MANUAL OF PROCEDURES/PROTOCOL

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A randomized controlled trial of permanent vs absorbable suture for uterosacral ligament suspension

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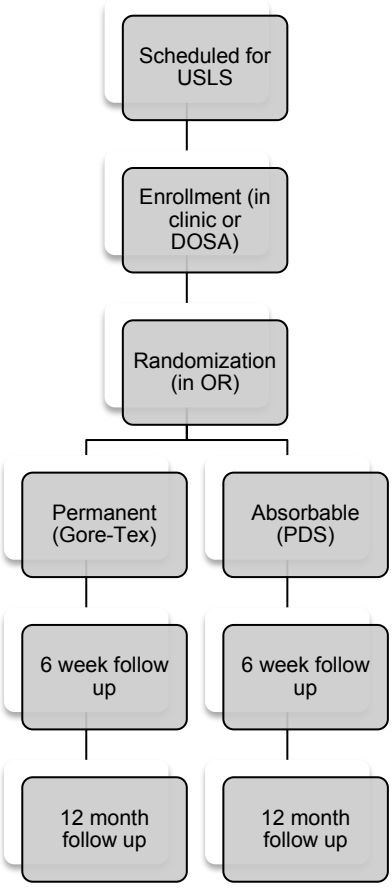
Section 1. *Study Overview*



Specific Aims

Primary: Demonstrate that absorbable 0 polydioxanone (PDS, Ethicon, Somerville, NJ, USA) suture is not inferior to permanent polytetrafluoroethylene (CV-2 Gore-Tex, WL Gore and Associates, Flagstaff, AZ, USA) suture for uterosacral ligament suspension (USLS) as measured by POP-Q point C at 12 month follow up.

We hypothesize that absorbable suture is not inferior to permanent suture for USLS as measured by POP-Q point C at 12 month follow up.

Secondary: (1) Compare suture-related complications between groups, including erosion, granulation tissue and need for suture excision. (2) Compare subjective outcomes between groups with the PFDI-20 questionnaire.

Background and Significance

The lifetime risk of surgery for pelvic organ prolapse (POP) or stress urinary incontinence (SUI) has been estimated to be as high as 20%.[1] USLS is a very commonly performed vaginal-approach surgical procedure for correction of apical vaginal prolapse. Anatomic cure rates for apical prolapse following USLS have recently been shown to be 89.7%.[2] The original description of the USLS procedure by Shull included the use of permanent sutures for the apical suspension.[6] Subsequent, high-quality trials evaluating USLS, such as the OPTIMAL trial, have also included the use of permanent sutures.[2] Thus, permanent apical sutures may be considered the “gold-standard”. Nonetheless, debate persists as to the optimal suture selection for this procedure.

Some have advocated choosing an absorbable suture.[3] This allows a full-thickness incorporation of the vaginal wall with the apical suture and may reduce suture-related complications. The procedure was initially described using permanent suture to suspend the fibromuscular apical vaginal tissue to the uterosacral ligaments. Symptomatic suture erosion rates of 22% in the permanent suture group were noted in one retrospective comparison of permanent and absorbable sutures.[3] No suture erosions were noted in the absorbable suture group. However, others have advocated continued use of permanent suture, citing increased failure rates with absorbable sutures.[4] The evidence for either approach is limited by having just a few retrospective studies.[3-4] A high-quality, randomized controlled trial to evaluate the optimal suture for this common procedure is needed. The IUGA grant is an ideal funding mechanism for answering this clinically relevant question with a focused randomized trial.

Section 2. *Participant Screening and Enrollment*

Adult women (age 18-99) scheduled for USLS can be approached for the study prior to surgery or at the time of the pre-operative clinic appointment or in DOSA. All women preparing for surgery can be given information (a study flier) prior to surgery once they are scheduled for USLS.

After review of eligibility criteria (see below), a study team member will determine eligibility and obtain informed consent. Once consent is obtained, the participant is enrolled into the study. However, a study ID number is not assigned until the patient is randomized.

Inclusion criteria will be: (1) scheduled for USLS.

Exclusion criteria will be: (1) age under 18 years, (2) non-English speaking, (3) prisoner, (4) cognitive impairment precluding informed consent and (5) planned hysteropexy. We will only plan to include post-hysterectomy procedures and procedures including a concomitant vaginal hysterectomy.

A screening log will be maintained for all potential participants for this study (i.e. all patients who are scheduled for USLS during the recruitment period) and whether they were enrolled into the study. The screening results from this log will be tallied at the conclusion of enrollment, and patient identifiers will be destroyed.

Section 3. *Randomization and Surgery*

Following enrollment, the subject will be randomized only after the subject is in the operating room. The study team member will then log on to the randomization software at www.randomize.net. The following steps are necessary to randomize the patient and obtain the treatment arm:

1. Sign in. Click “SIGN IN” in the upper right hand corner.
2. Enter user info. Your Login ID is your first initial followed by your last name (i.e. jkowalski). Your Password is uterosacral.
3. Click “ENROLL A PATIENT”.
4. Click “A randomized controlled trial of permanent vs absorbable suture for uterosacral ligament suspension”.
5. Note the assigned Patient ID. This is a three-digit number between 001 and 044. *Write this number on the cover sheet of the enrollment package. This step is critical.* Click “NEXT”.
6. Confirm the inclusion and exclusion criteria are met by selecting the appropriate yes or no boxes. Click “NEXT”.
7. Select the attending surgeon for the case. Click “NEXT”.
8. This final screen will display the treatment assignment and confirm the Patient ID number.

The surgery will then be completed. USLS with the assigned suture and any scheduled concomitant prolapse and anti-incontinence procedures will be performed. USLS will be performed as initially described by Shull *et al* with two important differences in technique. First, 2 sutures will be placed through the intermediate portion of each uterosacral ligament instead of 3. Second, when absorbable suture (PDS) is used, the suture will be placed through the full thickness of the anterior and posterior vaginal walls.

Following surgery, the patient should be scheduled for a follow up visit at 6 weeks with either Diane Elas (UIHC) or Nicole Myslinski (Quad Cities Outreach Clinic).

Section 4. *Follow-up and CRF Completion*

Patient demographics, relevant histories, baseline physical exam including POP-Q and PFDI-20 data will be abstracted from the electronic medical record following enrollment. The PI will place this information into a secure database.

Follow up exams will occur at 6 weeks and 12 months post-operatively and will include a POP-Q exam. All participants will also be assessed for any suture-related complications, such as erosion or granulation tissue. Follow up exams will be completed by one of two urogynecology nurse practitioners who will be blinded to the surgery and suture choice. Both nurse practitioners have extensive experience in performing POP-Q exams. The examiners will complete a follow up data abstraction form for each follow up appointment (6 weeks and 12 months).

The primary outcome will be measured by POP-Q point C. Specifically, the preferred method for measuring point C will be to identify point C visually with a speculum and to visually follow that point with the patient performing a Valsalva maneuver while simultaneously releasing pressure on the speculum. Should this method prove to not be feasible for any individual patient due to anatomy, the examiner will have the option to identify point C visually with the speculum in place, leave the Q-tip in place lying against point C, remove the speculum, and have the patient perform a Valsalva maneuver while allowing the Q-tip to descend against point C. As a last alternative, the provider may identify point C digitally, follow point C digitally while the patient performs a Valsalva maneuver and then measure the distance from the hymen to the tip of the finger with a Q-tip.

Subjects will also complete a set of questionnaires at each follow up appointment. See appendix 1.

Subjects will be provided with compensation following completion of the 12-month follow up. This will be provided in the form of a $100 check through the UIHC e-Voucher system.

We anticipate a volume of approximately 50-60 USLS procedures between July 2016 and June 2017. Based on enrollment rates in other ongoing studies at our institution, this volume should allow us to meet our recruitment goal of 44 subjects within a 1-year period.

Section 5. *Ethics and Patient Consent*

The study is approved with the University of Iowa Institutional Review Board. The study will be discussed in detail and the informed consent reviewed with potential subjects prior to enrollment.

Risk in this study is limited to loss of confidentiality of protected health information (PHI). However, maintaining records on a secure, password protected, local server will minimize this risk. Furthermore, no hard-copy forms will be utilized for this study that contain identifying data or PHI. Hard-copy data abstraction forms and questionnaires will only be labeled with the patient's unique study ID number. All necessary PHI will be abstracted to the secure database directly from the patient's electronic medical record.

There is true equipoise between groups in this study. Both permanent and absorbable sutures are commonly used around the world in USLS procedures. As described above, low-quality retrospective studies have reported conflicting prolapse outcomes with the use of alternative suture choices. Patients randomized to the permanent suture group potentially stand to benefit from a more durable repair. Patients randomized to the absorbable suture group may potentially benefit from fewer suture-related complications (erosion, granulation tissue, etc.) and an equally durable prolapse repair.