Video Article

Transvaginal Mesh Insertion in the Ovine Model

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Abstract

This protocol describes mesh insertion into the rectovaginal septum in sheep using a single vaginal incision technique, with and without the trocar-guided insertion of anchoring arms. Parous sheep underwent the dissection of the rectovaginal septum, followed by the insertion of an implant with or without four anchoring arms, both designed to fit the ovine anatomy. The anchoring arms were put in place using a trocar and an "outside-in" technique. The cranial arms were passed through the obturator, gracilis, and adductor magnus muscles. The caudal arms were fixed near the sacrotuberous ligament, through the coccygeus muscles. This technique allows for the mimicking of surgical procedures performed in women suffering from pelvic organ prolapse. The anatomical spaces and elements are easily identified. The most critical part of the procedure is the insertion of the cranial trocar, which can easily penetrate the peritoneal cavity or the surrounding pelvic organs. This can be avoided by a more extensive retroperitoneal dissection and by guiding the trocar more laterally. This approach is designed only for experimental testing of novel implants in large animal models, as trocar-guided insertion is currently not used clinically.

Video Link

The video component of this article can be found at https://www.jove.com/video/55706/

Introduction

Pelvic organ prolapse is clinically diagnosed in half of women who had at least one vaginal delivery, but subjectively, it bothers half of women overall[1]. The mainstay of therapy is surgical reconstruction using either native tissue or implant materials, but each of these methods has its limitations, including recurrence or local complications[2,3,4]. The ideal implant has not yet been identified; hence, there is an ongoing demand for product innovation and for the development of a proper pipeline for preclinical experimentation prior to the introduction of new products and techniques to the market. One of the steps in this track is experimental evaluation on suitable animal models[5,6]. Ideally, they should mimic the anatomical, biomechanical, and biological environments. When it comes to the experimental evaluation of novel implants, they are typically tested first in smaller models, either for biocompatibility or for the reconstruction of abdominal wall defects. That type of experiments has been criticized, because the implants are not inserted into the area of interest (*i.e.,* the vagina)[7]. Vaginal surgery models are more scarce, certainly when the goal of the experiment is to document the biomechanical characteristics of explants. For this reason, there was a move from rabbits to sheep[8]. Adult ewes are large-animal models with a reasonably sized and accessible vagina. They can be used for the mid-term evaluation of novel implants, and it is possible to reproduce vaginal exposures with certain materials[9,10,11,12,13]. Not only the dimensions and anatomy of the ovine vagina and pelvic floor are comparable to those in humans, but also the spontaneous occurrence of prolapse, which occurs in 15% of ewes. Prolapse risk factors are overlapping (*i.e.,* multiparity, previous history of POP, increased intra-abdominal pressure induced by a higher bodyweight or when grazing on hills, and comparable effects of (phyto)estrogens)[6,14]. In Europe, sheep are the only reasonable alternative, as research on non-human primates has been nearly completely banned. Here, the model was taken one step further by mimicking the transvaginal insertion of implants using trocars and guides for the tension-free placement of meshes into the recto-vaginal septum. This was followed by fixing the implant using anchoring with arms through the ligaments of muscles, which can be considered equivalent to clinical practice[15,16]. So far, this technique has not been studied, though many believe that specific complications may occur due to the use of these longer strips and/or the piercing of anatomical structures.

In an earlier detailed anatomical study, the ovine pelvic floor was compared to the female pelvis[17]. When it comes to anchoring the implant, sheep do not have the sacrospinous ligament, yet they do have a very well-developed and broad sacrotuberous ligament. The pudendal nerve runs ventrally over it, making it unsafe to use this landmark as a suspension point. Conversely, the coccygeus muscle and its fascia, as well as the obturator membrane, are accessible through the rectovaginal space. Here, the access and position of the anatomical structures for the fixation of anchoring arms is proposed. The instruments that can be used to position the mesh are discussed. Finally, the relationship of the arms or trocars to adjacent anatomical structures, such as vessels and nerves, as well as potential intraoperative complications, are also described.

Protocol

Ethical approval for this experiment was obtained from the Ethics Committee on Animal Experimentation of the KU Leuven (P065/2013). Animals were treated in accordance with current national guidelines on animal welfare.

1. Material and the Experimental Animal

1. **Surgery preparation**
    1. In the surgical theater cover a table with a sterile drape and prepare one sterile curved trocar (**Figure 1**, panel A), sterile surgical instruments, sutures, and sterile gauze. Perform the entire surgical procedure in sterile conditions if the experiment includes follow-up. Place all instruments on the table to be ready for use during surgery.
    2. Remove a sterile rectangular implant and/or an implant with anchoring arms from the sterile package and put them on the table covered with sterile drape (**Figure 1B**, **C,** and **D**).

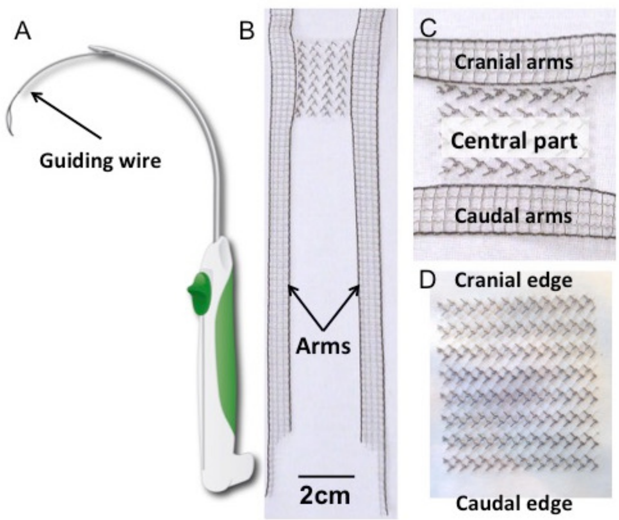

Figure 1: Trocar and Implants. (**A**) Schematic drawing of the trocar. (**B**) H-shaped polyvinylidene fluoride (PVDF) implant, with a detail of the central part (panel **C**). Its shape was inspired by the four-arm meshes currently available for transvaginal prolapse repair. The rectangular body (30 x 40 mm^2) is laterally extended by four outstretched arms (150 x 10 mm^2). The dimensions of the arms are designed to be long enough to pierce the relevant suspension structures, based on earlier anatomical studies[17]. (**D**) The rectangular implant (30 x 40 mm^2). Both implants were made of polyvinylidene fluoride; textile characteristics and properties are in **Table 1**.

2. **Experimental animal (Ewe, 45-60 kg)**
    1. Administer premedication of 1 mL of 15 mg/mL atropine sulfate and 1 mL/50 kg of xylazine HCl intramuscularly (i.m.) 30 min before the surgical procedure.
    2. After 30 min, ensure that the premedication has made the sheep lethargic and sleepy.
    3. Insert an intravenous catheter into the jugular vein and administer 0.075 mL/kg of ketamine 100 mg/mL HCl. Confirm deep anesthesia by observing the lack of reaction to painful stimuli.
    4. Move the animal onto the surgical table and secure its airways by intubation. Maintain the anesthesia with 2.5% isoflurane in 5 L/min oxygen.
    5. Keep the intravenous line inserted in the jugular vein and supply 500 mL of saline solution at a flow rate of 150 mL/h.
    6. Administer prophylactic antibiotics i.m. (amoxicillin clavulanate, 7 mg/kg) and post-operative analgesics (buprenorfin and chlorocresol, 1 mL) or the equivalent according to local protocols.
    7. Place the animal in lithotomy position on the end of the surgical table and secure its limbs, with the hips in hyper-flexion, using ropes (**Figure 2**, panel A).
    8. Manually empty the bladder and rectum by pushing on them trans-vaginally.
    9. Shave the perineum, the medial part of the thigh, and the tail folds and disinfect with polyvidone iodium 7.5% (**Figure 2**, panel B and C).

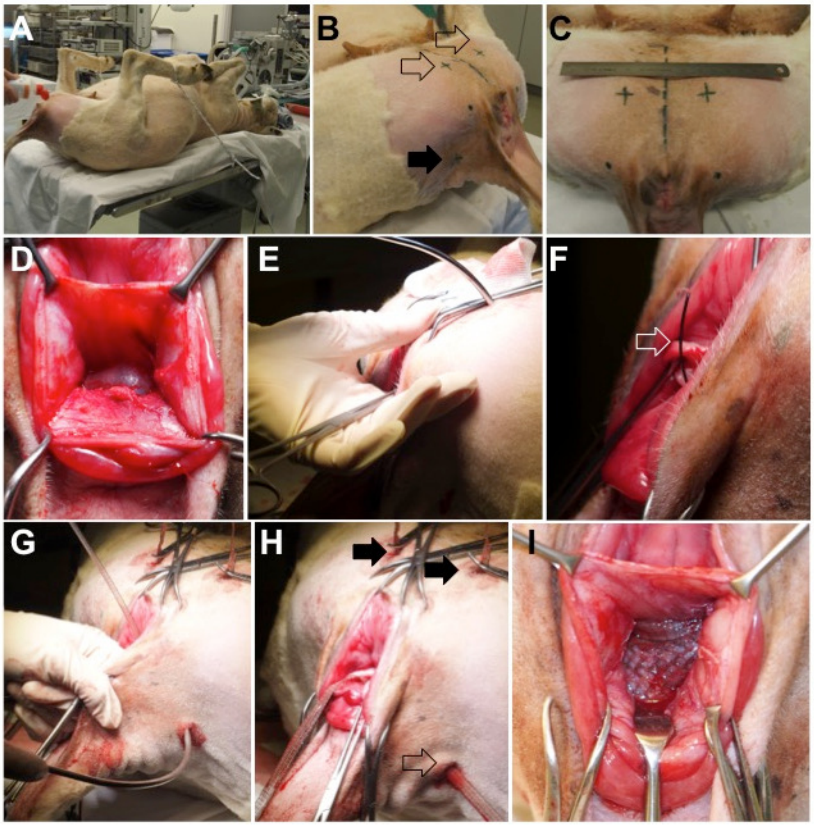

Figure 2: Animal Surgery. (**A**) A sheep placed in the supine position, with the hips hyper-flexed by securing the lower limbs. (**B**) The external entrance points for trocar insertion are on the ventral side (empty arrow) and dorsally on the lateral tail folds (full arrow). (**C**) Position of the ventral insertion points; the dashed line in the middle represents the midsagittal plane of the animal. (**D**) Dissected rectovaginal septum. (**E**) Insertion of the ventral trocar through the muscles on the medial side of the thigh, the obturator foramen, and the paravaginal space. The trajectory of the piercing trocar is controlled with the finger. (**F** and **G**) Once the trocar is in place, the wire sling (open arrow) is advanced and loaded with the arm of the vaginal mesh. (**H**) Final position of the ventral (full arrows) and dorsal (empty arrow) arms. (**I**) The central part is placed tension-free between the vaginal wall and the rectal adventitia.

10. Prepare personnel for a surgery in sterile conditions. Put on a surgical cap and mouth mask, wash hands for surgery, and put on a surgical gown and sterile gloves.
11. Cover the animal with a sterile drape and make an opening above the genital hiatus.

2. Surgical Procedure

1. **Preparation of the rectovaginal septum**
    1. Grasp the dorsal vaginal wall 3 cm cranial to the hymeneal ring using Allis forceps.
    2. Take a syringe loaded with 10 mL of saline and fitted with a 22 G needle. Insert it through the vaginal epithelium (approximately 3 - 4 mm deep) and into the midline of the rectovaginal septum, 1.5 cm cranial to the hymeneal ring.
    3. Perform "aqua-dissection" by injecting saline in the rectovaginal septum[11].
    4. Make a 3 cm-long midline incision on the vaginal epithelium, starting caudal to the Allis forceps (step 2.1.1) and ending at the hymeneal ring using a scalpel. Enter the recto-vaginal space through this incision.
    5. Place the self-retaining retractor (see the **Table of Materials**) over the perineum and place four sharp stay hooks in the vaginal incision to keep it open.
    6. With your finger, bluntly dissect the recto-vaginal fascia from the vaginal wall laterally towards the pelvic side walls and cranially up to the caudal aspect of the cul-de-sac. Create suitable space for the 30 x 40 mm^2 central part of the mesh (**Figure 2**, panel D).
    7. Perform haemostasis with haemostatic forceps or a crisscross haemostatic ligature whenever necessary.
    NOTE: Small bleeders can be clamped with the hemostatic forceps. This crushes the vessel and initiates the natural coagulation cascade. For stronger bleeding, grasp the bleeding vessel with forceps and place a crisscross ligature, securing it with a square knot. At this point, one can either insert the rectangular implant (step 2.2) or continue with the dissection to insert the implant with anchoring arms (step 2.3).

2. **Flat mesh insertion**
    1. Insert the vaginal retractor into the vaginal incision to allow a better view of the cranial part of the dissected area.
    2. Suture the left and right cranial corner of the implant with a simple interrupted 3/0 polypropylene suture on the left and right sides of the most cranial aspect of the dissected recto-vaginal space. Cut the residual suture material. Keep the suture away from the vaginal lumen (*i.e.,* do not penetrate the vaginal wall).

NOTE: The implant is always sutured to the connective tissue comprising the recto-vaginal septum. The vaginal wall is not penetrated if the suture material cannot be seen in the vagina.

3. Add one additional simple interrupted suture midway along the cranial aspect of the implant.
4. Suture the lateral edges of the implant midway onto the surrounding connective tissue with a simple interrupted 3/0 polypropylene. Keep the implant as flat as possible and tension-free.
5. Suture the left and right caudal corners with simple interrupted 3/0 polypropylene sutures on the left and right sides of the most caudal aspect of the rectovaginal space.
6. Add one additional simple interrupted suture midway along the caudal aspect of the implant.
7. Close the vaginal incisions with a running 3/0 polyglactin suture.

3. **Insertion and anchoring of implant with arms (trocar-guided technique).**
    1. Continue the dissection of the recto-vaginal space created in step 2.1 cranio-ventrally to reach the medial aspect of the obturator foramen, which can easily be palpated.
    2. Dissect the space caudo-laterally to reach the caudal aspect of the sacrotuberous ligament and the caudally located coccygeus muscle.
    3. With a no. 24 blade, make four 1 cm-wide incisions on the vulvar side, cutting through the skin and superficial muscular fascia (**Figure 2**, panel B and C).
    4. Make two “ventral” incisions on the medial aspect of the thigh, proximately 4 cm cranial from the caudal border of the sciatic arch (*i.e.*, the inferior border of the symphysis) and 3 cm lateral from the midline (**Figure 2**, panel C).
    5. Make two "dorsal" incisions at the level of the insertion of the tail folds, 2 cm medial to the tuber ischiadicum, which can be easily palpated (**Figure 2**, panel B).
    6. Place a curved trocar through one of the ventral incisions (**Figure 2**, panel E).
    7. Pass the trocar through the adductor magnus muscle, the external obturator, and the medial aspect of the obturator foramen.
    8. Control the progression of the trocar with a finger inserted through the vaginal incision. Guide its tip to the tendinous arc of the levator ani muscle (**Figure 2**, panel E).
    9. Expose the guiding wire in the vaginal wall incision and load it with the corresponding ipsilateral cranial mesh arm (**Figure 2**, panel F).
    10. Pull the trocar loaded with the mesh arm through the above structures. Keep the arm tension-free.
    11. Repeat the process with the second cranial arm through the ventral incision on the other side of the animal.
    12. Through one of dorsal incisions, pass the trocar through the coccygeus muscle, just distal to the sacrotuberous ligament (**Figure 2**, panel G).
    13. Expose the guide wire through the vaginal incision, grasp the dorsal arm of the mesh, and pull it out. Keep the arm tension-free and repeat on the other side.
    14. Adjust the position of the mesh by flattening it and applying tension to the arms, but keep the mesh tension-free (**Figure 2,** panel I; **Figure 3**).
    15. Fix the body of the mesh with a simple interrupted 3/0 polypropylene suture in the middle of its caudal border, securing it to the surrounding connective tissue.
    16. Cut the arms at the level of the skin and close all skin incisions with simple interrupted 3/0 polyglecaprone sutures (**Figure 2**, panel H).
    17. Close the vaginal incision with a running 3/0 polyglecaprone suture.

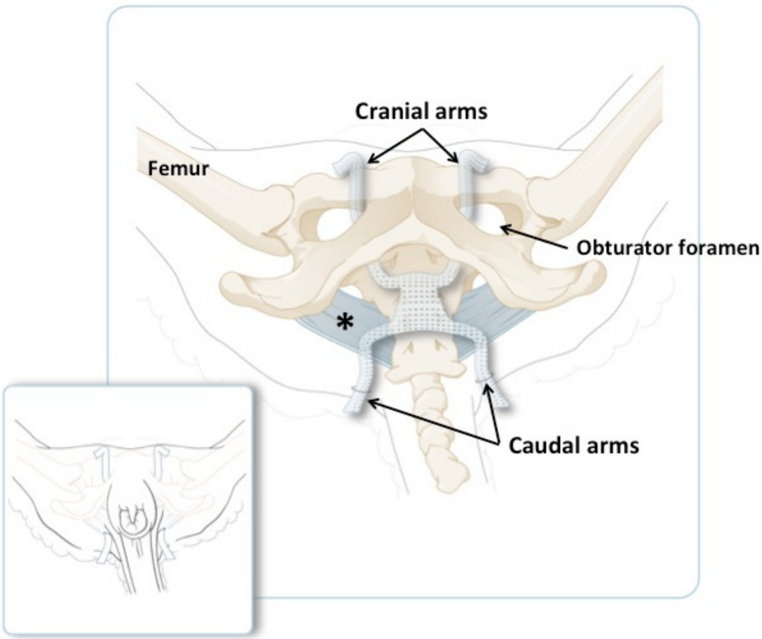

Figure 3: Schematic Illustration of the Ovine Pelvis, with the Cranial Arms Passing through the Obturator Foramen and the Caudal Arms Passing through the Tail Folds. The broad sacrotuberous ligament is in blue. The smaller panel illustrates the position of the arms on an animal in recumbent position, just before shortening the excessive amount of material. The main panel shows the same but with the skin and muscles removed.

Representative Results

Management in a Longer Observation Setup

Following the surgical procedure, vaginal packing (a saline-solution-soaked gauze package inserted in the vagina immediately after the surgery) may be inserted for 24 h to secure the implant position. The sheep should be placed in a recovery cage and its respiratory function followed until full recovery. Later, it is possible to place the sheep in the stable and to allow it to move freely and to drink and eat *ad libitum*. The vaginal packing, if present, must be removed 24 h after the surgery. The sheep should receive analgesics (buprenorfin and chlorocresol, 1 mL, i.m.) for at least three postoperative days. During the first postoperative week, the animal should be checked daily, and then every week until the end of the experiment.

Surgical Feasibility

During the procedure, there were no problems with mesh insertion in any of the animals. There was almost no bleeding during the dissection of the rectovaginal septum and paravaginal spaces. It was possible to identify the medial aspect of the obturator foramen through the dissection. Also, the trocar insertion was straightforward, with a difference in resistance between the more compliant muscles and the more resistant fascia of the individual muscles. Though the initial trajectory through the muscles was less controlled, the tip of the trocar became palpable once in contact with the obturator muscle. The dorsal arms were placed without complications or obstacles.

Mesh Positioning and Findings during Subsequent Dissections

To investigate the proper positioning of the implant with the anchoring arms, which was considered more difficult to achieve, three animals were euthanized by an intravenous injection of 1.0 mL of an embutramide-mebezonium-tetracaine hydrochloride mixture. Following euthanasia, the surgical area was carefully dissected to explore the mesh position and the effect of the insertion of the arms of the mesh through the relevant anatomical structures. The shortest distance of the ventral arms from the obturator artery and nerve to the internal pudendal vessel was measured with a ruler, and their relationship to the tendinous arc of the levator ani was investigated. Dorsally, the pudendal nerve and internal pudendal artery were identified, and the distance to them measured with a ruler.

Relevant bleeding did not occur in any of the ewes, nor was there any intra-operative nerve, intestinal, or bladder injury. In the first sheep, the cranial arm passed through the caudal aspect of the cul-de-sac, but the bowels remained intact. This was avoided in the next sheep by guiding the tip of the trocar more laterally away from the cul-de-sac. The other arm passages were identified in the anatomical structures previously described, far away from the pelvic nerves and vessels. The cranial arms passed through the caudal aspect of the obturator foramen (**Figure 4**, panel A). The entry point of the trocar was at the level of the tendinous arc of the levator ani, 2 - 2.5 cm caudal to the obturator canal and the obturator vessels and nerve (**Figure 4**, panel B). Once in the paravaginal space, the arm was located 1 - 1.5 cm ventral to the pudendal artery and vein and 1 cm lateral to the vaginal artery. The caudal arms passed 1 cm caudal to the caudal aspect of the broad sacrotuberous ligament, right through the coccygeus muscle. In that location, there are no major vessels or nerves anywhere close by. The pudendal nerve is located on the inner surface of the caudal part of the sacrotuberous ligament.

The central part of the mesh was placed flat, with its cranial part stretching retroperitoneally under the caudal end of the cul-de-sac and its caudal part down along the rectovaginal septum. No rectal perforations occurred (**Figure 4**, panel D).

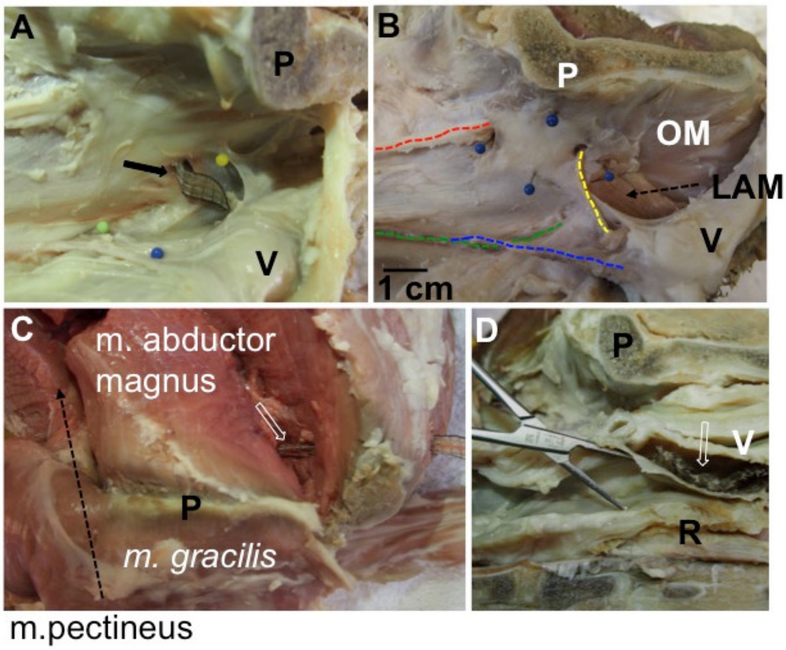

Figure 4. Anatomical Dissection on a Pelvic Hemisection. **A:** The lateral pelvic sidewall after the removal of the parietal peritoneum and the retroperitoneal fat tissue. The pubis (P) is at the top of the figure and the vagina (V) is moved medially to reveal the course of the cranial arm (full arrow). The arm passes through the tendinous arc of the levator ani. The green pin corresponds to the position of the internal pudendal vessels, the blue pin marks the vaginal artery, and the yellow pin is placed in the levator ani. **B:** The lateral pelvic sidewall after removal of the arm (course marked with a yellow line). The entrance point is located in the caudal aspect of the obturator foramen (marked with four blue pins). The obturator nerve and vessels (red line) pass through its cranial aspect. The internal pudendal and vaginal vessels (green and blue line, respectively) are dorsal to the arm. The obturator muscle (OM) and the levator ani muscle (LAM) are indicated as well. **C:** The course of the arm (open arrow) through the medial muscles of the thigh. The gracilis muscle is moved medially to display the course of the arm through the semitendinosus and the adductor magnus muscle. **D:** The central part of the implant (open arrow) is placed between the vagina (V), the parietal peritoneum, and the rectum (R).

	Rectangular mesh	**Arm mesh**	
		Central body	**Arms**
Dimensions (mm x mm)	30 x 40	30 x 40	10 x 150
Thickness (mm)	0.54	0.54	0.7
Weight (g/m^2)	83	83	73
Pore size (mm^2)	2.5 x 2.5	2.5 x 2.5	1.0 x 1.4
Stiffness (N/mm)	0.3	0.3	14.7
Anisotropic index	1.3	1.3	7.5

Table 1: Dry Material Properties.
The table shows the material properties of the rectangular mesh and the mesh with anchoring arms. The stiffness and anisotropic index were obtained from Maurer *et al*[18].

Discussion

Here, we describe an experimental procedure in sheep, aimed to mimic vaginal dissection and transvaginal mesh insertion of an implant with or without anchoring arms. The subsequent steps and instruments were inspired by surgical procedures done for POP and stress urinary incontinence[15,16,19,20]. After initial anatomical dissections, there were still some problems during experimental mesh insertion. In the first animal, a perforation in the peritoneal cavity at the level of de cul-de-sac was found. This has been previously described clinically in women[21]. In subsequent procedures, this was avoided by guiding the tip of the trocar more laterally (*i.e.,* closer to the pelvic side wall). In later sheep, no other complications were observed.

The most feared anatomical structures were the obturator nerve and artery. In humans, the distance between the trocar/implant and the obturator canal is 1.9 - 3.0 cm[22]. The high variability of the trocar/implant position in women was previously explained by the exact positioning of the legs or the needle trajectory. Therefore, the hind limbs of the sheep were secured in hyper-flexion at the hips to allow greater access to the vagina.

In this position the gracilis muscle is moved cranially. As a consequence, the trocar passed through the adductor magnus muscle, which is undivided but well-developed in sheep[23]. A more cranial passage of the trocar is possible yet may harm structures in the obturator canal.

Similarly to what is described clinically, the arms fixed the implant to given anatomical locations, corresponding to natural attachments of the rectovaginal septum in sheep[23]. The implant lay flat, apparently supporting the posterior vaginal wall without extending more laterally. Consequently, it did not have a tendency to fold. It may be possible to use larger implants. However, as demonstrated before in sheep, larger implants are associated with an up to 50% retraction and more local graft-related complications[9].

Previous investigation of novel implants in various animal models included the sheep as a model for vaginal surgery. One aim of this work was to fix implants in a manner similar to that done clinically (*i.e.,* by transfixing the arms of the mesh to anatomical structures in the pelvis). This procedure was not described earlier in a sheep model. This surgery follows a strategy similar to what was used to introduce new needle- and trocar-assisted surgeries into clinical practice[15]. However, these findings seem to be less relevant than a few years ago, as the use of vaginal implants and thus, trocar-guided procedures are quickly dropping due to the consecutive health warnings by the FDA and SCENIHR[24,25].

Though we describe herein the technique, the number of animals in this experiment was very limited, so the full level of anatomical variability may not be represented here. Another limitation is that this technique describes a posterior compartment procedure, which may be less practiced. There are a few reports on surgery in the anterior compartment in sheep[13], but smaller implants were usually used and complications were more frequent. Though these findings may be sufficient to plan further experiments, the feasibility of anterior vaginal mesh placement may also have been informative.

In conclusion, this is a description of a safe and feasible surgical technique in the ovine animal model for vaginal surgery that permits trans-vaginal and trocar-guided tension-free vaginal implant insertion. Relevant comparable structures could be blindly pierced without obvious risks for vessel, nerve, or organ injury. This model can of course also be used for simulated vaginal surgery using native tissue.

Disclosures

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