Impact of Ovarian Endometrioma *Per Se* and Surgery on Ovarian Reserve and Pregnancy Rate in *in Vitro* Fertilization Cycles

Jo KITAWAKI, MD, PhD
Professor and Chairman
Department of Obstetrics and Gynecology
Kyoto Prefectural University of Medicine,
Kyoto 602-8566, Japan
kitawaki@koto.kpu-m.ac.jp
Surgical Indication for Endometrioma

ESHRE Guidelines

- ≥4 cm
  - to confirm the diagnosis histologically
  - to reduce the risk of infection
  - to improve access to follicles
  - possibly to improve ovarian response

- >3 cm prior to in vitro fertilization (IVF)
  - it may interfere with follicle tracking and oocyte retrieval

Should EMoma Be Resected?

Pregnancy Rate:

- EMoma affects responsiveness to hyperstimulation, but the quality of the oocytes retrieved and the chances of pregnancy are not affected. – Still controversial
  
  (Benaglia L et al, *Fertil Steril*, 2013)

- ICSI outcomes did not differ between post-cystectomy and nonoperative groups. – RCT
  
Should EMoma Be Resected?

Recurrence:

- The reported recurrence rate of EMoma after laparoscopic cystectomy is 11.1–56%.
  
  (Busacca M et al, J Minim Invasive Gynecol, 2009)

- Cystectomy is superior to ablation – Meta-analysis: Reduced rates of recurrence, reoperation, and pain, and increased rate of spontaneous pregnancy.
  
  (Hart RJ et al, Cochrane Database Sys Rev, 2008)
Should EMoma Be Resected?

Ovarian Reserve:

- Lower ovarian reserve is associated with EMoma.  
  Shebl O et al, Gynecol Endocrinol, 2009)

- Cystectomy of EMoma reduces ovarian reserve, and repeated and bilateral cystectomy causes further reduction.  
  (Somigliana E et al, Hum Reprod, 2003; Fedele L et al, Fertil Steril, 2006;  

- Cystectomy carries a 2.4% risk of premature ovarian failure.  
Pros and Cons of Surgical Treatment of EMomas Before IVF–ICSI Cycles

Cystectomy

- Risk of pelvic abscess ruptured EMoma
- Risk of occult malignancy
- Retrieval difficulties
- Contamination of EMoma content
- Endo progression

Favors SURGERY

IVF-ET

- Surgical-related damage
- Minor and major surgical complications
- Economic costs
- Lack of evidence that surgery improves IVF pregnancy rates

Favors Expectant Management

(Adapted from Somigliana et al, Hum Reprod Update, 2006)
Questions

- Does resection of EMoma reduce ovarian reserve or affect the IVF-ET pregnancy outcome?

- Should EMoma be resected prior to IVF-ET?
Impact of EMoma per se and Surgery on Ovarian Reserve and Pregnancy Rate in IVF-ET Cycles

The Subcommittee of the Reproductive Endocrinology Committee of JSOG

A retrospective cohort study using questionnaires mailed to the all 579 ART clinics registered to the JSOG.

Enrollment

• Women who underwent IVF-ET/ICSI between Jan. and Dec. 2011
• Aged 25–40 years, with a regular menstrual cycle
• Exclusion factors: male factors and known gynecological factors other than endometriosis

Grouping

• Unexplained infertility (group UI)
• Current occurrence of EMoma, including recurrent cases (group CE)
• Past occurrence of EMoma but no current EMoma (group PE)
Impact of EMoma *per se* and Surgery on Ovarian Reserve and Pregnancy Rate in IVF-ET Cycles

Results

Enrollment: 5,124 cases from 94 (16.2%) of 579 clinics

- Group UI: 4,007 (3,279 appropriate cases)
- Group CE: 657
- Group PE: 442
# Impact of EMoma per se and Surgery on Ovarian Reserve, Number of Oocytes Retrieved, and Pregnancy Rate

<table>
<thead>
<tr>
<th>Unexplained infertility (n = 3279)</th>
<th>First and current onset of EMoma (n = 262)</th>
<th>Past occurrence of postsurgical EMoma (n = 401)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline FSH level (IU/L)</strong></td>
<td>7.9 ± 4.1</td>
<td>8.0 ± 3.9</td>
</tr>
<tr>
<td></td>
<td><strong>P &lt; 0.01</strong></td>
<td><strong>P &lt; 0.01</strong></td>
</tr>
<tr>
<td><strong>AFC (No.)</strong></td>
<td>6.2 ± 4.3</td>
<td>5.3 ± 3.8</td>
</tr>
<tr>
<td></td>
<td><strong>P &lt; 0.01</strong></td>
<td><strong>P &lt; 0.01</strong></td>
</tr>
<tr>
<td><strong>AMH (ng/mL)</strong></td>
<td>3.2 ± 2.6</td>
<td>2.8 ± 2.0</td>
</tr>
<tr>
<td></td>
<td><strong>P &lt; 0.01</strong></td>
<td><strong>P &lt; 0.01</strong></td>
</tr>
<tr>
<td><strong>FSH dose (IU)</strong></td>
<td>1514 ± 1074</td>
<td>1818 ± 825</td>
</tr>
<tr>
<td></td>
<td><strong>P &lt; 0.01</strong></td>
<td><strong>P &lt; 0.01</strong></td>
</tr>
<tr>
<td><strong>No. of oocytes retrieved</strong></td>
<td>9.4 ± 6.2</td>
<td>8.3 ± 6.5</td>
</tr>
<tr>
<td></td>
<td><strong>P &lt; 0.01</strong></td>
<td><strong>P &lt; 0.01</strong></td>
</tr>
<tr>
<td><strong>No. of embryos obtained</strong></td>
<td>5.4 ± 4.3</td>
<td>5.4 ± 4.3</td>
</tr>
<tr>
<td></td>
<td><strong>P &lt; 0.01</strong></td>
<td><strong>P &lt; 0.01</strong></td>
</tr>
<tr>
<td><strong>Rate of high-quality embryo (%)</strong></td>
<td>69.4 ± 28.3</td>
<td>71.2 ± 27.8</td>
</tr>
<tr>
<td><strong>No. of embryo transfer</strong></td>
<td>1.4 ± 0.6</td>
<td>1.3 ± 0.5</td>
</tr>
<tr>
<td><strong>Pregnancy rate (%)</strong></td>
<td>24.3</td>
<td>26.3</td>
</tr>
<tr>
<td><strong>Pregnancy rate per ET (%)</strong></td>
<td>35.8</td>
<td>36.8</td>
</tr>
<tr>
<td><strong>Miscarriage (%)</strong></td>
<td>23.3</td>
<td>30.1</td>
</tr>
</tbody>
</table>

Mean±SD

* P < 0.05, ** P < 0.01, analysis of variance (ANOVA) followed by the Scheffe F test or χ² test
**Impact of the Size and Unilateral/Bilateral Occurrence of EMomas on Ovarian Reserve and Number of Oocytes Retrieved**

<table>
<thead>
<tr>
<th></th>
<th>&lt;40 mm</th>
<th>≥40 mm</th>
<th>&lt;40 mm</th>
<th>≥40 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 165)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline FSH level (IU/L)</td>
<td>7.7 ± 3.0</td>
<td>7.4 ± 2.3</td>
<td>7.3 ± 2.9 **</td>
<td>11.1 ± 9.7</td>
</tr>
<tr>
<td>AFC (No.)</td>
<td>5.4 ± 4.0</td>
<td>4.6 ± 1.9</td>
<td>5.4 ± 4.2</td>
<td>4.4 ± 2.7</td>
</tr>
<tr>
<td>AMH (ng/mL)</td>
<td>3.2 ± 2.2 **</td>
<td>1.6 ± 1.1 *</td>
<td>2.0 ± 1.8</td>
<td>1.5 ± 1.4</td>
</tr>
<tr>
<td>Dose of FSH (mIU)</td>
<td>1781 ± 942</td>
<td>1602 ± 836</td>
<td>1601 ± 601</td>
<td>1761 ± 924</td>
</tr>
<tr>
<td>No. of oocytes retrieved</td>
<td>8.1 ± 6.7</td>
<td>7.1 ± 5.2 *</td>
<td>7.3 ± 4.8</td>
<td>5.2 ± 2.6</td>
</tr>
</tbody>
</table>

Mean ± SD
* P < 0.05, ** P < 0.01, ANOVA with the Dennett test
a P < 0.05, interaction was recognized with two-way ANOVA
b P < 0.05, significant difference with one factor, the size or laterality of ovarian endometrioma

The reduction of ovarian reserve was more evident in the cases with ≥40 mm and bilateral EMomas.
## Difference in the Number of Oocytes Retrieved between the Normal and Affected Ovaries According to the Size of Unilateral EMoma

<table>
<thead>
<tr>
<th>Size of EMoma</th>
<th>Contra lateral normal ovary</th>
<th>Affected ovary</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq 40 \text{ mm} (n = 36)$</td>
<td>$5.0 \pm 4.0$</td>
<td>$2.7 \pm 2.6$</td>
</tr>
<tr>
<td>$&lt; 40 \text{ mm} (n = 130)$</td>
<td>$4.0 \pm 3.9$</td>
<td>$3.6 \pm 3.3$</td>
</tr>
</tbody>
</table>

Mean±SD

* $P < 0.05$, paired $t$ test
### Factors that Affect No. of Oocytes Retrieved

<table>
<thead>
<tr>
<th></th>
<th>Unexplained infertility (n=661)</th>
<th>Current Occurrence of EMoma (n=82)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>γ</td>
<td>β</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>−0.221**</td>
<td>−0.207</td>
</tr>
<tr>
<td>Baseline FSH (IU/L)</td>
<td>−0.007</td>
<td></td>
</tr>
<tr>
<td>AMH (ng/mL)</td>
<td>0.285**</td>
<td>0.278</td>
</tr>
<tr>
<td>AFC (No.)</td>
<td>0.169**</td>
<td>0.160</td>
</tr>
<tr>
<td>FSH dose (mIU)</td>
<td>0.112**</td>
<td>0.102</td>
</tr>
<tr>
<td>Size of EMoma (mm)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

stepwise regression analysis

\[ F \geq 4 \quad * \ P < 0.05 \quad ** \ P < 0.01 \]
In the patients undergoing IVF-ET:

- the presence of untreated EMoma per se was associated with a reduced ovarian reserve.
- the reduction of ovarian reserve was more evident in the cases with EMomas ≥40 mm and bilateral EMomas.
- resection of EMoma caused further reduction of the reserve.
- the reduced ovarian reserve, as a result of the presence of EMoma or its resection, did not affect the IVF-ET pregnancy outcome.
- the presence of EMoma did not reduce the quality of oocyte or the rate of implantation, and its resection did not improve these parameters.
Limitation and Problems

- This study included the cases undergoing IVF-ET only, but not the cases of spontaneous pregnancy.
- This study did not compare the ovarian reserve of the cases undergoing cystectomy with those undergoing aspiration.
- This study was not a randomized study: Large EMomas might have been resected.
- This study did not investigate unfavorable complications of the cases with expectant management.

Further studies are needed to confirm the indications for the resection of EMoma.
Acknowledgements

Collaborators
Subcommittee of the Reproductive Endocrinology Committee of JSOG
Toshiro Kubota Tokyo Medical and Dental University
Tasuku Harada Tottori University
Mikio Momoeda St. Luke’s International Hospital
Yoshiharu Morimoto IVF Namba Clinic
Takashi Minegishi Gunma University
Koichi Iwasa Kyoto Prefectural University of Medicine
Kunihiro Hayashi Gunma University