ORIGINAL ARTICLE: ASSISTED REPRODUCTION

The arcuate uterus: is there an impact on in vitro fertilization outcomes after euploid embryo transfer?

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Objective: To study the impact of the arcuate uterus on euploid blastocyst-stage embryo transfer outcomes after comprehensive chromosomal screening (CCS).
Design: Controlled retrospective trial.
Setting: Tertiary care assisted reproduction technology (ART) center.
Patient(s): Consecutive patients undergoing in vitro fertilization and euploid embryo transfer after CCS during 2014.
Intervention(s): Ultrasound examinations and office hysteroscopy; array comparative genomic hybridization to perform CCS after a trophectoderm biopsy.
Main Outcome Measure(s): Implantation and live-birth rates.
Result(s): Patients were divided into two groups based on the presence (group 1) or absence (group 2) of arcuate uterus. Exclusion criteria were donor oocytes, evidence of other endometrial cavitary abnormalities, prior uterine surgery, and arcuate uterus <4 mm. Group 1 included 78 patients with arcuate uterus of mean depth 5.43 ± 1.81 mm (range: 4–9.5 mm) undergoing 83 transfer cycles. Group 2 included 354 controls undergoing 378 transfer cycles. There were no differences between the groups in baseline characteristics or mean number of euploid embryos transferred. Cycle outcomes were similar between the two groups: rates of implantation (63.7% vs. 65.4%), live birth (68.67% vs. 67.81%), biochemical pregnancy (8.4% vs. 7.65%), and spontaneous abortion (4.8% vs. 4.27%).
Conclusion(s): Arcuate uterus has no impact on ART outcomes after euploid embryo transfer subsequent to CCS, so arcuate uterus should be considered an incidental finding without an indication for surgical resection. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: Arcuate uterus, comprehensive chromosomal screening, implantation, in vitro fertilization

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The arcuate uterus is one of the most common congenital uterine anomalies. It was categorized in an initial classification system developed by the American Fertility Society in 1988 as consisting of a normal appearing uterine fundus with a small cavitary indentation (1, 2). The extent of this indentation, which would be used to differentiate the arcuate uterus from a septate or normal uterus, lacks a uniform definition (3–6).

A recent Practice Committee guideline from the American Society for Reproductive Medicine (ASRM) states that the arcuate uterus does not cause adverse fertility or reproductive outcomes (3). This conclusion is based on the paucity of conflicting data, which suggests that this anomaly either has no impact on IVF cycle outcome or results in significantly lower pregnancy rates than in controls (6, 7). Some investigators have recommended surgical resection as a means of improving outcomes (6, 8). The majority of investigations that have addressed IVF outcomes in patients with this anomaly do not focus solely on the arcuate uterus, but rather evaluate patients with an arcuate uterus as a subgroup in a broader analysis of a variety of other

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müllerian anomalies. In addition, there has not been a uniform approach employed to make the diagnosis. To our knowledge, no studies have controlled for the critical variable of embryo aneuploidy. This retrospective trial evaluated the impact of the arcuate uterus diagnosed using uniform criteria on the success of euploid blastocyst-stage embryo transfer after comprehensive chromosomal screening (CCS).

MATERIALS AND METHODS

This investigation is a retrospective trial performed in a single assisted reproduction technology center. All consecutive patients undergoing IVF and CCS with subsequent transfer of euploid embryos during the 2014 calendar year were assessed. All patients underwent serum ovarian reserve testing, which included day-3 follicle-stimulating hormone (FSH), estradiol, luteinizing hormone (LH), and antimüllerian hormone (AMH) levels. A baseline transvaginal two-dimensional (2D) ultrasound examination was performed that included calculation of antral follicle count. As part of our standard evaluation, all patients underwent three-dimensional (3D) ultrasound examination and office flexible hysteroscopy, both performed in the early follicular phase.

The patients were divided into two groups based on the presence (group 1) or absence (group 2) of an arcuate pattern. This was defined as a perpendicular depth from the interstitial line connecting the cornua ranging from 4 to <10 mm with a myometrial angle >90 degree as diagnosed by 3D ultrasound examination and confirmed by office hysteroscopy. An example is displayed in Figure 1.

All patients underwent controlled ovarian stimulation with an individualized protocol based upon consideration of age, ovarian reserve test results, and prior responses when applicable. Transvaginal ultrasound guided oocyte aspiration was performed 35 hours after gonadotropin-releasing hormone (GnRH) agonist and/or human chorionic gonadotropin (hCG) trigger (9, 10). As previously described elsewhere, intracytoplasmic sperm injection (ICSI) was performed on all mature oocytes, and resulting embryos were cultured to the expanded blastocyst stage before undergoing trophectoderm biopsy performed 5, 6, or 7 days after oocyte aspiration (11). We performed CCS using an array comparative genomic hybridization platform (Illumina). All embryos were then vitrified in Cryotops using the technique reported by Kuwayama (12).

The endometrium was prepared for embryo transfer using exogenous estrogens as has been described previously elsewhere (13). Euploid embryos were warmed on the day of transfer, and the transfer was performed under ultrasound guidance. Only euploid embryos were transferred.

Serum pregnancy tests were performed 9 days after embryo transfer. Ultrasound examinations to confirm pregnancy were typically performed both 2 and 4 weeks after evidence of appropriately rising serum hCG levels. Progesterone and estradiol support were initially maintained and then slowly tapered after evidence of an ongoing pregnancy (13).

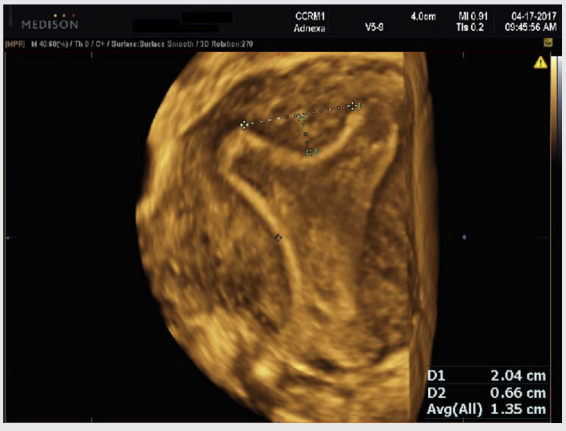
The exclusion criteria included patients who used donor oocytes or a gestational carrier, evidence of other endometrial cavitary abnormalities by 3D ultrasound or hysteroscopic examination, prior uterine surgery (with the exception of dilation and curettage), and a fundal indentation <4 mm.

Implantation rate was defined as the number of gestational sacs with ultrasound evidence of cardiac activity per number of embryos transferred. Live-birth rate was defined as the number of live births >26 gestational weeks per embryo transfer procedure. Biochemical pregnancy was defined as the number of embryo transfers resulting in an elevated serum hCG level at least 9 days after embryo transfer with subsequent decline before the first ultrasound examination. Pregnancy loss was defined as a nonviable intrauterine pregnancy subsequent to ultrasound confirmation of an intrauterine gestational sac.

Data analysis was performed using Student's group *t* and Fisher's exact tests, as appropriate. The results are expressed as mean ± standard deviation in conjunction with 95% confidence intervals (CI) unless otherwise indicated.

Institutional review board approval and informed consent were not obtained for data collection because of the retrospective nature of the study, use of deidentified data, and lack of experimental intervention. All patients were extensively counseled by their physician and a genetic counselor before standard informed consent was obtained before the IVF and CCS procedures.

FIGURE 1



Three-dimensional ultrasound image of an arcuate uterus. The perpendicular depth from the interstitial line connecting the cornua is 6.6 mm. The myometrial angle of the fundal indentation is >90 degrees.

Surrey. Arcuate uterus and IVF outcomes. Fertil Steril 2017.

RESULTS

Group 1 consisted of 83 transfer cycles performed in 76 patients with a diagnosis of arcuate uterus. The mean depth of the fundal indentation was 5.43 ± 1.81 mm (range: 4–9.5 mm). Group 2 consisted of 378 transfer cycles performed in 354 control patients with a normal uterine cavity. All consecutive cycles in patients who met inclusion criteria were evaluated. There were no differences in baseline characteristics between the two groups (Table 1). There were also no differences between the two groups with regards to the numbers of blastocysts biopsied, percentage of euploid