Project title: Reducing postoperative bleeding after hysterectomy via independent closure of vaginal cuff angles

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Hysterectomy is the most common surgical procedure in the United States, with over 600,000 performed annually.[1] There has been a dramatic improvement in expected postoperative course secondary to the advancement of minimally invasive gynecologic surgery.[2] With the advent of laparoscopy and robotic surgery, even the most complex cases can be successfully performed via a minimally invasive approach. What used to be a major surgery that required a prolonged inpatient stay has become an outpatient procedure where patients are discharged home a few hours after the operation.[3] Although the recovery period is shorter than in the past, there are still some postoperative complaints that are relatively common, and can impair quality of life. One of them is postoperative vaginal bleeding. Although this can be a sign of a more serious problem such as vaginal cuff dehiscence, the grand majority of times it is related to granulation tissue in the vaginal cuff that although may be self-limiting, can be bothersome and concerning to patients. Not only does this bleeding impair quality of life, but it's one of the most common reasons for emergency room visits after surgery. Multiple studies have shown that postoperative vaginal bleeding and return to the hospital significantly affect patient satisfaction. [4,5]

Anecdotally, bleeding originates from granulation tissue at the angles of the closure, although there hasn't been any studies specifically investigating this. A common approach to laparoscopic cuff closure involves a running barbed suture, with or without separate closure of the lateral angles.[6,7] Recently, laparoscopic closure of the vaginal cuff was found to be superior when compared to vaginal closure in terms of vaginal cuff dehiscence[8]. This RCT also evaluated vaginal cuff bleeding as a secondary outcome, but this was recorded as he presence of bleeding at 3 months after surgery. The closure technique in this study was a running non-barbed suture, without independent suturing of the angles. Although a running suture placed laparoscopically may provide adequate tensile strength throughout the cuff to promote healing, the tension at the corners may be less than at the center when using barbed suture, hence potentially increasing the risk of bleeding. Furthermore, the second angle may be more difficult to access when the remainder of the cuff is re-approximated.

We propose prospectively evaluating if adding separate sutures to the angles of the vaginal cuff before running barbed suture reduces the incidence of patient's perception of bleeding after surgery.

Primary Objectives:

Determine if closing angles of vaginal cuff separately during laparoscopic hysterectomy decreases incidence of vaginal bleeding after surgery.

Secondary objectives:

Determine if there is a difference in patient satisfaction after surgery by comparing results from SF-36 questionnaire

Determine if this technique changes the rate of vaginal cuff complications (cellulitis, dehiscence, vaginal cuff hematoma, and abscess)

Evaluate the difference in operative time between techniques for this portion of the procedure.

Hypothesis

Performing a separate closure of the vaginal cuff angles after hysterectomy will decrease incidence of postoperative bleeding

Inclusion Criteria-

- Pre-menopausal patients scheduled to undergo hysterectomy via laparoscopic/robotic approach for benign indications (Ages 18-60, who have had at least one menstrual cycle in the last year).

Exclusion Criteria-

- Patient's that incur in an intraoperative bowel or urologic injury during the hysterectomy that requires repair. If injury occurs after randomization (during vaginal cuff closure), this will be recorded and reviewed by the study's safety officer
- Patients scheduled to undergo a concomitant vaginal procedure (Mid-urethral sling, anterior/posterior repair)
- Patients scheduled to undergo pelvic floor repair (utero-sacral ligament suspension)
- Patients with known preoperative malignancy
- Patients in which a total hysterectomy is not completed

Sample Size

Sample size was calculated for primary outcome. Based on our experience when angles are not secured separately, incidence of at least mild spotting ranges around 20%. We expect the intervention to decrease this to an incidence of 5%, In order to detect the expected change with a significance level of 5% and a power of 80%, a sample of 154 patients is required (77 per group) using Kelsey's formula.

Methods

Participants will be enrolled based on eligibility criteria. They will be consented to participate in the office during their preoperative visit. Baseline demographic data collected will include Age, BMI, Diabetes status, HgbA1c within the last 3 months if available, and daily steroid use. Subjects will be allocated on a 1:1 ratio via block randomization in blocks of 4. Assignment will be performed after completion of hysterectomy, before cuff closure, via a pre-generated sequential masked randomized

list. An opaque sealed envelope containing group allocation will be opened by the circulating nurse prior to vaginal cuff closure, who will communicate contents to the surgeon.

Vaginal cuff-closure will be performed by high-volume surgeons with subspecialty training in minimally invasive gynecology who have similar operating techniques. If the subject's group corresponds to "Control group", the surgeon will re-approximate the cuff in a standard fashion, using a running-barbed suture (2-0 V-LOC 90 with tapered needle), starting at the right apex, moving towards the left, and then back-tracking once to further reinforce the closure. If the allocation corresponds to "Apical stitches", surgeon will use 0 polyglactin 910 suture on a tapered needle to place figure of 8 sutures on both (left and right) apexes. Knot tying technique (intra-corporeal vs extracorporeal) will be up to surgeon preference. After this is completed, barbed suture will be used to re-approximate the remainder of the vaginal cuff from right to left, backtracking once at the end for reinforcement. Time when vaginal cuff closure starts and ends will be noted. Surgeon will also examine vaginal introitus at the end of the case, noting any lacerations.

After the surgery, a survey will be filled out by the primary surgeon (See ANNEX 1).

Immediate postoperative care and discharge criteria will be performed per unit guidelines. All patients are instructed to abstain from heavy lifting (more than 30 lbs) and vaginal penetrative sex for 6 weeks.

When patients arrive for their postoperative visit (10-20 days after surgery), a member of the research team who is blinded to allocation will give out a short survey before the patient meets the physician (SEE ANNEX 2). Remainder of visit will occur in a routine fashion.

Between 90-114 days after surgery, patients will be called by a member of the research team and given a survey regarding bleeding and quality of life (See ANNEX 3 and SF-36 survey[9-11]).

A retrospective chart review will also be performed 3 months after enrollment to evaluate for any postoperative visits to the emergency department / re-admissions / re-operations / infections.

Data Handling

A master key will be generated during randomization. It will contain patient initials and medical record number, and a unique code. Only the primary investigator will have access to this master key which will be kept in an encrypted secure computer at Texas Tech.

A separate de-identified secure database (Redcap) using the unique code as index will be used for collection of data points. The baseline demographic data will transferred directly into the de-identified database after randomization. All collection forms /surveys will be destroyed after data is transferred into electronic database. Using the master key, we will perform a retrospective chart review to complete final data points (pathology results, return to ER, re-admissions, re-operations).

Data Analysis

All data analysis will be carried out in SPSS version 24 (IBM, Armonk, NY, USA). Continuous baseline demographic variables: (age, BMI, operating time and uterine weight) will be compared using t-student, and Chi square for categorical variables (steroid use, diabetes). Postoperative bleeding will first be evaluated as a binary categorical value, and compared using Chi Square. Inter-quartile ranges/t-student and logistic regression will be utilized to compare SF-36 results at 3 months. We will also use Chi Square to compare categorical values such as return to ER, Infection and re-admission.

Time frame

Based on the current volume of hysterectomies for the Minimally Invasive Surgery Division at Texas Tech, we expect to enroll 3 patients per week on average. We expect the data collection phase to span approximately 72 weeks (Taking into account the 3 month waiting period before the final satisfaction survey on the last patient enrolled). Data analysis will span an additional 12 weeks.

Strength/Innovation

Postoperative vaginal bleeding is one of the most common complaints after hysterectomy, and its negative impact on patient satisfaction has been demonstrated. Furthermore, if these symptoms prompt phone-calls to the office, nurse-visits, or a trip to the emergency department, valuable health-care resources are utilized. Although the technique of closing apexes separately is considered a standard variation, its impact on outcomes has never been evaluated in a controlled prospective fashion, where standardized surveys are given to patients to determine impact. The results from this trial will help surgeons determine the best technique for re-approximating the vaginal cuff after hysterectomy.

Limitations

The main confounding factors when comparing surgical techniques are difference in operating style between surgeons and baseline surgical characteristics (large uteri that may require more dissection and tissue manipulation, etc.). To control for this we are only recruiting patients from 3 surgeons who have a similar operating technique. In addition to this, we are documenting operating time and specimen weight, which can be used to compare both groups and assure that they are homogenous to these potential confounders. Baseline patient characteristics that can influence postoperative healing, such as diabetes and steroid use will also be accounted for. Post-hoc analysis will also be made specifically stratifying the data based on these characteristics.

Risks / Safety

There are no known risks associated to either method of vaginal cuff closure. Both are common variations that have been utilized throughout the country for several years. We are attempting to determine if one of the two methods has a higher risk of postoperative bleeding. To date, this has not been answered. We will have an assigned safety monitor that will perform an interim analysis of the cohort after every 20 subjects are enrolled. If the experimental arm demonstrates an increase of greater than 10% in visits to the emergency-room related to post-operative complaints, or an increase in unexpected complications (wound infection, wound dehiscence, etc.), the study will be halted.

There is also the potential risk of accidental disclosure of the health information that will be collected. To mitigate this, all stored data will be de-identified in a secure server using TTUHSC approved software (Red-Cap) that can only be accessed by members of the research team.

Benefits

This study will answer the question on whether including apical stitches results in a reduced incidence of postoperative bleeding.

Costs

Both methods of vaginal-cuff closure are routinely performed, albeit in an uncontrolled fashion, hence the cost of hysterectomies will not differ when compared to patients not undergoing a research protocol. In general, we expect that closing the apexes will add approximately 5 minutes of operating time. This will be measured during the study. The polyglactin suture is already routinely opened during hysterectomy cases. Research staff salaries are supported by the Department of Obstetrics and Gynecology at Texas Tech.

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ANNEX 1

Patient research ID:	EBL:
Surgery start time:	Surgery stop time:
Vaginal cuff start time:	Vaginal cuff stop time:
Vaginal lacerations visible at end of case? Y / N	Complications during cuff closure? Y / N

Vaginal cuff start time begins when first suture and sewing instruments are in abdomen. Cuff stop time is when last suture is cut.

ANNEX 2

English version:

On a scale of 0-10, with 0 being no pain and 10 being the worst pain ever, what number would you rate your current vaginal/pelvic pain at?

0 1 2 3 4 5 6 7 8 9 10

In the 6 months before surgery, do you consider yourself sexually active?

Yes No

Have you experienced vaginal bleeding/spotting after your surgery (not counting first 2 days after surgery)?

Yes No

If yes, with what frequency?

Daily Most days Infrequent

How would you best describe the bleeding?

Only when using restroom Spotting throughout day More than spotting

Spanish version:

En una escala del 0-10, con 0 siendo nada de dolor, y 10 siendo el peor dolor posible, ¿Qué número representaría su dolor pélvico/vaginal en este momento?

0 1 2 3 4 5 6 7 8 9 10

En los 6 meses antes de su cirugía, se considera sexualmente activa?

Si No

¿Ha tenido sangrado vaginal o manchado después de su cirugía? (Sin contar los primeros dos días después de la operación)

Si No

Si la respuesta fue sí, ¿con que frecuencia?

Diario La mayoría de los días Infrecuente

¿Cómo describiría su sangrado?

Solo al ir al baño Manchado durante el día Más que manchado

ANNEX 3

English Version

Have you experienced vaginal bleeding in the last 2 weeks?

Yes No

Have you had vaginal intercourse since your surgery?

Yes No

If yes, rate from 0-10 how painful the last time you had intercourse was? With 0 being no pain and 10 being the worst pain ever

0 1 2 3 4 5 6 7 8 9 10

Have you been to the emergency department after your surgery for any related surgical problems?

Yes No

Spanish Version

¿Ha tenido sangrado vaginal en las últimas 2 semanas?

Si No

¿Ha tenido relaciones sexuales vía vaginal desde su cirugía?

Si No

Si la respuesta fue sí, en una escala del 0 al 10, con 0 siendo nada de dolor y 10 siendo el peor dolor posible, ¿Cuánto dolor tuvo durante la última vez que tuvo relaciones sexuales?

0 1 2 3 4 5 6 7 8 9 10

¿Ha tenido que visitar el departamento de urgencias desde su cirugía, por problemas relacionados a la operación?

Si No