Trendelenburg, abdominal insufflation and time to completion of cystoscopy. A prospective randomized trial.

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Protocol Title: **Trendelenburg, abdominal insufflation and time to completion of cystoscopy. A prospective randomized trial.**

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Population: 136 female patients undergoing a planned cystoscopy after Minimally Invasive Gynecological procedure.

Number of sites: Two sites MHH-TMC and LBJ.

Study duration: 2 years

Subject duration: 6 weeks

General Information (PICO)

This is a randomized controlled trial assessing time to completion of cystoscopy in seconds after minimally invasive gynecologic surgery

We seek to compare the efficiency of the cystoscopy with two interventions:

after two interventions:

1- patient position during the cystoscopy (Trendelenburg (head down) or flat)

2- Abdominal insufflation (insufflation versus no insufflation).

Both interventions are used as usual care and depend on surgeon preference without evidence why one would faster at completing the cystoscopy. Also note that these two interventions are performed multiple times during the surgery itself and outside the cystoscopy procedure routinely.

Our main objective is to assess which intervention or combination of interventions is more efficient.

Background

Iatrogenic injury to the genitourinary tract is a rare, but significant cause of morbidity in patients undergoing gynecologic surgery for benign indications.1–3

In 2012, the American Association of Gynecologic Laparoscopists recommended that routine cystoscopy be performed after all laparoscopic hysterectomies, whereas the American College of Obstetricians and Gynecologists limited the endorsement to prolapse and incontinence procedures.4,5 Universal cystoscopy, where all women undergoing hysterectomy undergo cystoscopy, has been advocated because as many as 75% of genitourinary injuries occur in women without identifiable risk factors.

In one large study, cystoscopy was associated with a median increase in operative time of 17 minutes[6]. Increases in operative time and cost are the most commonly cited concerns regarding cystoscopy with recent estimates of operating room time, not including surgeon and anesthesiologist fees, at $37 per minute,[7] cystoscopy results in an additional $629 per hysterectomy in operating room time alone.

When performing gynecologic laparoscopy, the patient is in a Trendelenburg position (Head down) and the abdomen is normally insufflated to 15 mm Hg during the entire surgery that can take up to 4 hours.
Cystoscopy is done at the end to assure integrity of the bladder and ureteral function, Some surgeons like to do it with the patient in the Trendelenburg position and others flatten the patient position or insufflate the abdomen with the thought that it may reduce the time needed to complete the cystoscopy.

Theoretically, one would predict that performing the cystoscopy under low intra-abdominal pressure (no CO2 insufflation) and flat (with the added effect of gravity), would save time in the operating room.
In addition to those modifiable factors, additional factors may include fluid status (total urinary output during the surgery and fluid given intraoperatively as well as blood loss), duration of the surgery, manipulation of the ureters and the bladder (ureterolysis or bladder mobilization/presence of scar tissue) as well as blood loss overall.

Hypothesis:

Non Trendelenburg or flat position and Non insufflation of the abdomen significantly reduces cystoscopy procedure time after gynecologic laparoscopy.

Objective:

We seek to compare the efficiency of the cystoscopy with two interventions:
after two interventions:

1- patient position during the cystoscopy (Trendelenburg (head down) or flat)
2- Abdominal insufflation (insufflation versus no insufflation).

Population
All patients undergoing minimally invasive gynecologic surgery with planned cystoscopy to evaluate urinary tract injury at two main sites: LBJ and MHH-TMC

Inclusion:
Patient undergoing Planned cystoscopy in the benign gynecology service.

Exclusion:
Pregnancy
Known urologic anomaly
Unplanned cystoscopy

Cancer surgery
Urogynecology surgery
Patient with comorbidities including cardiac disease, chronic hypertension, any stage kidney disease (including abnormal creatinine level) and use of diuretics.
Patients undergoing extensive ureterolysis
Blood loss more than 500 mls
Contra-indications to position change and insufflation

Study design:
Prospective randomized controlled study 2X2 bloc randomized based on position status and Patient position as **the two interventions** being evaluated:

1. Patient Position: flat versus Trendelenburg
2. Insufflation status: Yes versus no insufflation,

Outcomes:
Primary outcome: Time in seconds to satisfactorily complete a cystourethroscopy (visualize the dome, the ureteral jets, the bladder mucosa scan and the urethra).

With additional detail in recording time as follows
T0: Start of cystoscopy
T1: time to see one of the ureteral jets
T2 as the second ureteral jet
T3: completion of cystoscopy

Exploratory outcome:
Surgeon satisfaction with the interventions (Likert scale questionnaire): The surgeon completes 6 Likert scale questions:

1- Global satisfaction (I will use this method routinely; it satisfies my requirements for cystoscopy).

Randomization
The randomization scheme is maintained by Redcap electronically at the time of consent.
Patients are randomized to 1 of 4 groups based on position and insufflation status

1- Position flat, No insufflation,
2- Position Trendelenburg, insufflation to 15 mm Hg
3- Position Flat, insufflation
4- Position Trendelenburg, No insufflation

Randomization occurs in preOp prior to rolling to the operating room.
Neither the surgeons nor the operating room team are blinded to the study group as it required changing position and insufflation.
Cystoscopy medium is sterile water.

Randomization will be performed by the research team (the research fellow who is part of the research team).
It will be performed via redcap using the permutated block method, with an allocation ratio of 1:1:1:1. Patients are blinded to what group they are randomized to.

If cystoscopy is not completed and additional dye is necessary for visualization (as would normally occur outside the setting of the study), then, subjects will be treated as per routine and receive sodium fluorescein (25 mg intravenous sodium fluorescein (concentration 500 mg in 5 mL).

Time will be recorded by the circulating nurse via a stopwatch.

Study duration:
Study duration will be for 6 weeks to allow to review the chart for postoperative outcomes, see variable list to be collected.

Adverse events:
None anticipated outside the routine procedure of cystoscopy.
Cystoscopy risks include possible urinary tract infection. Participation in the study does not increase the risk, as cystoscopy is planned.
There are no additional risks involved with this study beyond the risks discussed at the time of surgical consent. Both position changes (Trendelenberg) and insufflation are part of the laparoscopic procedure. This means that if a patient has a contra-indication to any intervention, she will not be undergoing the procedure. The cystoscopy portion of the procedure is expected to take minutes, in comparison to the procedure, which will take hours. Risks of insufflation and position changes include hemodynamic and respiratory changes that are closely monitored by the anesthesia and the surgical team. We have included this in the consent form.

Data:
Demographic characteristics are abstracted from chart review by study personnel. Characteristics included age, BMI, parity, race/ethnicity, indication for surgery, and medical history. Intervention and surgical data are collected, including type of surgery, surgical start and stop times, cystoscopy start and stop times, estimated blood loss, and whether furosemide or an intravenous fluid bolus was given to assist with assessment of ureteral jets.
Cystoscopy is performed using a 21F sheath and a 70-degree cystoscope. Per protocol, after determining the 12 o'clock position at the bladder dome via the air bubble, the ureteral jets were visualized until surgeon's confidence in the patency of the ureters was determined. Subsequently, a systematic global survey was performed of the bladder, followed by examination of the urethra as the cystoscope was withdrawn.

There are no anticipated adverse events for the two interventions evaluated, as the patient position and insufflation are two variables that routinely occur during surgery.

At the conclusion of the study (when the final randomized patient met the 6-week postoperative mark), all patient medical records will be reviewed for operative data including operative complications.

Statistical analysis

Continuous variables are described with mean (SD) or median (range) depending on the distribution of the data. Statistical tests for continuous data were based on 1-way analysis of variance for normally distributed data, or the Kruskal-Wallis test for nonnormal data. This is determined by histogram plots and Levene test. Categorical variables are described with numbers (percentages) and compared using the χ^2 test. All statistical tests were 2-tailed, and were based on the intent-to-treat principle.

Sample size analysis

Median and IQR cystoscopy duration is 168 (86-286) seconds[8], a clinically significant improvement in cystoscopy times would be 108 (69-160).

	Insufflation -	**Insufflation +**
Flat	Group1	Group2
T-Berg	Group3	Group4

Using analysis of variance, 28 subjects in each arm for a total of 112 subjects would be needed to detect an effect size of > 60 seconds, with 80% power and a 2-tailed alpha of 0.05 to achieve statistical significance using the frequentist method. To account for 20% drop outs, we will include 34 patients in each group for a total of 136 cystoscopy procedures,

The one minute decrease in operative time is used based on prior studies showing that the use of “Lasix” intraoperatively can significantly reduce cystoscopy duration by about 78 seconds.[8]

- CONSORT diagram will be performed
- We will evaluate for the presence of interaction between the different interventions as two interventions are employed at the same time.
- **Intention to treat analysis** will be performed
- All unadjusted outcomes will be reported descriptively (mean SD/ median IQR)
- For all outcomes, we will conduct intent-to-treat **Bayesian analysis** to calculate probabilities of intervention benefits and harms. We will use neutral priors and exclude large treatment effects. We will report posterior medians of group differences, their corresponding 95% credible intervals, and probability of treatment benefit.

Funding:

None

OVERSIGHT RESPONSIBILITIES
Oversight of the trial is provided by the Principal Investigator (PI), Dr. Randa Jalloul and Co-investigators Drs Mateo Leon and Aya Mohr-Sasson.

Ethics
- IRB approval will be sought for this study, and admin Approval sought from Harris Health and MHH approval as well as a departmental review.
- We are asking to obtain verbal consent for patients to participate. Position and insufflation are two interventions done routinely and changed by the surgeon many times during different parts of the surgery.
- Patient protected information is coded and protected using the Redcap software and destroyed once the study is published.
- The study is conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement, the Helsinki Declaration, and monitored by the Good Clinical Practice Unit
- Will register the trial once the IRB is approved.

Data handling and record keeping
- There will be a linking log maintained

Publication Plan
- Plan to publish in the JMIG
- Results are not returned to subjects

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