different insufflation pressures (6 versus 15 mmHg). Continuous variables will be compared between two groups using independent sample t-test or Mann-Whitney U test, as appropriate, and categorical variables will be compared using Chi-square test or Fisher's exact test, as appropriate.

During the previous feasibility study of RALPs at an insufflation pressure of 6 mmHg, we found that there was a significant difference in pain scores at 5-12 hours. The average score in the 6 mmHg group was 3.2, and that in 15 mmHg historical group was 3.9. Using these values and an assumed standard deviation within each group of 1.4 (effect size = 0.5), at a significance level of 0.05 to achieve 90% power, the estimated sample size will be 86 patients in each group (total 172 patients). However, to account for ineligible patients after enrollment (estimated 10%), we will enroll minimum of 192 patients.

Aim #1) Compare average postoperative pain medication use between groups, as measured in total morphine equivalents (MME) over time at pre-specified time intervals through follow-up at 1 week.

Postoperative medication use between the two groups will be assessed at the following time points: during the PACU stay, during the first 4 hours on the floor, next 8 hours, the following 8 hours, and following discharge through the 1-week follow-up visit. Both total and average medication use measured in total morphine equivalents at/during each time point will be calculated and compared between two groups (6 versus 15 mmHg) using independent sample t-test or Mann-Whitney U test, as appropriate.

Aim #2) Compare average and maximum postoperative pain scores between groups, as measured using the self-reported 11-point numerical rating scale (NRS), over time at pre-specified time intervals through discharge.

Similar to aim 1, postoperative pain scores will be assessed at following time points: during the PACU stay, during the first 4 hours on the floor, next 8 hours, and the following 8 hours, as well as the final scores immediately prior to discharge (or via phone call if discharged same-day). There will be only one measurement of pain at each bodily location during the PACU stay, as well as at discharge. However, the average and maximum postoperative pain scores will be calculated for each of the time intervals (the first 4 hours on the floor, next 8 hours, and the following 8 hours). The comparison of average and maximum scores at each time point between the two groups will be performed using independent sample t-test or Mann-Whitney U test, as appropriate.

The association between patient demographic or clinical characteristics and differences in medication use or pain scores will be assessed using multivariate regression. The appropriate type of regression (logistic or linear) used will be determined after data collection is complete.

Aim #3) Compare operative ventilation as measured by average tidal volume (ml) between groups.

Tidal volume is the lung volume representing the normal volume of air displaced between normal inspiration and expiration when extra effort is not applied (i.e., normal/resting breathing), and is measured continuously throughout the procedure by Anesthesia. Potential patient benefits to a lower pneumoperitoneal insufflation pressure include decreased postoperative pain and improved intraoperative ventilation. The average tidal volume for each patient will be compared between the two groups using independent sample t-test or Mann-Whitney U test, as appropriate.

Aim #4) Compare average length of stay (typically 0-1 days) between groups.

The average length of stay postoperatively will be compared between the two groups using independent sample t-test or Mann-Whitney U test, as appropriate. Also, the proportion of patients in each group who went home on day 1 versus day 0 will be compared using Chi-square test or Fisher's exact test, as appropriate. A difference of 10% in the proportion of patients will be considered clinically significant.

A p-value of less than 0.05 will be considered statistically significant for analysis. All of the analyses will be performed using SAS Enterprise Guide, version 7.1 (SAS Institute, Cary, NC).

3.0 – REFERENCES

1. A new Valve-Less Trocar for Urology Laparoscopy: Initial Evaluation. Journal of Endourology 2009;23: 1535-39.
2. Abbou CC, Hoznek A, Salomon L, et al. Laparoscopic radical prostatectomy with a remote controlled robot. J Urol 2001;165:1964-1966.
3. Cullen DJ, Coyle JP, Teplick R, et al. Cardiovascular, pulmonary and renal effects of massively increased intra-abdominal pressure in critically ill patients. Crit Care Med 1989;17:118-121.
4. Kashtan J, Green JF, Parsons EQ, et al. Hemodynamic effects of increased abdominal pressure. J Surg Res. 1981;30:249-255.
5. Mutoh T, Lamm JE, Embree LJ, et al. Abdominal distention alters regional pleural pressures and chest wall mechanics in pigs in vivo. J Appl Physiol. 1991;70:2611-2618.
6. McDougall EM, Monk TG, Wolf JS, et al. The effect of prolonged pneumoperitoneum on renal function in an animal model. J Am Coll Surg. 1996;182:317-328.
7. Ost MC, Tan BJ, Lee BR. Urologic laparoscopy: Basic physiological considerations and immunological consequences. J Urol 2005;174:1183-1188.
8. La Falce S, Novara G, Gandaglia G, et al. Low pressure robot-assisted radical prostatectomy with the airseal system at OLV hospital: results from a prospective study. Clin Gen Care. 2017;15(6):e1029-1037.
9. Umar A, Mehta KS, Mehta N. Evaluation of hemodynamic changes using different intra-abdominal pressures for laparoscopic cholecystectomy. Ind J Surg. 75(4):284-289.
10. Kanwer DB, Kaman L, Nedounsejiane M, et al. Comparative study of low pressure v. standard pressure pneumoperitoneum in laparoscopic cholecystectomy—a randomized controlled trial. Trop Gastroenterol. 2009;30(3):171-174.
11. Hua J, Gong J, Yao L, et al. Low-pressure v. standard-pressure pneumoeritoneum for laparoscopic cholecystectomy: a systematic review and meta-analysis. Am J Surg. 2014;208(1):143-150.
12. Modi PK, Kwon YS, Patel N. Safety of robot-assisted radical prostatectomy with pneumoperitoneum of 20mmHg: a study of 751 patients. J Endourol. 2015;29(10):1148-1151.