Title: The effect of abdominal binder use on postoperative pain and mobility in patients undergoing pelvic surgery: A randomized controlled trial

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Sponsor: Investigator-initiated

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Background and Rationale: Patients who seek surgical care for pelvic floor disorders have individual goals and expectations, including expectations about their postoperative recovery and return to their pre-surgical functional status. Effective pain management is key in postoperative healing (7). Inadequate pain control may lead to reluctance to taking deep breaths, to using an incentive spirometer, or to ambulate which increases the risk of postoperative atelectasis and thrombotic events (1). Inadequately controlled pain has a negative effect on quality of life and functional recovery. It also increases the risk of post-surgical complications and persistent post-surgical pain (2). Both narcotics and nonnarcotic medications should be used facilitate pain control given that narcotics can have side effects including nausea, vomiting, and constipation and over prescribing can contribute to narcotic addiction.

Elastic binders that surround the abdomen are commonly used after laparotomy and laparoscopic abdominal surgery with the aim of improving postoperative discomfort and pain, aiding in respiratory function, enhancing early mobilization, and decreasing seroma formation (3-5). While abdominal binder use has been studied after cesarean delivery, ventral hernia repair, and laparotomy for major abdominal surgery, its use has not been well studying in gynecology. Szender, et al., found that the use of an abdominal binder was well-tolerated and was relatively inexpensive and to increase ambulation after gynecologic surgery. However, the study did not find a statistically significant decrease in narcotic use (6). Additionally, the true effect of postoperative abdominal binder use on pain is unclear. Multiple studies have found improved pain scores, but there has been little data to correlate pain scores with actual postoperative narcotic usage. The aim of this study is to assess the effect of abdominal binder use on total postoperative narcotic use within seven days following pelvic surgery.

Objectives:
Primary objective: To assess the effect of abdominal binder use on total post-operative narcotic use within seven days following pelvic surgery.

Secondary objectives: To assess whether the use of an abdominal binder shortens the time to first ambulation after surgery.

Aims:

1. Determine postoperative total narcotic usage within the first seven days after pelvic surgery in patients who do not use an abdominal binder versus those who do use an abdominal binder.
2. Compare postoperative pain scores in postoperative patients with and without abdominal binder usage.
3. Compare length of time to first ambulation in postoperative patients with and without abdominal binder usage.
4. Describe associations between abdominal binder use and demographic data, medical comorbidities, indication for procedure, type of procedure, and perioperative/postoperative complications.

Hypothesis: Abdominal binder use will lead to improved postoperative pain scores, less total narcotic usage within seven days of surgery, and shorter time to first ambulation after surgery.

Patient selection:
Inclusion criteria
- Patients must be 18 years or older as well as willing and able to provide informed consent
- Patients undergoing going a scheduled pelvic surgery with plan to be admitted overnight (at least one night) after surgery.

Exclusion criteria
- Patients younger than 18 years old
- Patients unable or unwilling to provide informed consent
- Patients who are illiterate.
- Patients who are non-English speaking or reading
- Patients who are unable or unwilling to be contacted by phone after surgery on post-operative day seven
- Patients with chronic pain syndrome (evidence by daily intake of opioids for chronic low back pain, chronic headaches, or fibromyalgia).

No vulnerable populations will be approached for enrollment in this study.

Registration procedures:
Eligible subjects will be recruited by the process outlined below. Study team members will be emailed a list each week of the upcoming scheduled surgeries. The scheduled patients' electronic medical records will be reviewed and if the patient meets inclusion criteria, the patient will be approached by a study team member in the pre-anesthesia care unit on day of surgery for recruitment. Written informed consent will be documented by the use of a written consent form (attached). Each potential participant will have the opportunity to review the consent form with a physician co-investigator to discuss potential benefits and risks of participation. When all questions have been addressed, written consent will be officially obtained. All subjects will receive a copy of the signed consent form.

Protocol

Research-related procedures as part of this protocol:

[x] Device utilization/implementation – Not Investigational

Device utilization: Abdominal Binder – Category B device

Procedure Description and Details:

Screening/Eligibility Visit:

The determination for surgical procedure will be made by the patient's physician. The procedure will be scheduled by the patient's physician and then a list of all upcoming surgeries is sent to all members of the OBGYN department, including the study investigators. The list will be used to screen for patient who are eligible to participate in the study. The scheduled patients' electronic medical records will be reviewed and if the patient meets inclusion criteria, she will be approached for recruitment on day of surgery in the pre-anesthesia care unit. If patients agree to participate they will sign an IRB-approved informed consent at that time.

Randomization:

Randomization will be performed after the patient has agreed to participate, discussed the study, and signed the informed consent form. Using a random number generator, patients will be randomized in a 1:1 ratio into either the control (no abdominal binder) or the treatment (abdominal binder) group. Envelopes will be used to mask allocation to either the treatment group (abdominal binder) or the control group (no abdominal binder). Envelopes will be opened and allocation revealed after the conclusion of the procedure.

Risks:

There is a potential risk of breech of confidential information.

There is a risk of increased abdominal discomfort and skin irritation with abdominal binder use.

Benefits:

The potential benefit to subjects enrolled in the study includes improved pain control and quicker return to pre-surgery functioning. There is no financial benefit to participation. Although the patient may benefit from improved postoperative pain control and earlier ambulation, there may not be a direct benefit to study participation.

Day of Surgical Procedure

The surgical procedure will be performed using the standard procedures established in MacDonald Women's Hospital by an attending physician with a fellow and a resident. No deviation or alteration of the surgical procedure is needed to complete this study. Patients enrolled in the study to the experimental arm will have an abdominal binder ordered with their standard post-operative orders those enrolled in the control arm will not have a binder ordered.

Postoperatively, the patient will be encouraged to wear the abdominal binder continuously throughout their hospital stay, however if they wish to remove the binder for a period of time they will be able to do so. Patients will have standard narcotic and non-narcotic pain medications ordered for use after surgery. Patients will be given a Visual Analog Scale (VAS) to rate their pain at four time points during the study; pre-operatively, immediately (at 1 hour) post-operatively in the recovery area, twelve hours post-operation, and on the morning of post-operative day one. Additionally, the post-operative day number and exact time of the patient's first ambulation will be recorded.

After discharge home:
On discharge, patients randomized to the abdominal binder arm will be instructed to wear the binder while awake each day during the first seven days after surgery. Once the patient is more than seven days post-surgery, she may continue to wear the binder as much as she would like.

It will be discussed at the time of discharge that patients should expect a follow up phone call from a study investigator on post-operative day 7. All patients enrolled in the study will be contacted by phone by a study investigator on postoperative day seven regarding post-operative narcotic use (i.e. the number of remaining narcotic pills they have) and to give an estimate (percentage) of the amount of time the abdominal binder was worn during the first seven days. Study investigators will later review the patients' EMR to determine the quantity of narcotics they were discharged home with and calculate the total usage based on what the patient communicated on POD#7.

Patients will then continue to follow with their primary surgeon as scheduled for post-surgical follow up.

Alternatives to participation:
Subject participation in this study is voluntary. Subjects can refuse to participate or withdrawal at any time without stating a reason. Non-enrollment or withdrawal from the study will not affect their access to medical care of which they would otherwise be entitled.

Withdrawal from study participation:
There are no medical contraindications to binder use aside from a large wound that is left open to heal.

Withdrawal from the study is based on patient preference. Subjects may withdrawal at any time without stating a reason. Patients who withdrawal will remain included in the study as part of the "intention-to-treat" principle. If it is discovered that they did not give an accurate medical history or did not follow instructions for the study given by the study doctor and/or study nurse, the subject may be taken off the study at any time. Information that has already been collected will continue to be retained

Adverse Event Monitoring and Reporting:

This study will utilize the Common Terminology Criteria for Adverse Events (CTCAE) v4.03 for adverse event monitoring and reporting. The CTCAE v4.03 can be accessed from the CTEP homepage (http://ctep.cancer.gov). All appropriate treatment areas will have access to a copy of the CTCAE v4.03.

Adverse event monitoring and reporting is a routine part of every clinical trial. If an adverse event does occur, the first event will be clearly identified and the severity of the event will be graded using the CTCAE. Next, whether the event is expected or unexpected will be determined and whether the adverse event is related to the medical treatment or procedure will be clarified. With this information, it will be determined whether the adverse event should be reported as an expedited report. All expedited AE reports must also be sent to the local Institutional Review Board (IRB) according to local IRB's policies and procedures.

When assessing whether an adverse event is related to a medical treatment or procedure, the following attribution categories are utilized:

Definite - the adverse event *is clearly related* to the agent(s).
Probable - the adverse event *is likely related* to the agent(s).
Possible - the adverse event *may be related* to the agent(s).
Unlikely - the adverse event *is doubtfully related* to the agent(s).
Unrelated - the adverse event *is clearly NOT related* to the agent(s).

Clinical Safety Assessments
The following will be used in this study:
- Adverse event monitoring
- Vital signs, Pain and Distress questionnaires

Adverse Event Monitoring
For the purposes of this study, any clinical sign or symptom reported by the participant, abnormal laboratory result determined to be clinically significant by the principal investigator. Additionally, a medical diagnosis noted by medical personnel with onset or worsening from the time the participant signs the informed consent through completion of the follow up will be considered to be an AE, regardless of relationship to study procedures and treatments. More specifically, worsening of the patients baseline symptoms or function will be considered clinically significant and, as such, a reportable AE.

In addition, adverse events related to the procedures will be monitored clinically during the procedure (i.e. allergic reaction), as well as during short term follow up.
Relationship of an AE to the study intervention will be categorized as definite if the investigator feels it is incontrovertibly related to the treatment and,
- It follows a reasonable temporal sequence from administration of the treatment and,
- It could not be reasonably explained by the known characteristics of the participant’s clinical state, environmental or toxic factors, or other modes of therapy administered to the patient and,

Relationship of an AE to the study intervention will be categorized as probable if the investigator has a high degree of certainty that it is related to the treatment and,
- It follows a reasonable temporal sequence related to the procedure and,
- It cannot be reasonably explained by the known characteristics of the participant's clinical state, environmental or toxic factors, or other modes of therapy administered to the patient and,
- It follows a known pattern of response to treatment.

Relationship of an AE to the study intervention will be categorized as possible if the investigator has a low suspicion that it is related to the treatment, but it cannot be entirely ruled out and 2/3 of the following are met:
- It follows a reasonable temporal sequence related to the procedure
- It cannot be reasonably explained by the known characteristics of the participant's clinical state, environmental or toxic factors, or other modes of therapy administered to the patient
- It follows a known pattern of response to the treatment

Relationship of an AE to the study intervention will be categorized as not likely if the investigator deems it unrelated to the treatment, and 2/3 of the following are met:
- It does not follow a reasonable temporal sequence from administration of the MSCs
- It can be readily explained by the known characteristics of the participant's clinical state, environmental or toxic factors, or other modes of therapy administered to the patient
- It does not follow a known pattern of response to the treatment.

Relationship of an AE to the study intervention will be categorized as unrelated if it is clearly and incontrovertibly related to extraneous causes.

Adverse Event Severity

An AE is classified as serious if it meets any of the following criteria (in accordance with 21 United States Code of Federal Regulations Part 312.32 and the recommendations of the International Conference on Harmonization):
- Death.
- Life-threatening event, i.e., an event that places the participant, in the view of the site investigator, at immediate risk of death from the event as it occurred (does not include an event that, had it occurred in a more severe form, might have caused death).
- Requires or prolongs in-patient hospitalization.
- Results in persistent or significant disability/incapacity.
- Congenital anomaly/birth defect diagnosed in a child of a participant who participated in this study.
- Other medically important events that in the opinion of the investigator may jeopardize the participant or may require intervention to prevent one of the other outcomes listed in the definition above.

An AE is considered non serious if it does not meet the above criteria.

Adverse Event Recording

All AEs reported by the participant or observed by study site personnel from the time the participant signs the informed consent through completion of the follow up will be recorded in the participant's study record. Laboratory values that are deemed clinically

significant will be recorded as AEs. AEs are to be recorded regardless of relationship to study procedures and treatments. The information to be recorded will include, but not be limited to, relationship of the AE to study procedures and treatments, severity, and whether the event was serious.

Adverse Event Reporting
Any serious AE and Immediately Reportable AE will be reported to the Principal Investigator. An AE form will be completed. The Principal Investigator or designee will notify the IRB, and FDA, as necessary, within the required time frames. The reporting of any serious AE will not be delayed in order to obtain additional information. Any additional information, if collected, will be reported as a follow-up to the initial report. Serious AEs will be reported using standard forms. Follow-up information on a previously reported AE will be processed using the Follow-up forms. Follow-up information includes additions, deletions, and corrections to the initial report. Previously signed, dated, and faxed forms will not be altered to provide follow-up SAE information of any type. Any serious AE that has onset after enrollment and that is unresolved at the time the participant completes or permanently discontinues the study will be followed until the event resolves or until the participant's clinical course has stabilized.

For deaths that occur following a participant’s enrollment into the study, a Record of Death as well as a copy of the autopsy report (when/if available) will be submitted to the Principal Investigator. A copy of all documentation related to the event will be kept in the site's study files.
The Principal Investigator will notify the local review committee, i.e., the Institutional Review Board (IRB) as per local IRB requirements. Documentation of these reports will be kept in the site's study files

Stopping Criteria
The trial can be stopped at any point if safety concerns arise.

Statistical Considerations:
Based on retrospective data, a power analysis was performed and it was determined that a total of 88 patients (44 in each arm) would be required to achieve a power of 80% with an alpha error of 0.05 in order to detect a true difference in opioid (morphine equivalent) use between the groups. When an appropriately sized group is obtained, we will analyze the prospective data for difference in morphine use via univariate analysis, by either a t-test or Mann-Whitney U depending upon the distribution. Additionally, data will be evaluated with descriptive statistics, including means, medians, standard deviations, and ranges.

Study Parameters:
Age
Body Mass Index (BMI)
Medical Co-Morbidities
Past Surgical History
Type of procedure

Indication for procedure
Length of procedure
Post-operative complications
Pain assessment using Visual Analogue Scale (preoperatively, immediately after surgery in PACU, 12 hours postoperatively, and 24 hours postoperatively (POD#1)
Time to first ambulation
Total postoperative narcotic usage (Morphine equivalents, will be calculated based on inpatient usage and outpatient usage. Outpatient usage will be determined by calling the patient on POD#7 and asking how many narcotic pills they have remaining and then comparing that to what the EMR shows the narcotic prescription dispense number.)

Data / Record Keeping

Paper or written study data will have a study number rather than PHI. Subsequently, collected study data will be managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Case Western Reserve University. REDCap is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

No identifiable information with be shared outside of UH and all non-identifiable information will be pooled and released as a group for the final study after statistical analysis is complete. Identifiers will be kept until completion of data analysis to allow for review of additional information that may become necessary during the statistical analysis phase. Patient MRN and unique study specific identifier will be kept until completion of data analysis or <2 years, whichever is greater. The file containing study specific identifier and other study, as well as pooled statistics data, will be kept for a period of greater than 3 years per UH policy to allow additional statistical analysis as may be required for final manuscript revisions.

Physical elements of the study, including signed consent forms will be maintained in a locked cabinet within the Obstetrics and Gynecology administrative office as per standard protocol. This cabinet will only be accessible by the division secretary or the investigators. At times when this paper chart requires direct inspection and data retrieval, study personnel will access it and use it only within the Obstetrics and Gynecology administrative office. REDCap will be used to safely contain all HPI and will be accessible to study staff only.

Data and safety monitoring will be performed by the primary investigators throughout the study to ensure all above policies are being followed. The primary investigators will meet monthly to review patient enrollment and potential adverse event. Adverse events in obstetrics patients are defined institutionally and we will use the definitions employed by MacDonald Women's Obstetric Quality Assurance. Any unexpected or significant adverse event may prompt a preliminary statistical analysis and/or immediate halt in enrollment or cancellation of the study.

Financial Information:
This prospective study investigates two different standard of care practices to determine whether there is a clinically significant difference. Subjects will receive no compensation for participation in this study.

Subjects will incur no costs associated with participation with this study. Regardless of participation in this study, the patient is responsible for the cost of surgery and post-operative treatment. Postoperative care will be per usual care standards and as such, if randomized to an abdominal binder, it will within the standard postoperative hospitalization cost.

Compensation for Research Related Injuries:
This prospective study investigates two different standard of care practices to determine whether there is a clinically significant difference. As such, subjects are at minimal risk of incurring a research related physical injury. As currently literature does not support a real risk, no expected compensation is necessary.