Original Study

The Interest of Women with Mayer–Rokitansky–Küster–Hauser Syndrome and Laparoscopic Vecchietti Neovagina in Uterus Transplantation

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A B S T R A C T

Study Objective: The goal of this study was to assess a group of women with Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome with surgically created neovaginas in the interest of uterus transplantation (UTx) and to recruit the first group of applicants for a UTx trial.
Design and Setting: This was an original prospective study using semistructured interviews.
Participants: A study group of 50 women with MRKH syndrome with Vecchietti neovaginas was recruited via letter of invitation.
Interventions and Main Outcome Measures: Interest of MRKH women in obtaining experimental UTx for the treatment of absolute uterine factor infertility.
Results: A total of 50 women responded via e-mail and 31 (62% [31 of 50] of the study group) expressed serious interest in UTx after complete information about its risks and benefits was provided during the first semistructured interview. They subsequently agreed to participate in additional interviews and further examinations. Because of various reasons, only 9 women were prepared to enter our UTx trial (18% [9 of 50] of the study group). Three recipients/donors were accepted into the living donor arm and 6 into the deceased brain donor arm of the trial.
Conclusion: Nearly two-thirds of our MRKH syndrome study group women with surgically created neovaginas were interested in UTx and motivated to undergo this method of absolute uterine factor infertility treatment. Therefore, this group of women might be approached to participate in ongoing and future UTx trials. Future studies of women with MRKH syndrome might confirm or disprove the results of our survey.
Key Words: Mayer–Rokitansky–Küster–Hauser syndrome, MRKH, Absolute uterine factor infertility, AUFI, Neovagina, Uterus transplantation, Infertility

Introduction

Uterus transplantation (UTx) as a quality of life-enhancing and life-propagating vascularized composite allotransplantation is the only potential causal treatment for absolute uterine factor infertility (AUFI). It is also the first ephemeral transplantation whereby the uterus is removed after childbirth. Only one Swedish UTx trial was performed with the deliveries of healthy but premature children from transplanted wombs.[1–4] All but 1 UTx in this group were performed in women with Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome with uterine agenesis.

There are several reasons for AUFI, congenital and acquired, with different reasons for hysterectomy, which mostly include growing leiomyomas, cervical cancer, and emergency peripartum bleeding. The occurrence of some congenital uterus malformations can be found in 6.7% of all women, in 7.3% of infertile women, and in 16.7% of women with recurrent abortions.[5] Uterine agenesis (with 46, XX karyotype, functioning ovaries, typical female secondary sex characteristics, and upper two-thirds vaginal aplasia) is the least frequent congenital uterine anomaly. One of the subtypes of MRKH syndrome occurs in approximately 1 in 4500 women.[6,7] Most reported cases occur sporadically but there are also reports describing familial occurrence.[8] Women with MRKH syndrome can have normal vaginal intercourse from nonsurgical dilation or surgical creation of a neovagina.[9,10]

The management of vaginal agenesis is currently determined by location and center preference. A multidisciplinary approach is required to support women with MRKH syndrome from the initial diagnosis to maturity. The optimal treatment is unknown and most articles on neovagina techniques and outcomes focus on personal case series. The recommendation from the American College of Obstetricians and Gynecologists for primary treatment is on the basis of nonsurgical methods.[9] On the contrary, the absolute majority of patients treated in our center undergo a Vecchietti neovagina procedure, a tissue expansion technique, which causes little surgical trauma and demands a high degree of postoperative cooperation to provide permanent effects. The procedure is therefore performed usually on emotionally mature women with a steady partner and a strong desire to have vaginal intercourse immediately after surgery. The aim of each treatment of vaginal agenesis is not only the creation of a vagina that is functional in terms of its length and sexual satisfaction for the couple, but also improved quality of life and

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psychological well-being of women with MRKH syndrome. Unfortunately, in women with neovagina, fertility is still compromised and infertility is the most difficult aspect of the disorder to accept. Surrogacy (commercial or altruistic) by means of assisted reproductive techniques and adoption are potential alternatives for women with MRKH syndrome who desire to become mothers.[11] Young women with MRKH syndrome with neovaginas are healthy with good results of in vitro fertilization (IVF) through surrogate pregnancies and no higher incidence of congenital uterus malformations in their own genetic female offspring have been documented.[12,13]

Because of advances in microsurgical techniques and innovations, tissue preservation possibilities, and improved understanding of transplantation immunity, UTx might be a source of hope for women with congenital and acquired AUFI to fulfill their maternal desires. The presence of a formed vagina is a necessary preexisting condition to UTx in women with AUFI. Uterovaginal anastomosis especially enables outflow of menstruation blood, cervical biopsy to reveal potential uterine rejection, and embryo transfer. The main objective of our study was to assess a group of women with MRKH syndrome with laparoscopic Vecchietti neovaginas in the interest of UTx, which should become available as an infertility treatment option in women without a uterus in the near future. The second objective was to recruit the first group of applicants into the UTx trial.

Materials and Methods

Between 2003 and 2013, a total of 95 women with MRKH syndrome underwent laparoscopic Vecchietti neovagina surgery at our Obstetrics and Gynecology Department. In November 2014, 2 months after the announcement of the first delivery of a healthy child from a transplanted womb in Gothenburg, Sweden, invitation letters (e-mail addresses were not available for all women who received surgery) for personal semistructured interviews regarding experimental UTx as an AUFI treatment method were sent via post to all patients who received surgery. The study was approved by the ethics committee of the principal institution and informed consent was fully explained to all of the participants and obtained before the study. The women were asked to reply via e-mail with the option to send a letter by post. Between December 2014 and February 2015, all of the interested women with MRKH syndrome underwent a first interview and completed a baseline questionnaire.

At first, the patients were given complete information about our UTx trial, including administrative, theoretical, and practical preparations. They were informed about the fact that our experimental trial was still in the preparation phase and may not be eventually approved by the Ministry of Health. The women with MRKH syndrome were also informed about other parenthood options in the Czech Republic, such as adoption and altruistic surrogacy. All of the key questionnaire issues were discussed in detail with at least 2 members of the study team (the gynecologists and transplantation surgeon). All women were informed about the current status of knowledge worldwide and our experience with UTx to exclude potential recipients with excessive and unrealistic expectations. We repeatedly stressed the ethical issues on the basis of the concept of nonmaleficence. Applicants were informed about the Montreal criteria for the ethical feasibility of UTx published in 2013 and possible consequences.[14] All of the potential risks, especially those regarding the IVF procedure, and a minimum of 3 surgeries (UTx, cesarean section, and hysterectomy), exposure to immunosuppressive therapy, rejection risk, complications in pregnancy, and the risk of premature labor were fully described. All of the women (and their partners) were invited for the second interview and asked to seek potential uterus donors among their relatives, but this was not a condition for further participation in the study. The principal aim of this step was only to shorten the time before the start of our UTx trial, which was open to living donor (LD) and deceased brain donor (DBD).

Only women with persistent interest, their partners, and potential donors underwent the second interview. They received the same complete information and additional questions were answered by the members of the study team. All of the potential donors were fully informed and ultrasound examinations were performed to reveal uterine pathologies.

The third interview was arranged for the highly interested and motivated participants. During this visit, blood groups were examined, detailed medical history of potential uterus recipients and donors were taken, and proper gynecological (including Pap smears) and repeated ultrasound examinations were performed.

A fourth visit was scheduled for the group of women (with donors and partners) who were accepted into the LD and DBD arms of the UTx trial. To provide full information and prevent possible misunderstandings regarding the risks and benefits of UTx for the treatment of AUFI, the final group of women underwent 4 detailed semistructured interviews and discussions with the members of the study team. All interviews were arranged in monthly intervals and each lasted 90-120 minutes.

Results

Of 95 invitation letters sent to the last known permanent addresses, 9 were returned undelivered. Patients who also could not be reached via e-mail were excluded from the study. Overall, 36 women did not answer (for the purpose of the study; they were excluded as well) and 50 patients (58%,

Table 1
Group of MRKH Women Interested in UTx (n = 31)

Characteristic	Mean	Range	Median	SD
Height, cm	166.5	150-181	166.5	9.46
Weight, kg	64.6	50-91	66	11.76
BMI	23.2	18.2-32.6	24.1	4.25
Vaginal length, mm	64.0	55-85	65	8.67
Age at time of surgery, years	18.5	16-25	18	1.92
Age at time of study, years	24.2	19-31	24	3.10
Time from surgery, years	6.7	2-12	6	3.16
Partnership length, years	5.6	2-12	5	2.58

BMI, body mass index; MRKH, Mayer–Rokitansky–Küster–Hauser; UTx, uterus transplantation.