A prospective randomized trial comparing vaginal hysterectomy and laparoscopic supracervical hysterectomy at the time of sacrocolpopexy for the treatment of uterovaginal prolapse

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Background and Significance:

For young women who are sexually active with symptomatic pelvic organ prolapse, reconstruction with a sacrocolpopexy procedure is beneficial because the success rates are high as the procedure adequately restores support of the vaginal apex and maintains vaginal length (Walters). Minimally invasive abdominal sacrocolpopexy has become an alternative to open abdominal sacrocolpopexy as this mode of surgery bridges the gap between the advantages of vaginal surgery, namely decreased morbidity and faster patient recovery, with the surgical success rates of abdominal sacrocolpopexy (Ganatra).

Sacrocolpopexy involves suspension of the vagina to the anterior longitudinal ligament of the sacrum at the level of S1 using a bridging graft which can be made of biologic or synthetic materials. The graft is sutured to the anterior as well as the posterior vagina and then attached to the anterior longitudinal ligament of the sacrum. The surgery can be performed for uterovaginal prolapse or post-hysterectomy vaginal vault prolapse. In cases of uterovaginal prolapse, hysterectomy is often performed unless uterine preserving surgery is desired and a hysteropexy is performed. When concurrent hysterectomy is done, a supracervical or total approach may be taken.

In 2014, there was a de facto change in practice patterns after the Food and Drug Administration advised against power morcellation for extraction of the uterine specimen after minimally invasive supracervical hysterectomy. At that time, surgeons performing prolapse surgery had to choose to continue performing concurrent supracervical hysterectomy at the time of sacrocolpopexy using an extended abdominal incision to remove the uterus. An alternative solution became to perform total vaginal hysterectomy followed by a combination of mesh attachment vaginally (to the vagina) and laparoscopically (to the sacrum) versus mesh attachment performed laparoscopically only

(to the vagina and sacrum). Very few studies have looked at the outcomes of these two ways to perform minimally invasive sacrocolpopexy with concurrent hysterectomy. One study published by Nosti et al. did compare the two groups retrospectively and found that there was no difference in mesh-related complications between the groups and that vaginal mesh attachment following vaginal hysterectomy decreased operative time significantly with no differences in intraoperative complications, reoperation for recurrent prolapse, and subjective or objective outcomes compared to concurrent supracervical hysterectomy (Nosti). In our practice, both techniques are currently used, and while we also believe there are no differences in complications and outcomes between the two modes of surgery, anecdotally our group feels that surgical time may be the same between the two types of prolapse repairs.

Cost of health care has become a hot topic in the medical community. One of the focuses of cost containment in medicine has centered around operating room efficiency. Several studies have looked at OR time nonutilization (Weinbraum) in order to determine the economic value of saving OR time. Surgeons can make significant contributions to these types of savings by reducing equipment needs, facilitating case set-up times, and focusing on intraoperative efficiency. This includes choosing a mode of hysterectomy and technique for mesh attachment at the time of sacrocolpopexy that may make the entire procedure faster and more efficient.

Given the sparse data that exist, it remains unclear if one type of concurrent hysterectomy and subsequent mesh attachment at the time of sacrocolpopexy is more efficient. Furthermore, because no prospective studies exist, we also do not know with any degree of certainty if one approach reduces the risk of intraoperative and postoperative mesh-related complications as well as the risk of prolapse recurrence. Therefore, the primary objective of the proposed study is to determine the difference in surgical time between minimally invasive (laparoscopic) sacrocolpopexy performed with concurrent vaginal hysterectomy versus laparoscopic supracervical hysterectomy. The secondary objectives are to determine if there are differences in intraoperative adverse events and postoperative mesh-related complications and prolapse recurrence between the groups.

Hypothesis: There is no clinically difference in surgical time in patients undergoing vaginal hysterectomy versus laparoscopic supracervical hysterectomy at the time of sacrocolpopexy

Study Design: Randomized trial

Primary Outcome: Surgical time defined as time of incision to time of sacrocolpopexy completion (abdominal incisions closed)

Secondary Outcomes:

1. Intraoperative, peri-operative and post-operative complications up to 6 weeks after surgery

2. Pelvic floor symptoms (urinary, bowel, prolapse, sexual function): PFDI, ISI, PISQ) at 6, 12, and 24 months
3. Patient satisfaction (PGII) at 6, 12 and 24 months
4. Prolapse recurrence at 12 and 24 months
5. Mesh-related complication defined by mesh erosion on vaginal examination or report of reoperation for any type of sacrocolpopexy mesh excision within 24 months of the index surgery

Study Population: Study subjects will be recruited from patients that present to the Center for Urogynecology & Pelvic Reconstructive Surgery in the Department of Obstetrics and Gynecology at the Cleveland Clinic Main campus, Hillcrest Hospital and Fairview Hospital, and their surgeries will be performed at either one of these sites.

Inclusion Criteria:

- Age ≥ 18, who are to undergo laparoscopic sacrocolpopexy for uterovaginal prolapse and desire concurrent hysterectomy at the time of surgery
- Other concomitant laparoscopic or prolapse and anti-incontinence procedures (cystocele repair, rectocele repair or mid-urethral sling procedures) will be performed at the primary surgeon's discretion.
- Patient's must have an up-to-date PAP smear on record, or a PAP smear is performed in the office and verified to be normal pre-enrollment

Exclusion Criteria:

- Inability to comprehend written and/or spoken English
- Inability to provide informed consent
- Medical illness precluding laparoscopy
- Need for concomitant surgeries not related to pelvic organ prolapse or incontinence
- Sacrocolpoperineopexy
- Patients desiring uterine preservation (hysteropexy)

Study Procedures:

Study Identification and Recruitment

Potential subjects will be identified by members of the Center for Urogynecology & Pelvic Reconstructive Surgery at the Cleveland Clinic Main campus, Hillcrest Hospital and Fairview Hospital. Eligible patients who agree to participate will be provided written informed consent administered by the collaborators listed on this IRB.

Randomization

All subjects will be predetermined by their surgeon to undergo a laparoscopic sacrocolpopexy. The participants will then be randomized to either concurrent vaginal hysterectomy or laparoscopic supracervical hysterectomy according to a computer-generated randomization schedule with the use of the SAS statistical software package (SAS Institute, Cary, NC).

Office Interventions

All patients will be seen for a preoperative visit and then postoperatively at 6, 12 and 24 months. The 6 month visit will be standard of care, the 12 month and 24 month visit will be a research visit. At each visit, a vaginal exam and a complete Pelvic Organ Prolapse Quantification (POP-Q) exam will be performed. In addition, patients will be asked to complete the Pelvic Floor Distress Inventory (PFDI-20), Incontinence Severity Index (ISI), Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) and Patient Global Impression of Improvement (PGII) questionnaires at the pre-operative visit as well as the 6, 12, and 24 month postoperative visits. Completion of these questionnaires is the only additional assessment that is specific to participation in this study and is not usually included as part of the standard care of sacrocolpopexy. It should take no more than 10-15 minutes to complete the questionnaires. The study subjects will not be exposed to any additional risk by participating in this study except for the inconvenience of completing the questionnaires.

Surgical Interventions

The laparoscopic portions of the surgery will be performed using four ports: an umbilical port for the laparoscope (either 5 or 10/12mm), two ports (either 5, 8 or 10/12 mm) in the bilateral lower quadrants, and one 5-mm port placed at the level of the umbilicus, lateral to the rectus muscle on either side for retraction.

If a supracervical hysterectomy is to be performed, it will be done in a standard fashion. A uterine manipulator will be placed inside of the uterus. The round ligaments will be transected using cautery. The fallopian tubes and ovaries will be left in situ or removed at the time of hysterectomy depending upon the preoperative decision made between the surgeon and patient. The uterine arteries and cardinal ligaments will be cauterized laparoscopically. The uterus will be amputated at the level of the internal cervical os and the endocervical canal will be cauterized. The specimen will be extracted in a laparoscopic endocatch bag and removed through an extended incision at the umbilicus at the end of the case. Dissection of the vagina anteriorly and posteriorly will be done laparoscopically with the use of an end-to-end anastomosis (EEA) sizer in the vagina. Dissection of the presacral space will also be done laparoscopically. Five to six 2-0 PDS sutures will be placed to secure the mesh to the anterior vagina as well as the posterior vagina for a total of 10-12 sutures on the vagina; the arm of the mesh will be secured to the anterior longitudinal ligament of the sacrum using two 0 Prolene sutures. The Coloplast® Restorelle Y mesh will be used for all cases. The peritoneum will be closed with 0 or 2-0 vicryl sutures.

If a vaginal hysterectomy is performed, it will be done in a standard fashion using a traditional clamp and suture technique starting at the uterosacral ligaments and ending with the utero-ovarian ligaments. The specimen will be extracted through the vagina. Dissection of the vagina anteriorly and posteriorly will be done vaginally. The mesh will be attached vaginally using five to six 2-0 PDS sutures on the anterior and posterior vagina for a total of 10-12 sutures on the vagina. The Coloplast® Restorelle Dual flat mesh will be used. The vagina will then be closed in two layers using 0 or 2-0 vicryl suture. Laparoscopic entrance will then be gained and set up will be done as described above. The presacral space will be dissected laparoscopically and the mesh attached to the anterior longitudinal ligament of the sacrum using two 0 Prolene sutures. The peritoneum will be closed with 0 or 2-0 vicryl sutures.

Data Collection & Management:

Preoperative data will include the following:

- Patient age, race, vaginal parity, menopausal sate, BMI, comorbid conditions, tobacco use, preoperative prolapse stage, preoperaetive use of vaginal estrogen
- PFDI-20, ISI, PISQ-12

Data points recorded during the procedure will include:

- Total OR time = operating room time of entry and exit
- Surgical time = time from incision to end of sacrocolpopexy (abdominal incisions closed)
- Total Case time = time from incision to end of procedure
- Hysterectomy time= time from start of hysterectomy to end of hysterectomy
- Concomitant procedures
    - Lysis of Adhesions >45 min
    - Anterior colporrhaphy
    - Posterior colporrhaphy
    - Perineorrhaphy
    - Midurethral sling
    - Other
- Estimated blood loss
- Intraoperative complications
    - Vascular Injury
    - Cystotomy
    - Ureteral Injury
    - Bowel Injury - small bowel, large bowel, rectal

Postoperative data will include the following: 6, 12, 24 months

- POP-Q exam (performed by a provider who did not perform the surgery)
- Vaginal exam, inspection for mesh exposure
- PFDI-20, ISI, PISQ-12
- Assessment of use of postoperative vaginal estrogen

- Review of electronic medical record (inpatient notes, d/c summary, ER visits), assessing for postoperative complications
    - Reoperation for immediate complications = reoperation within 30 days of surgery
    - Abdominal Wound infection = fascial, subcutaneous, cutaneous infection requiring antibiotic treatment
    - Hematoma = intrapelvic/abdominal
    - Vaginal cuff cellulitis/Pelvic Abscess = requiring IV/PO antibiotic therapy and/or transvaginal, trangluteal or percutaneous drainage
    - DVT/PE = diagnosed with Doppler US or CT scan
    - Reoperation for SUI with pubovaginal sling (synthetic or fascial), colposuspension, injection with periurethral bulking agents
    - Reoperation for mesh exposure
    - Reoperation for recurrent POP
    - Bowel Injury/Bowel Obstruction = enterotomy, perforation, ileus, partial/complete obstruction
    - Port site or incisional hernia
    - Need for any radiologic imaging
    - Lower urinary tract injury = bladder, ureteral
    - Neurologic Injury = brachial plexus, abdominal wall (ilioinguinal, iliohypogastric), lower extremity (femoral, sciatic, common peroneal)
    - Pulmonary complications = pneumonia, pulmonary hypertension, pulmonary edema within 14 days of surgery
    - Cardiac = ACS, MI, HF within 14 days of surgery
    - Postoperative ICU admission

Protection of each subject's personal health information will be a priority in this study. One master excel file containing subject personal information including name and medical record number will be kept in a password-protected file, on a designated protected research drive on a password-protected computer in a locked office at the Cleveland Clinic. In that file, each subject will be assigned a subject identification number that will be used for the purposes of data collection in order to de-identify subjects.

All paper forms used for data collection will be kept in a research cabinet dedicated to this project which will be locked at all times, in a locked office at the Cleveland Clinic. All forms will contain de-identified information – identification numbers will correspond to the subjects listed in the master excel file.

All study data will be transferred and managed electronically using REDCap (Research Electronic Data Capture). Each subject will be entered into REDCap using the assigned identification number from the master excel file. REDCap is a secure, web-based application designed to support data capture for research studies, providing user-friendly web-based case report forms, real-time data entry validation, audit trials, and a de-identified data export mechanism to common statistical packages. They system was developed by a multi-institutional consortium which was initiated at Vanderbilt University and includes the Cleveland Clinic. The database is hosted at the Cleveland Clinic Research Datacenter in the JJN basement and is managed by the Quantitative Health Sciences Department. The system is protected by a login and Secure Sockets Layers (SSL) encryption. Data collection is customized for each study as based on a study-specific data dictionary defined by the research team with guidance from the REDCap administrator in Quantitative Health Sciences at the Cleveland Clinic.

Analysis Plan:

There will be 2 arms to this study: laparoscopic supracervical hysterectomy and sacrocolpopexy with Restorelle® Y mesh and vaginal hysterectomy and sacrocolpopexy using the Restorelle® Dual flat mesh.

We determined that 30 subjects in each arm were needed to detect a difference of 30 minutes or more (standard deviation 30 minutes) in surgical time between the two groups with 80% power and a significance level of .05. We will account for potential subject drop out and loss to follow-up as well as unforeseen factors in recruiting and will plan to recruit 35 subjects to each arm, for a total of 70 subjects.

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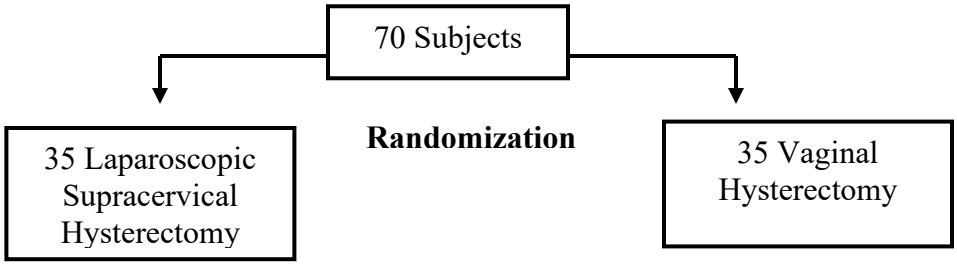

All statistical analyses will be done using jmp 14. We will use descriptive statistics to show our demographic and baseline data: categorical variables will be presented as n/N (%) with 95% confidence intervals and continuous variables will be presented as mean+/- SD [range]. The two types of hysterectomy (laparoscopic supracervical and vaginal) will be compared. With a continuous outcome and two categorical independent factors, a two-way analysis of variance will be used to evaluate differences between the groups. The results will be presented in a standard ANOVA table, which should be sufficient to determine if differences exist. A linear regression will be done to demonstrate actual changes in surgical time attributed to each variable.

Summary of tasks for study:

	Preop	Day of Surgery	6 mo	12 mo	24 mo
Enrollment/Informed consent	X				
Demographic data	X				
PFDI-20	X		X	X	X
ISI	X		X	X	X
PISQ-12	X		X	X	X
POP-Q	X		X	X	X
Vaginal exam			X	X	X
Randomization		X			
Intraoperative Data		X			
Review of d/c summary, chart, complications (ER visits, etc)			X		

References:

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3. Nosti PA, Carter CM, Sokol AI, et al. Transvaginal versus transabdominal placement of synthetic mesh at time of sacrocolpopexy. Fem Pelvic Reconstr Surg 2016; 22(3):151-155.
4. Weinbraum AA, Ekstein P, Ezri T. Efficiency of the operating room suite. Am J Surg 2003;185:244-250.