Uterine viability in the baboon after ligation of uterine vasculature: a pilot study to assess alternative perfusion and venous return for uterine transplantation

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Objective: To assess, in two separate groups of baboons, uterine viability after ligation of the uterine veins and uterine viability after ligation of both the uterine arteries and veins, respectively.
Design: Prospective, observational study.
Setting: Baboon breeding colony.
Animal(s): Six naïve female *Papio hamadryas* baboons with indicators of normal reproductive function.
Intervention(s): Three baboons underwent surgical interruption of the uterine veins bilaterally, and three baboons underwent surgical interruption of the uterine arteries and the uterine veins bilaterally. All baboons also underwent colpotomy, cervico-vaginal reanastomosis, and intraoperative near-infrared fluorescence imaging after vessel ligation. In the postoperative period, transabdominal sonography, vaginoscopy, and endocervical biopsy were performed on all animals.
Main Outcome Measure(s): Postoperative uterine and ovarian viability.
Result(s): Near-infrared imaging confirmed intraoperative perfusion of the uterus and cervico-vaginal anastomosis in all cases. In all subjects, sonography revealed normal uteri, and vaginoscopy revealed well-healed anastomoses. Endocervical biopsies (five of six) demonstrated pathologically normal endocervical tissue without evidence of necrosis. Cyclical sex skin turgescence and menstruation were unanimously observed.
Conclusion(s): Disruption of bilateral uterine vessels does not affect uterine or ovarian viability in the baboon. Bilateral uterine artery and vein ligation furthers development of a minimally invasive approach to donor hysterectomy. (Fertil Steril® 2017;107:1078–82. ©2017 by American Society for Reproductive Medicine.)
Key Words: Baboon model, donor hysterectomy, uterine transplant

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Absolute uterine factor infertility afflicts women with surgical absence of the uterus, women with a nonfunctioning uterus, and women with congenital absence of the uterus, as in Mayer-Rokitansky-Kuster-Hauser syndrome (1). Uterine transplantation is the first available treatment for absolute uterine factor infertility. Dr. Brännström and his team pioneered allogenic human uterine transplant in Sweden and achieved the first live birth to a transplant recipient in 2014 (1). Procuring the uterus from a live donor is the rate-limiting step of uterine transplant as described in the Swedish protocol (2). The recovery surgery consists of a midline laparotomy through which the uterus is isolated with long bilateral uterine artery and uterine vein pedicles.

Received November 25, 2016; revised January 9, 2017; accepted January 20, 2017; published online March 7, 2017.
M.L.S. is a consultant for Medtronic and Applied Medical. S.Z. is a consultant for Medtronic and Applied Medical. M.S. has nothing to disclose. K.A. has nothing to disclose. B.B. has nothing to disclose. K.R. has nothing to disclose. P.E. has nothing to disclose. A.T. has nothing to disclose. T.F. has nothing to disclose.
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Fertility and Sterility® Vol. 107, No. 4, April 2017 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2017.01.014

Dissection of the internal iliac arteries and veins begins proximally at the bifurcation and extends distally to incorporate the uterine vessels. The lengthy 10–13 hours of operative time required for live donor surgery is a direct result of meticulous vascular dissection, which requires attention to the uterine vein's circuitous course to the deep pelvis and its close proximity to the ureter (2).

Developing a uterine procurement technique that avoids dissection of the uterine vein is crucial to lessen operative time and minimize surgical risks to live donors. Alternative venous drainage of the uterus has been demonstrated in ex vivo studies documenting extensive anastomotic flow between the uterine and the utero-ovarian vessels (3), so we developed two hypotheses. First, we hypothesized that the uterus can be drained without the uterine veins, exclusively via the utero-ovarian veins bilaterally. Second, we hypothesized that neither the uterine vein nor the uterine artery are necessary for perfusion and drainage of the uterus, respectively. Therefore, the objective of this study was to assess uterine and ovarian viability in a baboon model after [1] ligation of the uterine veins bilaterally, and [2] ligation of the uterine veins and the uterine arteries bilaterally. By ensuring that these unique perfusion and drainage prototypes can sufficiently support a uterus in vivo, we may further development of a minimally invasive approach to donor hysterectomy.

MATERIALS AND METHODS

Animals

The baboon, *Papio hamadryas*, shares similar menstrual cycle characteristics to human females, making it an ideal model for uterine studies (4). Six reproductive-aged female baboons were selected for this pilot study, which was approved by the Institutional Animal Care and Use Committee of Mannheimer Foundation in Homestead, Florida. The Mannheimer facility is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, and baboons were housed and handled in accordance with the Animal Welfare Act. All animals were 5 years of age, sexually naïve (never having been exposed to male baboons), and weighed between 12 and 16 kg. They all demonstrated indicators of normal reproductive function preoperatively, including cyclic sex skin turgescense and deturgescence and predictable bloody vaginal discharge. Subjects were observed outdoors before the start of the study and brought indoors for isolated monitoring 1 to 2 weeks before surgery.

Perioperative Considerations

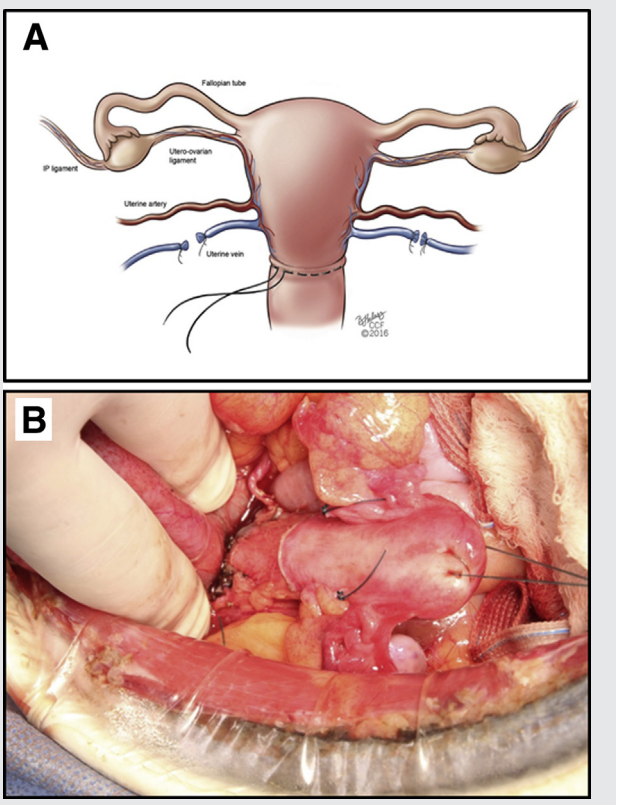
In the selected *Papio hamadryas* females, anesthesia was induced with IM ketamine HCl (5-10 mg/kg) and glycopyrrolate (0.0004-0.008 mg/kg). Intubation was performed using an endotracheal 5.5-mm, 24-Fr tube, and anesthesia was maintained by spontaneous breathing of isoflurane (2%–5%) in oxygen. Respiratory rate and heart rate, as well as rectal temperature, were monitored during the surgery. Hydration was maintained throughout the surgery by continuous IV infusion of warmed 0.9% sodium chloride at a rate of 10 mL/kg/h, and the bladder was continuously drained by an indwelling catheter. All subjects received antibiotic prophylaxis IM with ceftiofur (Naxcel, Zoetis Services; 2.2 mg/kg) on the day of surgery and daily for 6 days postoperatively.

Surgical Procedure

All six baboons underwent laparotomy via a midline vertical incision under sterile technique. General anesthesia was administered by a veterinarian as described above. The uterus was elevated, and the ovarian vasculature was skeletonized but not interrupted. Normal fallopian tubes were identified and left in situ to allow for spontaneous conception. The uterus was then placed on traction, and incisions were made in the bilateral broad ligaments, extending from the utero-ovarian vessels to the uterine vessels. In the first set of three baboons (group 1), the uterine veins were skeletonized, suture ligated, and incised bilaterally (Fig. 1). In the second set of three baboons (group 2), both the uterine arteries and veins were isolated bilaterally, suture ligated, and incised (Fig. 2).

After ligation of the uterine veins and ligation of the uterine arteries and veins in both groups, respectively, attention was turned toward the cervix. Colpotomy was begun with a monopolar electrosurgical pencil and extended

FIGURE 1



(**A**) Ligation of bilateral uterine veins. Surgical technique used on the first group of subjects (n = 3), notable for preservation of the uterine arteries. (**B**) In vivo uterus after ligation of bilateral uterine veins. Suture knots at uterine veins are visible.

Shockley. Uterine viability and bilateral uterine vessels. Fertil Steril 2017.