



# Outcomes of in vitro fertilization cycles following fertility-sparing treatment in stage IA endometrial cancer

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## Abstract

**Purpose** This study aimed to present cases involving in vitro fertilization (IVF) cycles in patients with stage IA endometrial adenocarcinoma (EC) who underwent fertility-sparing conservative treatment.

**Methods** Twenty-two patients who underwent IVF cycles in a single fertility center between May 2005 and February 2017 after progestin treatment for stage IA EC were chosen for this study. Outcomes of IVF cycles were analyzed retrospectively.

**Results** Women of a median age of 34 years (range 26–41 years) underwent a total of 49 embryo transfers within an average of 2 months after their last progestin treatment. The clinical pregnancy rate per transfer was 26.5%, implantation rate was 16.7%, and live birth rate was 14.3%. The cumulative clinical pregnancy rate was 50% (11/22), resulting in 6 live births (27.3%) within 3 cycles of embryo transfer. The median endometrial thickness on the day of human chorionic gonadotropin injection in 34 fresh cycles was 9.0 mm (range 4–10 mm) in live births, 7.5 mm (range 6–9 mm) in miscarriages, and 6.0 mm (range 4–15 mm) in no pregnancy cases. During a median post-cancer treatment follow-up period of 41 months (range 9–150 months), 6 (27.3%) women underwent definitive hysterectomy for EC relapse.

**Conclusions** This study showed an acceptable cumulative pregnancy rate after the IVF procedure in patients with early-stage EC who were treated conservatively. Considering the high relapse rate, it is of great importance that these patients are closely monitored after the IVF cycles.

**Keywords** Assisted reproductive technology (ART) · Endometrial cancer · In vitro fertilization (IVF) · Levonorgestrel-releasing intrauterine system (LNG-IUS) · Progesterone

## Introduction

Endometrial adenocarcinoma (EC) is one of the most common types of gynecologic malignancy in Western countries and the incidence of EC is rapidly increasing in Westernizing countries. Although the majority of cases are diagnosed in the postmenopausal period, 14–25% of cases are diagnosed in the premenopausal period and 2–14% are diagnosed in patients less than 40 years of age [1, 2]. As over 70% of women aged 40 years or younger are nulliparous, the

optimal infertility treatment has taken on greater importance for these patients [3].

The standard treatment for EC is total hysterectomy with bilateral salpingo-oophorectomy, peritoneal cytology, and/or lymph node dissection. In early-stage EC, the 5-year survival rate after this surgical treatment is over 93% [4]. However, this definitive treatment may not be acceptable to young women due to their desire for childbearing. In young patients (aged < 40 years), EC is associated with a very favorable prognosis because the tumors are likely to be early-stage, well-differentiated endometrioid-type adenocarcinomas and hormone dependent [2]. Therefore, conservative treatment with oral progestins or levonorgestrel-releasing intrauterine system (LNG-IUS) is recommended to patients of this age group with stage IA and grade 1 EC desiring fertility preservation [1, 5, 6]. Recent studies reported that complete response rate is between 66.7% and 79.7% with conservative therapy for stage IA, grade 1 endometrioid EC [7, 8].

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After conservative treatment, prompt pregnancy is encouraged to avoid cancer recurrence. Assisted reproductive technology (ART) such as in vitro fertilization (IVF) is recommended as a good option for immediate conception [8, 9]. There are several studies reporting overall acceptable pregnancy outcomes after conservative treatment in early-stage EC patients; the clinical pregnancy rate was reported to be up to 73% and the live birth rate was 37.4% [10]. However, limited case series have investigated the pregnancy outcomes of IVF cycles in EC patients and they are mostly of United States or European population [11, 12]. In this study, we report the outcomes in 22 women conservatively treated for stage IA EC followed by IVF in the Korean population.

## Materials and methods

The authors reviewed the medical records of patients who underwent IVF cycles after conservative treatment for early-stage EC at CHA Gangnam Medical Center between May 2005 and February 2017. A total of 22 women who underwent IVF cycles following conservative management for early-stage EC were identified. Of the 22 patients, 6 were from the authors' previous case series comparing the outcome of IVF cycles [13]. The diagnosis and treatment of EC in all the patients were according to standard FIGO guidelines [14]. Histologic diagnosis was made using samples obtained with dilatation and curettage (D&C) under intravenous anesthesia. All the patients were evaluated by pelvic examination, ultrasonography, abdominal and pelvic computed tomography (CT), and magnetic resonance imaging (MRI). The status of pelvic/aortic lymph node involvement or extrauterine lesions was also confirmed.

The patients who decided to undergo fertility-sparing therapy were administered oral progestins [megestrol acetate (MA) or medroxyprogesterone acetate (MPA)] with or without insertion of LNG-IUS. Follow-up evaluation for treatment response was performed at 3-month intervals and included history taking, physical examination, and D&C. In cases where LNG-IUS was inserted, D&C was done between removal and reinsertion of LNG-IUS. In the histologic interpretation of treatment response, complete remission (CR) was defined as a condition with no cancerous or hyperplastic lesions. Partial response (PR) was defined as the presence of residual lesions with degeneration or atrophy of endometrial glands or endometrial hyperplasia. No change (NC) was defined as the presence of residual lesions without degeneration or atrophy of endometrial glands. Progressive disease (PD) was defined as the appearance of grade 2 or 3 endometrial carcinoma.

Patients in CR after treatment were recommended for pregnancy trial at the earliest possibility. Women with persistent PR were selectively permitted for pregnancy trial

after maintenance of longer periods of progestin therapy. Women desiring to use ART were offered treatments such as conventional IVF with controlled ovarian stimulation using GnRH antagonist protocol, natural cycle IVF, in vitro maturation (IVM) or cryopreserved embryo transfer (ET). An embryo was described as a good quality embryo if it had a 4-cell embryo on day 2 and a 7- or 8-cell embryo on day 3, contained < 20% anucleate fragments, and exhibited no apparent morphological abnormalities. Clinical pregnancy was determined by observation of a gestational sac with fetal heart beat on transvaginal ultrasound scan at 6 weeks of pregnancy. All the women were followed up for pregnancy status and cancer recurrence. The data were analyzed by SPSS version 22 (SPSS Inc., Chicago, IL, USA). Mann–Whitney *U* test and Fisher's exact test were used for comparisons between patient groups with or without cancer recurrence. *P* value < 0.05 was regarded as statistically significant. This study protocol was approved by the institutional review board of CHA Gangnam Medical Center (GCI-17-11). Informed consent was waived due to the retrospective design of the study.

## Results

Baseline patient characteristics are summarized in Table 1. The median age at diagnosis was 31 years (range 26–40 years) and 21 patients were nulliparous. Thirteen (59.1%) women had been diagnosed with polycystic ovary syndrome (PCOS). Of a total of 22 patients, 7 (31.8%) complained of symptoms associated with EC. The other 15 patients had no specific symptoms and were incidentally diagnosed during infertility work-up which included ultrasonography and hysteroscopy. After cancer diagnosis, 3 patients were treated with oral progestins (MPA and/or MA) only and 19 with MPA plus LNG-IUS. The median number of D&C was 4 times (range 2–9 times) and median duration of treatment was 11 months (range 6–42 months). All the women responded to treatment with a median time to CR of 9 months (range 3–37 months).

Patient pregnancy outcomes after 49 IVF cycles are shown in Table 2. IVF treatment was administered at a median patient age of 34 years (range 26–41 years) after a median duration of 1 month (range 0–29 months) after the last progestin administration. Embryo transfer (ET) cycles were cancelled 12 times due to the presence of thin endometrium in 4 patients and 2 times due to ovarian hyperstimulation syndrome in 2 patients, and finally a total of 49 ET cycles were performed. Each woman underwent a median number of 2 ET cycles (range 1–9 ET cycles) and had a mean number of 2.4 (range 1–3) embryos transferred during 49 ET cycles (27 conventional IVFs with short GnRH antagonist protocol, 5 IVMs, 2 natural IVFs,

**Table 1** Baseline characteristics of patients during treatment of early-stage EC ( $N=22$ )

Variables	Mean, median or $N$ (%)
Age at diagnosis (years)	31 (26–40)
BMI ( $\text{kg}/\text{m}^2$ )	$23.7 \pm 4.8$
PCOS	13 (59.1%)
Oligomenorrhea	14 (63.6%)
Nulliparity	21 (95.5%)
Medical comorbidity <sup>a</sup>	4 (18.2%)
Cancer presentation	
Irregular menstruation	7 (31.8%)
Incidental finding on ultrasound	10 (45.5%)
Incidental finding on hysteroscopy	5 (22.7%)
Histology	
Grade 1	18/22 (81.8%)
Grade 2	4/22 (18.2%)
Treatment regimen	
Oral progestin	3 (13.6%)
MPA plus LNG-IUS	19 (86.4%)
Time to complete remission (months)	9 (3–37)
Duration of progestin treatment (months)	11 (6–42)
Median number of D&C procedures	4 (2–9)

PCOS polycystic ovarian syndrome, BMI body mass index, D&C dilatation and curettage, MPA medroxyprogesterone acetate, LNG-IUS levonorgestrel-releasing intrauterine system

<sup>a</sup>Diabetes mellitus, hypertension, thyroiditis

and 15 cryopreserved ETs). During the conventional IVF cycles, the patients underwent ovarian stimulation for a median duration of 8 days (range 5–11 days) with a mean estradiol level of 1973.0 pg/mL (range 276.9–5035.8 pg/mL) on human chorionic gonadotropin injection (hCG) triggering day. The mean number of total retrieved oocytes was 11.2 (range 3–39) during conventional IVF and IVM protocols.

Per ET cycle, the clinical pregnancy rate was 26.5%, the implantation rate was 16.7%, and the live birth rate was 14.3%. In a total of 49 ET cycles, 11 patients (50%) achieved clinical pregnancies and 6 (27.3%) gave birth to 10 healthy live neonates within 3 ET cycles. One patient had singleton and twin deliveries during consecutive IVF cycles. Five patients suffered six spontaneous abortions with no evidence of residual tumor following dilatation and evacuation. All the women aged 40 and above at the time of initial IVF cycle ( $N=6$ ) failed to have a live birth.

The median number of D&C was generally higher in women with failed IVF cycles: 3 (range 2–6) live births, 5 (range 3–6) spontaneous abortions and 4 (range 3–9) no clinical pregnancies. In 34 fresh cycles, the median endometrial thickness on hCG injection day was generally higher in successful cycles: 9.0 mm (range 4–11.2 mm) in live births, 7.5 mm (range 6–9 mm) in spontaneous abortions, and

6.0 mm (range 4–15 mm) in no clinical pregnancies (data not shown).

During a median follow-up period of 41 months (range 9–150 months) after cancer treatment, 11 women underwent definitive hysterectomy. Of the 11 patients, 6 (27.3%) had confirmed cancer recurrence with a median time interval of 8 months (range 6–60 months) after the last progestin administration and a recurrence rate of 6.3% per person-year. The patients with EC relapse had generally been given higher doses of gonadotropin (median 2325 IU) during IVF and were more likely to be nulliparous than those without relapse though the difference did not reach statistical significance (Table 3).

## Discussion

This case series revealed acceptable IVF outcomes in women conservatively treated for early-stage EC. All the women who succeeded in having live births were free of obstetric complications such as placenta accreta and postpartum bleeding. In a recent review of the outcomes after fertility preservation with oral progestin or LNG-IUS in EC patients, the pregnancy rate was 79.0% (128 pregnancies) and the live birth rate was 44.4% (72 live births) in 162 patients [15]. In another meta-analysis, the live birth rate was 23.6% (61 live births) in 258 EC patients after conservative oral progestin therapy [16]. Park et al. reported a 73% pregnancy rate and a 66% live birth rate in 70 women with early-stage EC treated with oral progestin in a multicenter study [7]. There are few studies about pregnancy outcomes following ART use and they are mostly in the form of case reports. Elizur et al. reported IVF outcomes of a relatively large number of 8 EC patients after conservative oral progestin therapy: a pregnancy rate of 75% in the patients, 29.2% per ET and a live birth rate of 50% in the patients, 19.4% per ET during a total of 31 IVF cycles [17].

Age and endometrial receptivity are known as major factors for successful IVF pregnancy outcomes. In this study, all 6 women aged 40 or more years failed to successful pregnancy during 11 cycles of ET as suggested in other reproductive studies of women with EC [18]. Considering these results, it might be suggested that women aged under 40 are more adequate candidates for fertility-sparing treatment for EC, whereas women aged 40 or more are for definitive surgery.

Women with EC might have impaired endometrial response to infertility treatments because of their primary endometrial cancerous conditions, the post-high-dose progestin therapy status, and repeated endometrial curettages [12, 18]. Endometrial thickness on ultrasonography is recognized as an important parameter of endometrial receptivity. Many researches emphasized the positive correlation

**Table 2** Patient pregnancy outcomes following a total of 49 ET cycles (*N*=22)

Variables	Mean, median or <i>N</i> (%)
Age at first IVF (years)	34 (26–41)
Age at ET (years)	
< 35	24/49 (49.0%)
35–39	8/49 (16.3%)
40 ≥	17/49 (34.7%)
AMH (ng/mL)	3.0 ± 2.8
Duration of infertility (years)	2 (0–8)
Time interval between cancer treatment and first IVF (months)	1 (0–29)
ET trial per woman	2 (1–9)
≤ 3	20/22 (90.9%)
3 >	2/22 (9.1%)
ART method	
Conventional IVF/ET	27/49 (55.1%)
Natural IVF/ET	2/49 (4.1%)
IVM/ET	5/49 (10.2%)
Cryopreserved ET	15/49 (30.6%)
Gonadotropin use in conventional IVF (IU)	1463 (825–2325)
Endometrial thickness (mm)	
On hCG injection day in fresh cycles	7.0 ± 2.5
On the day of luteal support start in cryopreserved ET cycles	7.3 ± 2.0
Retrieved oocytes in conventional IVF and IVM cycles	11.2 ± 7.3
Transferred embryos per ET	2.4 ± 0.7
Transferring good quality embryo per ET	37/49 (75.5%)
Pregnancy outcome per ET	
Clinical pregnancy rate	13/49 (26.5%)
Live birth rate	7/49 (14.3%)
Miscarriage rate	6/49 (12.2%)
Implantation rate	16.7%
Hysterectomy	11/22 (50%)
For recurrence	6/22 (27.3%)
For completion of childbearing	3/22 (13.6%)
No more desire for pregnancy trial	2/22 (9.1%)

ET embryo transfer, IVF in vitro fertilization, ART assisted reproductive technology, IVM in vitro maturation, hCG human chorionic gonadotropin, AMH anti-Mullerian hormone, IU international units

between endometrial thickness (usually > 5 mm) and successful IVF outcomes [19–22]. D&C procedures may cause endometritis, intrauterine adhesions, and endometrial thinning. Thicker endometrium can be achieved with less D&C procedures as in this study and as reported by Inoue et al. [18]. Even with adequate endometrial preparation, lower numbers of D&C are considered favorable to IVF success.

Exogenous progestin therapy for EC induces reduction of glandular cells with decidualized and spindled stroma, appearing as quiescent endometrial tissue without mitotic activity. Also, endometrial tissue exposed to increased levels of progesterone shows a loss of nucleoli and cytoplasmic metaplasia [23]. Therefore, it is possible that long-term exogenous progestin exposure can cause histologic alteration in the endometrium, which may affect the reproductive

function of the endometrium as well as EC therapy. In this study, the longest duration of progestin therapy resulting in a live birth was 24 months and beyond that period there was no clinical pregnancy even in women of younger age.

Some studies have suggested a relationship between the use of fertility drugs and the risk of EC, because there is concern that ovarian stimulation with gonadotropins results in high serum estradiol concentrations which in turn impact EC incidence. Regarding relapse in cancer survivors who underwent ART treatments, two retrospective studies of young women with EC reported that there was no association between the use of ovulation induction drugs and the risk of recurrence [7, 24]. Considering the recurrence rate of 23.1–71.4% in women who got naturally pregnant after conservative EC treatment [25], the recurrence rate obtained

**Table 3** Characteristics of patients with or without recurring endometrial cancer after IVF cycles. All the variables were compared between the two groups using non-parametric tests

Variables	Patients without recurrence ( <i>N</i> =16) Mean, median or <i>N</i> (%)	Patients with recurrence ( <i>N</i> =6) Mean, median or <i>N</i> (%)	<i>P</i> value
Age at diagnosis (years)	31 (26–40)	34 (26–40)	1.000
BMI (kg/m <sup>2</sup> )	23.8±5.2	23.6±4.3	0.941
PCOS	10 (62.5%)	3 (50%)	0.655
Medical comorbidity <sup>a</sup>	2 (12.5%)	2 (33.3%)	0.292
Cancer presentation			
Irregular menstruation	3 (18.7%)	4 (66.8%)	0.103
Incidental finding on ultrasound	9 (56.3%)	1 (16.6%)	
Incidental finding on hysteroscopy	4 (25.0%)	1 (16.6%)	
Histology			
Grade 1	13 (81.3%)	5 (83.3%)	1.000
Grade 2	3 (18.7%)	1 (16.7%)	
Treatment regimen			
Oral progestin	1 (6.5%)	2 (33.3%)	0.169
MPA plus LNG-IUS	15 (93.5%)	4 (66.7%)	
Time to complete remission (months)	9 (3–37)	8 (3–14)	0.590
Total duration of progestin treatment (months)	12 (6–42)	9 (6–20)	0.370
Duration of infertility (years)	2 (0–8)	1 (0–5)	0.329
Nulliparity after IVF			
Yes	11 (68.8%)	5 (83.3%)	0.634
No	5 (31.2%)	1 (16.7%)	
Total duration of gonadotropin use during IVF (days)	9 (0–24)	10 (6–99)	0.630
Total gonadotropin use during IVF (IU)	1700 (0–5850)	2325 (0–12,225)	0.196
Follow-up period after progestin treatment (months)	40 (9–150)	71 (24–104)	0.203

PCOS polycystic ovarian syndrome, BMI body mass index, IVF in vitro fertilization, MPA medroxyprogesterone acetate, LNG-IUS levonorgestrel-releasing intrauterine system, IU international units

<sup>a</sup>Diabetes mellitus, hypertension, thyroiditis

from our study was comparable to that from earlier studies. Though no statistical significance was observed, the patients with EC relapse were followed up for longer periods and received higher total doses of gonadotropin during IVF in our study in comparison to earlier studies. In considering the totality of the findings, it should be noted that fertility drugs can be used safely, but with caution regarding the total dosage, after successful conservative progestin therapy and longer durations of close follow-up are mandatory to avoid missing possible relapses. Further large-scale studies are necessary to confirm the safe margin for the total gonadotropin dosage and the factors affecting cancer recurrence following IVF.

In conclusion, the cumulative pregnancy and live birth rates were acceptable following IVF cycles in young women who were conservatively treated for early-stage EC. Further prospective studies are expected to confirm these findings. Considering the high EC relapse rate, long-term continuous follow-up after IVF cycles will be of great importance in these patients.

**Author contributions** YSK: project development, data collection, manuscript writing. MJK: data collection, data analysis, manuscript writing. S-AC: manuscript writing, manuscript editing. MKK: data collection, manuscript editing. BSY: data collection. SJS: project development, manuscript editing.

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### Compliance with ethical standards

**Conflict of interest** The authors report no conflicts of interest.

**Informed consent** All the procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

### References

1. Kaku T, Yoshikawa H, Tsuda H, Sakamoto A, Fukunaga M, Kuwabara Y et al (2001) Conservative therapy for adenocarcinoma and atypical endometrial hyperplasia of the endometrium in

- young women: central pathologic review and treatment outcome. *Cancer Lett* 167:39–48
2. Ramirez PT, Frumovitz M, Bodurka DC, Sun CC, Levenback C (2004) Hormonal therapy for the management of grade 1 endometrial adenocarcinoma: a literature review. *Gynecol Oncol* 95:133–138
  3. Soliman PT, Oh JC, Schmeler KM, Sun CC, Slomovitz BM, Gershenson DM et al (2005) Risk factors for young premenopausal women with endometrial cancer. *Obstet Gynecol* 105:575–580
  4. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB (1987) Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. *Cancer* 60:2035–2041
  5. Pinto AB, Gopal M, Herzog TJ, Pfeifer JD, Williams DB (2001) Successful in vitro fertilization pregnancy after conservative management of endometrial cancer. *Fertil Steril* 76:826–829
  6. Yang YC, Wu CC, Chen CP, Chang CL, Wang KL (2005) Reevaluating the safety of fertility-sparing hormonal therapy for early endometrial cancer. *Gynecol Oncol* 99:287–293
  7. Park JY, Seong SJ, Kim TJ, Kim JW, Kim SM, Bae DS et al (2013) Pregnancy outcomes after fertility-sparing management in young women with early endometrial cancer. *Obstet Gynecol* 121:136–242
  8. Zhou R, Yang Y, Lu Q, Wang J, Miao Y, Wang S et al (2015) Prognostic factors of oncological and reproductive outcomes in fertility-sparing treatment of complex atypical hyperplasia and low-grade endometrial cancer using oral progestin in Chinese patients. *Gynecol Oncol* 139:424–428
  9. Chao AS, Chao A, Wang CJ, Lai CH, Wang HS (2011) Obstetric outcomes of pregnancy after conservative treatment of endometrial cancer: case series and literature review. *Taiwan J Obstet Gynecol* 50:62–66
  10. Park JY, Nam JH (2015) Progestins in the fertility-sparing treatment and retreatment of patients with primary and recurrent endometrial cancer. *Oncologist* 20:270–278
  11. Azim A, Oktay K (2007) Letrozole for ovulation induction and fertility preservation by embryo cryopreservation in young women with endometrial carcinoma. *Fertil Steril* 88:657–664
  12. Han AR, Kwon YS, Kim DY, Kim JH, Kim YM, Kim YT et al (2009) Pregnancy outcomes using assisted reproductive technology after fertility-preserving therapy in patients with endometrial adenocarcinoma or atypical complex hyperplasia. *Int J Gynecol Cancer* 19:147–151
  13. Kim MK, Seong SJ, Kim YS, Song T, Kim ML, Yoon BS et al (2013) Combined medroxyprogesterone acetate/levonorgestrel-intrauterine system treatment in young women with early-stage endometrial cancer. *Am J Obstet Gynecol* 209(358):e1–4
  14. Pecorelli S (2009) Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynecol Obstet* 105:103–104
  15. Zapardiel I, Cruz M, Diestro MD, Requena A, Garcia-Velasco JA (2016) Assisted reproductive techniques after fertility-sparing treatments in gynaecological cancers. *Hum Reprod Update* 22:281–305
  16. Gallos ID, Yap J, Rajkhowa M, Luesley DM, Coomarasamy A, Gupta JK (2012) Regression, relapse, and live birth rates with fertility-sparing therapy for endometrial cancer and atypical complex endometrial hyperplasia: a systematic review and metaanalysis. *Am J Obstet Gynecol* 207(266):e1–12
  17. Elizur SE, Beiner ME, Korach J, Weiser A, Ben-Baruch G, Dor J (2007) Outcome of in vitro fertilization treatment in infertile women conservatively treated for endometrial adenocarcinoma. *Fertil Steril* 88:1562–1567
  18. Inoue O, Hamatani T, Susumu N, Yamagami W, Ogawa S, Takemoto T et al (2016) Factors affecting pregnancy outcomes in young women treated with fertility-preserving therapy for well-differentiated endometrial cancer or atypical endometrial hyperplasia. *Reprod Biol Endocrinol* 14:2
  19. Zhang X, Chen CH, Confino E, Barnes R, Milad M, Kazer RR (2005) Increased endometrial thickness is associated with improved treatment outcome for selected patients undergoing in vitro fertilization-embryo transfer. *Fertil Steril* 83:336–340
  20. Wu Y, Gao X, Lu X, Xi J, Jiang S, Sun Y et al (2014) Endometrial thickness affects the outcome of in vitro fertilization and embryo transfer in normal responders after GnRH antagonist administration. *Reprod Biol Endocrinol* 12:96
  21. Kasius A, Smit JG, Torrance HL, Eijkemans MJ, Mol BW, Opmeer BC et al (2014) Endometrial thickness and pregnancy rates after IVF: a systematic review and meta-analysis. *Hum Reprod Update* 20:530–541
  22. Fang R, Cai L, Xiong F, Chen J, Yang W, Zhao X (2016) The effect of endometrial thickness on the day of hCG administration on pregnancy outcome in the first fresh IVF/ICSI cycle. *Gynecol Endocrinol* 32:473–476
  23. Mentrikoski MJ, Shah AA, Hanley KZ, Atkins KA (2012) Assessing endometrial hyperplasia and carcinoma treated with progestin therapy. *Am J Clin Pathol* 138:524–534
  24. Ichinose M, Fujimoto A, Osuga Y, Minaguchi T, Kawana K, Yano T et al (2013) The influence of infertility treatment on the prognosis of endometrial cancer and atypical complex endometrial hyperplasia. *Int J Gynecol Cancer* 23:288–293
  25. Park JY, Kim DY, Kim TJ, Kim JW, Kim JH, Kim YM et al (2013) Hormonal therapy for women with stage IA endometrial cancer of all grades. *Obstet Gynecol* 122:7–14

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