Fertility preservation in young patients with endometrial cancer!

ISFP Vienna
17. November 2017

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Klinik für Endokrinologie und Reproduktionsmedizin

Epidemiology

Endometrial cancer is the most common gynecologic malignancy typically in the postmenopausal women.

### Common Types of Cancer

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated New Cases 2017</th>
<th>Estimated Deaths 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer (Female)</td>
<td>252,710</td>
<td>40,910</td>
</tr>
<tr>
<td>Lung and Bronchus Cancer</td>
<td>222,050</td>
<td>151,870</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>180,580</td>
<td>29,270</td>
</tr>
<tr>
<td>Colon and Rectum Cancer</td>
<td>135,430</td>
<td>59,260</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>87,110</td>
<td>9,720</td>
</tr>
<tr>
<td>Bladder Cancer</td>
<td>76,030</td>
<td>18,870</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>72,440</td>
<td>20,110</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis Cancer</td>
<td>63,990</td>
<td>14,430</td>
</tr>
<tr>
<td>Leukemia</td>
<td>42,370</td>
<td>11,920</td>
</tr>
<tr>
<td><strong>Endometrial Cancer</strong></td>
<td><strong>61,380</strong></td>
<td><strong>10,970</strong></td>
</tr>
</tbody>
</table>

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**Endometrial cancer represents 3.6% of all new cancer cases in the U.S.**

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**Median Age at Diagnosis:** 62

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People™

Dr. Kazem: Medizinische Universität Wien, UFK
Risk factors!

- Infertility and nulliparity
- Hypertension and diabetes
- Hyperestrogenic state
- Endometrial cancer

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Dr. Kazem Nouri Medizinische Universität Wien, UFK

Hyperestrogenic state

1. Obesity
2. PCO
3. Anovulation
4. Irregular menses
5. Functional ovarian tumors

Presence of two or more polyps in patients with polycystic ovary syndrome increases the probability of pre-malignant and malignant changes!

Key Symptoms?

1. Abnormal bleeding!
2. Prolonged anovulation
Subset of young women with endometrial cancer are slim with regular menses!

**Gynecologic Oncology**
DOI: 10.1006/gyno.2001.6434, available online at http://www.idealibrary.com on 120, 100 Blossom Street, Boston, MA 02114. Fax: (617) 724-6898. E-mail: Gynecologic Oncology
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Endometrial Cancer in Women 40 Years Old or Younger
Linda R. DeSouza, M.D.;* Audrey Garrett, M.D.;‡ Bo R. Rueda, Ph.D.;* Jacqueline Hau, M.D.;‡ Yachiao Chang, Ph.D.; and Adam F. Pollak, M.D.;†

*Division Gynecology, Service of Gynecologic Oncology, Department of Obstetrics, and Section Plastic Evaluation Center, Department of Obstetrics, and Division Gynecologic Oncology, Department of Obstetrics, and Reproductive Medicine, Massachusetts General Hospital, Boston, Massachusetts 02114; and Division Gynecologic Oncology, Brigham and Women’s Hospital, Boston, Massachusetts 02115.

In the current study the normal-weight woman does seem to be at higher risk to develop higher stage disease and is more likely to have high-risk histology!

**Other malignancy!**

**Ovarian malignancy**
Young women with endometrial cancer are at significant risk for concomitant adnexal disease:
1- Synchronous primary ovarian tumors (10–29.4 %)
2- Endometrial metastases to the ovary (5%)

Lynch/HNPPCCh

CASE REPORT

Endometrial carcinoma in a young patient with polycystic ovarian syndrome: first suspected at time of embryo transfer

At the time of embryo transfer, a small but steady trickle of blood was noted as soon as the embryo transfer catheter was introduced into the uterine cavity. There had been trauma in the insertion of the catheter which we believed had explained this loss. A repeat ultrasound scan was subsequently negative. Based on this, irregular bleeding was thought to be suspicious and prompted further investigations. The embryo transfer was abandoned and all the embryos were frozen.

Figure 1. Hysterectomy specimen showing intra-endometrial adenocarcinoma (original magnification ×200).

Figure 2. Endometrial hyperplasia showing severe atypical hyperplasia and intra-endometrial adenocarcinoma (original magnification ×200).

Endometrial Hyperplasia
Precursor of EM-Ca!

Simple hyperplasia without atypia - 1%
Complex hyperplasia without atypia - 3%
Simple atypical hyperplasia - 8%
Complex atypical hyperplasia - 29%
Staging FIGO 2010

Carcinoma of the Endometrium

IA  Tumor confined to the uterus, no or <1/2 myometrial invasion
IB  Tumor confined to the uterus, >1/2 myometrial invasion
II  Cervical stromal invasion, but not beyond uterus
IIIA Tumor invades serosa or adnexa
IIIB Vaginal and/or parametrial involvement
IIIC1 Pelvic node involvement
IIIC2 Para-aortic involvement
IVA Tumor invasion bladder and/or bowel mucosa
IVB Distant metastases including abdominal metastases and/or inguinal lymph nodes

ER+/PR+ (by either ligand binding or immunohisto-chemistry)

Grade

Grade 1 tumors have 95% or more of the cancerous tissue forming glands.

Grade 2 tumors have between 50% and 94% of the cancerous tissue forming glands.

Grade 3 tumors have less than half of the cancerous tissue forming glands.

Early endometrial carcinoma is defined as low-grade cancer limited to the uterus!
**Good prognosis**

The available data suggest relative safety and efficacy of progestin treatment for a short window to allow the woman to achieve her reproductive goals!

- Early stage and low grade
- 5-year disease-specific survival rate of 95% in younger patients, in contrast to older patients (86%)

**Fertility Preservation!**

- Complete resolution rates ranging from 65.8% to 74% for CAH and 48.2% to 72% for EM Cancer patients

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**Staging of endometrial carcinoma**

1. Pelvic exam
2. Pap smear
3. D&C / Endometrial Biopsy
4. Hysteroscopy
5. Transvaginal ultrasound
6. CT/MRI
7. CA125
8. LSK

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simple endometrial biopsy?
Only D & C?

Underdiagnose!

Incorrectly grading: 25%
Missing higher-grade tumors: 10%

Hysteroscopy with D&C

1-Hysteroscopy with directed biopsies and D&C
2-Following the lesion during the course of therapy
3-Sensitivity and specificity of hysteroscopy
in diagnosis of endometrial carcinoma: 86.4% and 99.2%


Conservative surgical management of stage IA endometrial carcinoma for fertility preservation

Ivan Mazzon, M.D.,* Giacomo Corrado, M.D., Ph.D.,* Valeria Masciullo, M.D., Ph.D.,* Daniela Morri, M.D.,* Gabriella Ferrandina, M.D.,* and Giovanni Scambia, M.D.,*

*Endoscopic Gynecologic Unit, Nuova Villa Claudia, Rome; 1Department of Oncology, Catholic University of the Sacred Heart, Campobasso; and 2Division of Gynecologic Oncology, Catholic University of the Sacred Heart, Rome, Italy

Objective: To describe an innovative method to preserve fertility in young women with stage IA endometrial cancer with use of hysteroscopic resection followed by administration of 160 mg of megestrol acetate.

Design: Prospective study.

Setting: Division of Gynecologic Oncology, Catholic University of the Sacred Heart, and the Endoscopic Gynecologic Unit, Nuova Villa Claudia, Rome, Italy.

Patients: Six young patients with stage IA endometrial cancer.

Intervention(s): Conservative microsurgical treatment using a three-step technique in which each step is characterized by a pathologic analysis of the removed lesion (step 1), the removal of the endometrium adjacent to the lesion (step 2), and the removal of the myometrium underlying the lesion (step 3).

Main Outcome Measure(s): Therapy of stage IA endometrial cancer and pregnancy.

Results: The conservative surgery was effective because of transvaginal ultrasound examination and diagnostic hysteroscopy with targeted biopsies at 3, 6, 9, and 12 months after surgery were negative for atypia or malignancy. Moreover, four out of six patients (66%) achieved childbearing.

Conclusion(s): This method, under a close postsurgical follow-up, might represent a novel therapeutic option for those women with stage IA endometrial cancer who wish to preserve fertility. (Fertil Steril 2010;93:1286-9. ©2010 by American Society for Reproductive Medicine.)

Key Words: Endometrial cancer, fertility preservation, hysteroscopy, hormone therapy.
Eligible patients were counseled extensively for the option of conservative therapy and the possibility of recurrence or progression of disease. After informed consent was obtained, an operative hysteroscopy was performed with the patients under general anesthesia; the cervix was dilated to 10 mm with Hegar’s dilator, and a 9 mm resectoscope with 0°/C14 lens was introduced. The uterus was distended with 1.5% glycine solution under gravity inflow of 70 mm Hg pressure. Irrigant fluid was collected in 3-L graduated cylinders and monitored carefully. A 5-mm cutting loop electrode and 100 W of pure cutting output power were used to resect the tumor lesion, the endometrium near the lesion, and the myometrium under lesion.

If the pathologic analysis confirmed a well-differentiated adenocarcinoma of the endometrium with no invasion of myometrium and of resection margins, hormone therapy regimen of megestrol acetate (160 mg) daily was initiated 5 days after operative hysteroscopy and continued for 6 months. Patients were allowed to attempt childbearing immediately after completing their therapy with megestrol acetate.

Complete response was defined as total absence of tumor cells during the follow-up diagnostic hysteroscopy with biopsy after hormone therapy. If the patient did not respond on the first assessment, the plan was to switch to traditional surgery.

After documentation of complete remission, the patients then were closely followed up in the outpatient clinic. Vaginal ultrasonography and diagnostic hysteroscopy with biopsy were performed every 3 months for the first year and every 6 months for the next 2 years.

**RESULTS**

Clinical characteristics of patients are detailed in Table 1. Median patient age was 33 years (range 27–39 years). None of the patients was obese; four out of six referred a primary infertility. Pathologic diagnoses at diagnostic hysteroscopy were six grade 1 endometrioid adenocarcinoma FIGO stage IA. All tumors were estrogen and progestin receptor positive. Median follow-up time was 50.5 months (range 21–82 months). None of these patients had any problem during and after both endoscopic surgery and hormonal therapy. All patients responded to conservative therapy after 3 months of hormonal therapy, and none had recurrent disease during the follow-up time (Table 2).

As with most young patients with endometrial cancer, our patients were nulliparous at diagnosis. At present, four out of six have given birth to five infants, 24 months on average from the end of therapy (range 14–46 months) without assisted reproductive technology (ART). The other two actively are attempting to conceive.

One patient had two pregnancies. Four babies were born by cesarean section at 39 weeks of gestation, and one was born spontaneously at 41 weeks. Four out of five were male, and the average weight was 3,600 g (range 3,200–4,500 g). Of the two patients who are not pregnant yet, one is undergoing several fertility tests to establish whether she would be able to get pregnant, whereas the second one because of changes in her personal life decided to forgo pregnancy altogether. After counseling with these patients, three out of six declared not to

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**TABLE 1**

Clinical characteristics of our 6 patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>BMI</th>
<th>Parity</th>
<th>Infertility</th>
<th>Menarche (y)</th>
<th>Symptomatology</th>
<th>Ultrasound scan</th>
<th>HYS + biopsy</th>
<th>ER/PR</th>
<th>Stage of disease assessed by MRI</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>22</td>
<td>0</td>
<td>I</td>
<td>12</td>
<td>Haematic endless bleeding</td>
<td>Increased endometrial thickness EEA G1</td>
<td>EEA G1</td>
<td>++</td>
<td>IA</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>23</td>
<td>0</td>
<td>I</td>
<td>11</td>
<td>Haematic endless bleeding</td>
<td>Increased endometrial thickness EEA G1</td>
<td>EEA G1</td>
<td>++</td>
<td>IA</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>0</td>
<td>0</td>
<td>I</td>
<td>15</td>
<td>Haematic endless bleeding</td>
<td>Increased endometrial thickness EEA G1</td>
<td>EEA G1</td>
<td>++</td>
<td>IA</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>22</td>
<td>0</td>
<td>I</td>
<td>12</td>
<td>Haematic endless bleeding</td>
<td>Increased endometrial thickness EEA G1</td>
<td>EEA G1</td>
<td>++</td>
<td>IA</td>
</tr>
<tr>
<td>5</td>
<td>36</td>
<td>23</td>
<td>0</td>
<td>I</td>
<td>11</td>
<td>Haematic endless bleeding</td>
<td>Increased endometrial thickness EEA G1</td>
<td>EEA G1</td>
<td>++</td>
<td>IA</td>
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<tr>
<td>6</td>
<td>30</td>
<td>25</td>
<td>0</td>
<td>I</td>
<td>12</td>
<td>Haematic endless bleeding</td>
<td>Increased endometrial thickness EEA G1</td>
<td>EEA G1</td>
<td>++</td>
<td>IA</td>
</tr>
</tbody>
</table>

Note: HYS = hysteroscopy; MRI = magnetic resonance imaging; EEA = endometrioid endometrial adenocarcinoma; G1 = grading 1.

1- Removal of the tumor
2-Removal of the endometrium adjacent to the tumor
Successful surgery: If the results of the first pathologic analysis are positive (neoplastic lesion) and the other two are negative!

Hysteroscopy with D&C

Fluid based hysteroscopy could cause retrograde seeding of the peritoneal cavity with malignant cells, the prognostic significance of positive peritoneal cytology in clinical stage I endometrial adenocarcinoma remains controversial!
Imaging?

**MR VS CT**

Grade 1 Endometrial carcinoma

- Pelvic lymph-node involvement (3%)
- Para-aortic lymph node involvement (1.7%)
- Deep myometrial invasion (9%)
- Spread of tumor to the adnexa (6%)
- Coexisting ovarian neoplasms (19%)
MRI?

1-For the detection of myometrial invasion, contrast-enhanced MRI, is superior to ultrasonography and computed tomography scan (Sensitivity and specificity of 74%)

2-MRI can also be used to evaluate lymph nodes. Lymph nodes over 1 cm and with central necrosis are suspicious.

The Role of Laparoscopy

- Extrauterine disease
- Peritoneal cytology
- Pelvic lymphadenectomy


Coexisting Ovarian Malignancy in Young Women With Endometrial Cancer

Christine Walsh, MD, Christine Holchneider, MD, Yen Hoang, MD, Khai Tieu, MD, Beth Karlan, MD, and Ilana Cass, MD

OBJECTIVE: In premenopausal women with endometrial cancer, ovarian preservation may be a consideration. Our objective was to examine the occurrence of coexisting ovarian malignancy and to identify predictors of advanced involvement.

METHODS: With institutional review board approval, a retrospective chart review was conducted of young women with endometrial cancer identified at 4 affiliated institutions from 1996 to 2004.

RESULTS: Among 102 young women (aged 24–45 years) who underwent hysterectomy for endometrial cancer, 26 (25%) were found to have coexisting epithelial ovarian tumors. Of these, 23 were classified as neoplasms in situ, and 3 were metastases. Ovarian cancer histology was endometrioid in 92% of cases. Among the 26 cases of coexisting ovarian involvement, 12 (46%) had grade 1 endometrial cancer on preoperative biopsy. Four (15%) had normal-appearing ovaries at the time of intraoperative assessment. On final pathology, 18 of 26 cases (69%) occurred in patients with grade 1 endometrial cancers, and 15 (58%) occurred with inner myometrial invasion. Our study further highlights the risk of conservative management with a case of ovarian cancer diagnosed 9 months after hysterectomy with ovarian conservation for stage T1b, grade 1 endometrial cancer and a case of advanced endometrial cancer metastatic to the ovaries developing 3 years after successful resolution of a grade 1 endometrial cancer treated with megestrol acetate (megace).

CONCLUSION: Careful preoperative and intraoperative assessment of the adnexa is mandatory in young women with endometrial cancer. Those who desire ovarian preservation should be counseled regarding the high rate of coexisting ovarian malignancy.

METHODS AND MATERIALS

Institutional review board approval was obtained at each participating institution. To determine the frequency of coexisting ovarian malignancies in young women with endometrial cancer, we conducted a retrospective chart review of young women with endometrial cancer identified at 4 affiliated institutions from 1996 to 2004.

RESULTS

Among 102 young women (aged 24–45 years) who underwent hysterectomy for endometrial cancer, 26 (25%) were found to have coexisting epithelial ovarian tumors. Of these, 23 were classified as neoplasms in situ, and 3 were metastases. Ovarian cancer histology was endometrioid in 92% of cases. Among the 26 cases of coexisting ovarian involvement, 12 (46%) had grade 1 endometrial cancer on preoperative biopsy. Four (15%) had normal-appearing ovaries at the time of intraoperative assessment. On final pathology, 18 of 26 cases (69%) occurred in patients with grade 1 endometrial cancers, and 15 (58%) occurred with inner myometrial invasion. Our study further highlights the risk of conservative management with a case of ovarian cancer diagnosed 9 months after hysterectomy with ovarian conservation for stage T1b, grade 1 endometrial cancer and a case of advanced endometrial cancer metastatic to the ovaries developing 3 years after successful resolution of a grade 1 endometrial cancer treated with megestrol acetate (megace).

CONCLUSION: Careful preoperative and intraoperative assessment of the adnexa is mandatory in young women with endometrial cancer. Those who desire ovarian preservation should be counseled regarding the high rate of coexisting ovarian malignancy.
Coexisting Ovarian Malignancy

Stage I ovarian cancer
Excellent prognosis

2-4.6%
In Women
>45

10-29% in
Women
<45

Higher stage tumors
and poorer prognosis

Conservative management:

1- With what?
2- How long?

- Progestin medications:
  - Medroxyprogesterone acetate (MPA): 500-1000 mg/d
  - Megestrol acetate: 80-160 mg/d


Uses of gonadotrophin-releasing hormone agonists, anti-estrogens and aromatase inhibitors have also been reported!
Risks of conservative management!

1. The risk of disease progression during conservative management of grade 1 endometrial carcinoma: 6%
2. Clinical understaging of a more advanced cancer
3. Presence or development of a simultaneous primary ovarian malignancy
4. Fertility options?

Deferral of definitive surgery to achieve childbearing, but no replacement!!

Complications of Progestin therapy?

1. Thrombophlebitis
2. Weight gain
3. Mood or libido changes
4. Headaches
5. Breast tenderness
6. Sleep disorders
7. Leg cramps
8. Liver dysfunction

**IUD?**

1- high-risk surgical patients with grade I endometrial cancer and no evidence of extrauterine disease.
2- It releases 20 mcg of levonorgestrel per day, generating a localized effect within the endometrium!
3- higher concentrations of progestin to the uterine mucosa compared to oral MA,
4- Superior results in endometrial hyperplasia compared with oral MA

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**How long?**

10 weeks to 12 Months!

- Surveillance?
- Sampling or D & C or HSC every 3 to 6 months

**Regression: Conception (3 Months reevaluation)**
RESEARCH

GENERAL GYNECOLOGY

Regression, relapse, and live birth rates with fertility-sparing therapy for endometrial cancer and atypical complex endometrial hyperplasia: a systematic review and metaanalysis

Ines B. Dallmaier, MD; Irene Yang, MD; Marianna Murovecova, MD; David M. Leekley, MD; Ari L. Greenberg, MD; Jodi L. Zeyler, MD

OBJECTIVES: The objective of the study was to evaluate the regression, relapse, and live birth rates of early-stage endometrial cancer (EC) and atypical complex hyperplasia (ACH) with fertility-sparing treatment.

STUDY DESIGN: This was a systematic review of the proportions from observational studies with systematic review and meta-regression to assess their methodology.

RESULTS: Thirty-four observational studies, including the regression, relapse, and live birth rates of early-stage EC (400 women) and ACH (106 women) with fertility-sparing treatment. Fertility-sparing treatment for EC achieved a pooled regression rate of 75.2%, a relapse rate of 40.7%, and a live birth rate of 28.6%. For ACH, the pooled regression rate was 85.4%, a relapse rate of 24.6%, and a live birth rate of 36.3%.

CONCLUSION: Fertility-sparing treatment of EC and ACH is feasible, and selected women can achieve their reproductive outcomes.

Keywords: atypical complex hyperplasia, endometrial cancer, fertility-sparing treatment, live births, pregnancies.

Assisted reproduction versus spontaneous pregnancy

From the 451 women that had fertility-sparing treatment for EC or ACH, 142 had assisted reproduction to achieve pregnancy and 36 of them achieved successful live birth. This amounts to a 26.4% live birth rate. The remaining 309 women are presumed to have tried to spontaneously conceive and 46 women achieved at least one live birth, with a rate of 14.9%. There was no difference between assisted reproduction and spontaneous conception in achieving a live birth was statistically significant (P = 0.041) in meta-regression analysis.
Other options?

Gestational carrier!

1- Egg/embryo freezing prior to hysterectomy,
2- Hysterectomy with lymph node dissection and preservation of ovaries with the future use

Disadvantages:

1- Diminish ovarian reserve or reduce accessibility to the ovaries for oocyte retrieval.
2- Risk of microscopic metastatic or concurrent disease to the ovaries or development of metachronous ovarian cancer

Reproductive and oncologic outcomes after progesterone therapy for endometrial complex atypical hyperplasia or carcinoma.

Multidisciplinary management team

Reproductive Endocrinology
Gynecologic Oncology
Maternal–Fetal Medicine
Conclusiones

1- Detailed informed consent

2- Both physician and patient should be aware of the potential risks of deviation from standard therapy. Current recommendations are based on a small number of case series and case reports, but no prospective data!

3- Careful oncologic, psychotherapeutic, genetic and reproductive counseling is essential before starting conservative management.

Thank you for your attention!
Complete remission?

A thinning of the endometrium as seen on transvaginal ultrasound is associated with an increased chance of responding to progestin therapy.

Total absence of tumor cells during the follow-up diagnostic hysteroscopy with biopsy after hormone therapy!
If the patient does not respond on the first assessment, recommendation to switch to traditional surgery should be performed.

Fertility outcomes of patients with early stage endometrial carcinoma

Huriye Ayse Parlakgumus, Esra Bulgar Kilidag, Erhan Simsek, Bulent Haydardedeoglu, Tayfun Cok, Pinar Caglar Aytac and Tayfun Bagis

1 Department of Obstetrics and Gynecology, Baskent University Faculty of Medicine, Ankara, and 2 Department of Obstetrics and Gynecology, Acibadem University Faculty of Medicine, Istanbul, Turkey
Table 1. Patients who preferred surgery

<table>
<thead>
<tr>
<th>Age at</th>
<th>Parity</th>
<th>Risk factors for endometrial cancer</th>
<th>Risk factors for infertility</th>
<th>Accompanying gynecologic disease</th>
<th>First suspicion at</th>
<th>Polyp Histology</th>
<th>Grade</th>
<th>Treatment</th>
<th>Medical treatment</th>
<th>Stage IVF</th>
<th>Medical treatment</th>
<th>Pregnancy course</th>
</tr>
</thead>
<tbody>
<tr>
<td>63</td>
<td>G: 1</td>
<td>Oligomenorrhea</td>
<td>Epiphragma</td>
<td>Yes</td>
<td>Surgical (Type 2)</td>
<td>Adenocarcinoma</td>
<td>60</td>
<td>3</td>
<td>--</td>
<td>1A</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>77</td>
<td>G: 1</td>
<td>Oligomenorrhea</td>
<td>Anovulation + tubal factor</td>
<td>None</td>
<td>Medical</td>
<td>160 mg/day</td>
<td>3 months</td>
<td>1A</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>57</td>
<td>G: 0</td>
<td>Oligomenorrhea</td>
<td>Uterine septum</td>
<td>Yes</td>
<td>Endometrioid</td>
<td>100%</td>
<td>6 months</td>
<td>1A</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>56</td>
<td>G: 0</td>
<td>Oligomenorrhea</td>
<td>Uterine septum</td>
<td>Yes</td>
<td>Endometrioid</td>
<td>100%</td>
<td>6 months</td>
<td>1A</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2</td>
<td>G: 0</td>
<td>Oligomenorrhea</td>
<td>None</td>
<td>None</td>
<td>Medical</td>
<td>160 mg/day</td>
<td>3 months</td>
<td>1A</td>
<td>--</td>
<td>--</td>
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Table 2. Patients who had medical treatment

<table>
<thead>
<tr>
<th>Age at</th>
<th>Parity</th>
<th>Risk factors for endometrial cancer</th>
<th>Risk factors for infertility</th>
<th>Accompanying gynecologic disease</th>
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<th>Medical treatment</th>
<th>Pregnancy course</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>G: 2</td>
<td>Premature ovarian ageing</td>
<td>Myoma uteri</td>
<td>Yes</td>
<td>Medical, later surgical</td>
<td>160 mg/day</td>
<td>3 months</td>
<td>1A</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>36</td>
<td>G: 0</td>
<td>Male Factor</td>
<td>Ovarian cyst</td>
<td>Yes</td>
<td>Endometrioid</td>
<td>80 mg/day</td>
<td>3 months</td>
<td>Stage 2B</td>
<td>clear ovarian carcinoma</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>28</td>
<td>G: 0</td>
<td>Oligomenorrhea</td>
<td>Uterine septum + tubal factor</td>
<td>None</td>
<td>Medical</td>
<td>160 mg/day</td>
<td>-- times</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>38</td>
<td>G: 3</td>
<td>Premature ovarian ageing</td>
<td>None</td>
<td>Yes</td>
<td>Medical</td>
<td>160 mg/day</td>
<td>6 months</td>
<td>1A</td>
<td>--</td>
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<td>G: 0</td>
<td>Oligomenorrhea</td>
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<td>None</td>
<td>Medical</td>
<td>160 mg/day</td>
<td>6 months</td>
<td>1</td>
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Reevaluating the safty?

Concomitant Ovarian disease at Laparoscopy!

4 Patients with endometrium. ca persistent to progestin


CASE REPORT

Endometrial carcinoma in a young patient with polycystic ovarian syndrome: first suspected at time of embryo transfer

At the time of embryo transfer, a small but steady trickle of blood was noted as soon as the embryo transfer catheter was introduced into the uterine cavity. There had been no trauma in the insertion of the catheter which could have explained this loss. Hence this unprovoked bleeding was thought to be suspicious and merited further investigations. The embryo transfer was abandoned and all the embryos were frozen.

1. Medexprogesterone acetate 30 mg twice daily for 6 months
2. Hysteroscopy and D&C was
3. Well-differentiated adenocarcinoma with no myometrial invasion.
4. HE Cum Adenxe + LN

The patient has since requested that her sister-in-law acts as a ‘host’ to her frozen embryos from the IVF cycle.
No evidence of disease by post-partum serial endometrial samplings or hysterectomy.

Worst case scenario

- synchronous ovarian malignancy
- Persistence
- Progression
- Poor outcome
Epidemiology

Endometrial cancer is the most common gynecologic malignancy in the United States, with over 40,000 cases diagnosed each year, typically in the postmenopausal women. In 2013, the National Cancer Institute estimates 49,560 new cases in the United States and 8190 deaths.

25% of cases affect premenopausal women.

14% of endometrial cancers are diagnosed in women younger than 45 years old

5% of these tumors are diagnosed in women younger than 40 years old
Disease free window!

The available data suggest relative safety and efficacy of progestin treatment for a short window to allow the woman to achieve her reproductive goals!
Regression rate!

Metaanalysis of the 32 studies (408 women) of women with EC managed with fertility-sparing treatment found that 301 women regressed with a pooled regression rate of 76.2% (95% CI, 68–85.3)

Endometrial Cancer in Women 40 Years Old or Younger

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Received Jan 7, 2011

Majority of women had stage I and grade I disease. However, 19 of 95 patients (20%) had disease beyond the uterus, including 10 with advanced disease. Four women died as a result of their disease!
Relapse rate!

In 29 studies (267 women), women were followed up over time with the median ranging from 11 to 76.5 months. 89 women after an initial regression of the EC relapsed during follow-up, which amounts to a pooled relapse rate of 40.6% (95% CI, 33.1–49.8).

Hysteroscopy and direct resection