Treatment of endometrioma
Conflicts of interest

- Head of the Obstetrics and Gynecology department
  Päijät-Häme Central Hospital

- Laparoscopic surgery training collaboration with Olympus
Endometriosis and endometrioma

- Endometriosis is seldom a one nodule or lesion disease

- 1% of patients have only ovarian disease
  
  Redwine 1999

- Ovarian endometriosis is often a marker for more extensive pelvic and intestinal disease
  

- Endometrioma is important as an individual endometriotic lesion as it is located inside the ovary
Endometrioma

- Is a common finding
  17 - 44% of patients with endometriosis have endometriomas
  Jenkins et al. 1986, Redwine 1999, Busacca and Vignali 2003

- More frequently located on the left ovary
  Vercellini et al. 2002, Ferrero et al. 2005

- Does nor disappear by itself

- Medical treatment leads only to a temporary reduction in volume
  Donnez et al. 1989, Ferrero et al. 2013

- Drainage leads to a quick recurrence
  Donnez et al. 2004

- Surgery is the only way to remove endometrioma
• When deep endometriosis is detected in the appendix, appendix can be removed but when endometrioma is detected in the ovary, in most of the cases, ovary can not be removed

• Surgical excision of endometrioma from the ovary would provide immediate removal of the disease but the safety of endometrioma excision in terms of damage to ovarian reserve has been questioned
Endometrioma and ovarian physiology

• Findings are controversial:

The presence of endometrioma is associated with decreased antral follicle count and with a reduction in the number of oocytes retrieved for IVF

More recent findings: the number of antral follicles and oocytes retrieved is not affected by the presence of endometriomas

The presence of endometrioma may negatively influence embryo quality
Yanushpolsky et al. 1998, Kumbak et al. 2008

Endometriotic ovarian cysts does not negatively influence embryo quality
Endometrioma and ovarian physiology

• Maggiore et al.  
  *Endometriotic ovarian cysts do not negatively affect the rate of spontaneous ovulation.*  

• women desiring to conceive but not infertility patients  
  ultrasonographic diagnosis of unilateral ovarian endometriotic cysts  
  largest diameter of endometrioma 5.3+1.7 cm (mean+SD)  
  no previous surgery  
  regular menstrual cycle (24–35 days)  
  male partners with normal semen analysis

• The rate of ultrasonographically documented ovulation was similar between the healthy and the affected ovary during 6 cycles

• The rate of ovulation between the two ovaries was not affected by laterality of endometriomas  
  number and size of endometriomas  
  ultrasonographic diagnosis of deep endometriosis

• 43.0% of the patients conceived spontaneously during the 6-month study period
Ovarian reserve and endometrioma

- Serum AMH= anti-Mullerian hormone levels and AFC = antral follicle count by ultrasound

  AMH 2 ng/ml is considered as abnormal in women aged < 30 years old
  Bologna criteria "poor responders": AMH levels 0.5–1.1 ng/ml, AFC 5–7 follicles

- The presence of endometrioma seems to be associated with a decrease in ovarian reserve

<table>
<thead>
<tr>
<th>Age</th>
<th>Patients with endometrioma (n=30)</th>
<th>Patients without endometrioma (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>29.0 (5.4)</td>
<td>30.1 (4.4)</td>
<td>0.39</td>
</tr>
<tr>
<td>AMH (ng/ml)</td>
<td>2.81 (2.15)</td>
<td>4.20 (2.26)</td>
<td>0.02</td>
</tr>
<tr>
<td>Total AFC</td>
<td>9.73 (4.77)</td>
<td>14.7 (4.11)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Uncu et al. Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve. Human Reproduction 2013

<table>
<thead>
<tr>
<th>Endometrioma (n=40)</th>
<th>Other benign cyst (n=22)</th>
<th>Tubal factor infertility (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH (ng/ml)</td>
<td>1.53 ± 1.37</td>
<td>2.20 ± 1.23</td>
</tr>
</tbody>
</table>

The impact of surgery on ovarian reserve

- Significant decline in serum AMH levels 1 – 3 months after endometrioma excision
  Raffi et al. 2012

Weighted mean difference in serum AMH after surgery for endometrioma: pooled results for all studies.
The impact of surgery on ovarian reserve

- Persistent decline in AMH levels ≥ 6 months after endometrioma excision
  Tsolakidis et al. 2010, Biacchiardi et al. 2011

- Progressive decline in AMH levels in two studies during 6 months after excision
  Celik et al 2012, Uncu et al. 2013

- Bilateral excision causes a greater decline in serum AMH levels than unilateral
  Hirokawa et al. 2011, Uncu et al. 2013

- Second surgery for recurrent unilateral endometrioma causes even lower AMH levels and AFC of the affected ovary than before surgery
  Ferrero et al 2015
Infertility patient and endometrioma

- The presence of endometrioma seems to be associated with a decrease in ovarian reserve in patients with infertility

- Further decline in ovarian reserve if endometrioma is surgically removed

- Recurrence rate of endometrioma after surgery is between 11.7 and 30.4% at 2 –5 years follow-up (Busacca et al. 1999, Ghezzi et al. 2001, Jones and Sutton 2002, Koga et al. 2006)

- Detrimental effect of repeated surgeries on ovarian reserve

- In Finland, infertility treatment is available in all women < 40 years and who have tried to conceive one year without pregnancy

- IVF offers the highest pregnancy rates for endometriosis patients (Vercellini et al. 2009)

- No data supporting endometrioma surgery before ART in terms of improved pregnancy rates

- ESHRE guideline 2013:
  In case of single ovarian endometriotic cysts with diameter between 3 and 6 cm, surgery may not be useful before ART

- Patients should primarily be referred to infertility treatment and surgical excision of endometrioma should preferably be delayed, until women have completed their families.
Is surgery always bad for infertility patient?

- Infertility patients are sometimes operated before infertility treatment because of severe pain caused by endometriosis
  very large endometrioma
- Patient may not want to undergo infertility treatments
- ESHRE guideline:
  In infertile women with ovarian endometrioma undergoing surgery, clinicians should perform excision of the endometrioma capsule, instead of drainage and electrocoagulation of the endometrioma wall, to increase spontaneous pregnancy rates

  Hart et al. 2008, based on two RCT studies Beretta et al. 1998, Alborzi et al. 2004

  In infertile women with AFS/ASRM Stage III/IV endometriosis, clinicians can consider operative laparoscopy, instead of expectant management, to increase spontaneous pregnancy rates

  Nezhat et al. 1989, Vercellini et al. 2006
- Prospective cohort study by Bianchi et al 2009 of patients with DIE:

  Extensive laparoscopic excision of DIE before IVF significantly improved IVF pregnancy rates
  41% vs 24%, p = 0.004

  IVF without undergoing laparoscopic surgery n=105 or extensive laparoscopic excision of DIE before IVF n = 64, (endometrioma excision 29 patients (45%)
Endometrioma in patients with severe pain

- Endometrioma does not cause pain Chopin et al. 2006, Vercellini et al. 2006

- Pain in women with endometrioma is associated with coexisting deeply infiltrating and/or peritoneal endometriosis Chapron et al. 2012, Khan et al. 2013 or adenomyosis

- Appropriate evaluation of the extent of the disease

- Laparoscopic excision of all endometriosis has been shown to result a significant reduction of pain and improvement of quality of life Sutton et al. 1994, Garry et al. 2000, Redwine & Wright 2001, Abbott et al. 2003, Dubernard et al. 2006, Darai et al. 2010, Ribeiro et al 2014, Taboul et al. 2015

- Surgery should always be considered as a treatment of severe pain

- If patient with severe pain is to be operated, all endometriotic lesions including endometrioma, should be removed

- Appropriate preoperative work-up in order to plan the surgical interventions
Endometrioma in asymptomatic young patients

• Endometrioma is one of the few endometriotic lesions that can be diagnosed without the operation

• Endometrioma is accurately diagnosed with transvaginal ultrasound


• Endometrioma may be accidentally found in asymptomatic patients as ultrasound examination is performed in almost all patients referred to gynecological unit in Finland

• CA-125 levels are often increased in women with endometrioma (60.8 ± 63.5 U/mL) and DIE (55.2 ± 68.7 U/mL) Santulli et al. 2015

but the probability of cancer is low in young patients
Endometrioma in asymptomatic young patients

- Small endometriomas with low CA 125 levels does not have to be operated immediately but patient has to be followed-up. Eventually endometrioma has to be surgically removed.

- Mean increase of 3.9% (3.1 –4.7% 95% CI) in the largest diameter of the ovarian endometriotic cysts between baseline (5.3+1.7 cm mean+SD) and sixth ovarian cycle (5.6+1.8 cm; P < 0.001)

  Maggiore et al. 2015

- Larger endometrioma and higher CA 125 levels surgical treatment
Endometrioma in patients ≥ 40 – 45 years

• The need to confirm the diagnosis and histological examination to rule out early ovarian cancer?

• Endometrioma is accurately diagnosed with transvaginal ultrasound also in these patients.\(^1\) Maisnet al. 1993, Patel et al. 1999, Ash & Levine 2007

• The risk of ovarian cancer seems to be elevated among patients with long standing history (< 10 years) of ovarian endometriosis.\(^2\) Brinton et al. 1999

• Surgery is the treatment of choice in most of the cases

• Removal of endometrioma or oophorectomy
  - age of the patient
  - previous ovarian surgery
  - US findings typical/atypical
  - Ca 125 level

---


Surgical treatment

- Laparoscopic cyst excision with striping technique is considered the best treatment


  Pregnancy rates are better and recurrence rates lower than after ablation with electrocoagulation

  Two RCT studies Beretta et al. 1998, Alborzi et al. 2004

- Stripping technique leads to a decline in ovarian reserve

- Proposed mechanisms:

  Inadvertent removal of follicles adjacent to the endometriotic cyst wall

  Electrocoagulation of the cyst bed, may disrupt ovarian circulation
Surgical treatment

- The number of ovarian follicles on surgical specimens did not correlate with the decline in serum AMH levels Hirokawa et al. 2011, Celik et al. 2012, Uncu et al. 2013

- Damage to the ovarian circulation could be the most important determinant of the loss of ovarian reserve? Especially bipolar dissection near the ovarian hilus. Ata et al. 2015


  - Suturing of the cyst bed unclear whether suturing is better than BD (bipolar dissecation)
  - Application of a hemostatic sealant hemostatic sealant could be better than BD (human or bovine plasma-derived product, risk of viral transmission)

Surgical treatment

• Proper surgical technique is the most important factor affecting ovarian outcome

• Hemostasis should be selective and very careful. Coagulation of entire ovarian stroma should never be performed.

• The first operation is probably crucial for the prognosis.

Incomplete and/or unduly traumatic procedures probably greatly reduce the ovarian reserve and change of spontaneous pregnancy and increase the risk of endometrioma recurrence = persistence.

Vercellini et al. 2004