Surgical Removal of Endometrioma: When Is It Worth the Risk?

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Learning objectives

At the conclusion of this presentation, participants should be able to:

• Discuss the impact of endometrioma surgery on fertility outcome
• Discuss the impact of endometrioma surgery on ovarian reserve
Management of Endometriomas
Why remove endometriomas?
Relief of pain

• Clinical presentation: Porpora et al. 2010
  • Dysmenorrhea: 76 %
  • Chronic pelvic pain: 53 %
  • Dyspareunia: 43 %

• Objective endometrioma surgery
  • Histologic confirmation
  • Eliminate all endometriotic tissue but preserve normal tissue
Why remove endometriomas? Possible Malignancy

- Pearce et al. Lancet Oncol 2012
  - Association with ovarian cancer
  - Clear-cell (odds ratio 3·05, 95% CI 2·43–3·84, \( p<0·0001 \)), low-grade serous and endometrioid invasive ovarian cancers

- Buis et al. Human Reproduction 2013
  - Dutch nationwide database- subfertile women with endometriosis
  - HR 12.4 (95% CI 2.8-54.2) ovarian cancer
  - HR 5.5 (95% CI 1.6-11.2) Borderline ovarian tumors

- Exclusion of malignancy
  - Risk is small
  - Ultrasound may be confusing
Why remove endometriomas?
Exclude malignancy

Recurrent endometrioma - significantly higher rate of unexpected ovarian cancer in patients older than 40 years

Why remove endometriomas prior to IVF?

• Increases the risk of infection after oocyte retrieval
  • Puncture of endometrioma
  • Ovarian abscess
• Contamination of oocyte obtained with endometriosis cyst contents
• Difficulties in the retrieval
Endometrioma and Fertility

• Does the intrinsic presence of an endometrioma decrease ovarian reserve?

• **Endometrioma removal**: Is there a decrease in ovarian reserve after surgery?

• How does the endometrioma removal affect pregnancy rates
  • Spontaneous & ART
Untreated Endometrioma and Ovarian Reserve

• **Unilateral endometriomas**-
  • Benaglia et al Human Reproduction 2011
    - Only the first cycle of IVF per patient (N=84)
    - Mean size 21 mm (all less than 4 cm)
    - No difference in ovarian responsiveness

• **Almong et al F&S 2011**
  - Only first IVF cycle (N=81)
  - No difference in the number of oocytes retrieved
    • Compared with the contralateral ovary
    • Control group without endometriosis
  - Mean diameter of the endometrioma was 2.8 cm
Untreated Endometrioma and Ovarian Reserve

• Bilateral endometriomas

• Benaglia et al F&S 2013
  - Case (un-operated bilateral endometrioma N=39) vs. Control (no cysts-N=78)
  - Serum AMH pre-IVF was 2.8 vs. 3.0 (NS)
  - Mean Diameter 22-23 MM
  - Total # of oocytes retrieved 7.1 vs. 9.8
  - Implantation & PR similar
Un-operated Ovarian endometrioma: Oocyte quality

- Filippi et al 2014
- The fertilization rate in the affected and intact gonads was 64% and 64%, respectively.
- The cleavage rate was 58% and 51%, respectively.
- The rate of high-quality embryos was 31% and 21%, respectively.
Follicular density

- Kitajima et al 2011
- Cortical biopsy specimens
- Follicle density lower in the cortex from ovaries with endometriomas than **unaffected contralateral ovary**
- Maneschi et al 1993 & Schubert et al 2005
  - Lower follicular density in endometrioma than other benign cysts
Ovarian Reserve & Endometriomas:
Cleveland Clinic data- Am J Obstet Gynecol May 2016

<table>
<thead>
<tr>
<th></th>
<th>Endometrioma (n = 58)</th>
<th>Control (n = 58)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline AMH ng/ml</td>
<td>1.8 (1.2 – 2.4)</td>
<td>2.8 (2.0 – 3.5)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Table 3: All values are means (95% Confidence intervals), superscripts are p-values compared with pre-operative values

Mean size 5 cm
Is stripping technique the Gold standard?

• Cochrane database 2008 Hart R et al.
  - Excision of cyst associated with a reduced rate of recurrence; reduced symptom recurrence and increased spontaneous pregnancy rates (OR 5.1) compared with ablative surgery.

• Clinicians can consider performing cystectomy rather than CO2 laser vaporization in women with ovarian endometrioma, because of a lower recurrence rate of the endometrioma (ESHRE Endometriosis Guideline Development Group September 2013).

RCT = randomized controlled trial
TABLE
Anti-Müllerian hormone, endometrioma, pelvic peritoneal endometriosis, and no endometriosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Endometrioma (n = 58), mg/mL&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Pelvic peritoneal endometriosis (n = 29), mg/mL&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No endometriosis (n = 29), mg/mL&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.77 (1.18–2.37)</td>
<td>2.29 (1.34–3.25)</td>
<td>3.20 (1.96–4.43)</td>
<td>.06</td>
</tr>
<tr>
<td>1 Month</td>
<td>1.12 (0.81–1.45)&lt;sup&gt;.01&lt;/sup&gt;</td>
<td>2.38 (1.26–3.50)&lt;sup&gt;.41&lt;/sup&gt;</td>
<td>3.22 (2.04–4.49)&lt;sup&gt;.78&lt;/sup&gt;</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>6 Months</td>
<td>1.41 (0.97–1.85)&lt;sup&gt;.22&lt;/sup&gt;</td>
<td>2.76 (1.58–3.95)&lt;sup&gt;.12&lt;/sup&gt;</td>
<td>3.14 (1.83–4.43)&lt;sup&gt;.67&lt;/sup&gt;</td>
<td>.01</td>
</tr>
</tbody>
</table>

Superscripts indicate probability values compared with baseline preoperative values.

<sup>a</sup> Data are given as mean (95% confidence interval).

Other markers of decreased ovarian reserve

- Exacoutos et al; 2004
  - Reduction in ovarian volume
- Biacchiardi et al 2011 – Laparoscopic stripping
  - Decreased ovarian volumes & AMH at 9 months
  - Does experience matter?

Operated-Bilateral Endometriomas

- Somigliana et al. HR 2008
- Endometrioma group = 68 patients
- Control group (no ovarian surgery) = 136 patients
- Day-3 FSH of cases > controls
- Number follicles/oocytes/embryos decreased/implantation rate lower
- PR/DR cases per transfer (14%/8%) vs. controls (28%/25%)
- POF 2.4% risk

FSH = follicle-stimulating hormone; DR = delivery rate
Impact of Excision on Ovarian Reserve

• Raffi et al JCEM 2012
  • Meta-analysis using AMH & AFC
  • 8 studies- excisional surgery
  • Cysts were more than 3-4 cm; mean 4-6 cm
  • Up to a 30 % fall in AMH in unilateral cystectomy & 44% fall in bilateral cystectomy
  • Gradient effect of increasing size of the endometrioma on the magnitude of the fall in AMH
• Muzii L et al HR 2014: meta-analysis= no change in AFC after non-excisional surgery
Second Surgery for recurrent Endometrioma

• Muzii et al F&S 2015

• Prospective- trial-primary vs. secondary surgery
  • Control was the unoperated side
  • Lower AFC & volume vs. unoperated side in the repeat surgery group
  • Histology- more ovarian tissue removed with secondary surgery
Adherent to pelvic side wall - Lysis of adhesions
What about the other ovary?
Where is the blood supply in relation to the cyst
Technical Consideration—cleavage plane

• Muzii et al. 2007 histological analysis
  • **Ovarian tissue removed with the cyst.**
  • Endometriosis of the inner cyst rarely penetrates more than 1.5 mm into the cyst capsule.

• Muzii et al. 2005
  • Circular incision and then stripping vs. simply stripping
    • Circular incision removes more follicles.
Fibrosis
Risk for ovarian reserve: Technical considerations
Risk for ovarian reserve: Technical considerations-vasopressin

• RCT – control, saline or vasopressin injection
  Vasopressin reduced use of
  electrosurgery
  Saeki A et al  J Reprod Infertil
  2010;17:176-9

• RCT – control, saline or vasopressin injection-
  Vasopressin limited tissue damage and
  prevented postop increase in FSH
  Qiong-Zhen R et al  J Min Invas
  Gynecol  2014;21:266-71

• RCT –saline or vasopressin injection
  NSD - OR time, electrosurgery use,
  change in FSH or AFC
  Ghafarnejad M et al  J Reprod Infertil
  2014;15:199-204
Alternative Techniques to Minimize Damage

- Angioli R et al. JMIG 2009
  - Use of hemostatic agent
- Tsolakidis et al 2010-3 stage procedure
  - surgery 1-drained/GnRHa=3 months/surgery 2-laser vaporization
  - 20% recurrence rate
Ablative Therapy- alternative energy forms

- Partial cystectomy & ablation of the hilum
  Muzii L & Panici PB. Reprod Biomed Online 2010;20:300–2

- Roman et al. Fert Steril 2011-Plasma energy-coagulation mode-10-40W
  • recurrence 5-9 %
Endometrioma removal: alternative technique

Recurrence rate at 6 months 5.9% vs. 2% (P = 0.62)
- AFC same- AMH not measured
- Postop pain recurrence 17%
- No postop suppression
Electrosurgical approach

• Capsule may be up the 3 mm
• Bipolar can penetrate 10-12 mm
• Deep coagulation may destroy follicles
Technique to Minimize Damage

- Ding W et al RBO 2015: Impact on ovarian reserve of hemostasis by bipolar coagulation vs. suture following surgical stripping of ovarian endometrioma: 21 studies - 312 patients
  - Bipolar coagulation did more harm to ovarian reserve than suture hemostasis
- Ata et al JMIC 2015 - Systematic reviews -
  - 5/6 studies decrease in ovarian reserve after bipolar electrosurgery
  - In all 3RCT- desiccation groups had greater loss in AMH than hemostatic sealant; in 2 RCT bipolar had a greater loss than suturing groups.
Treatment of endometriomas: uncontrolled studies

- Vercellini et al. 2009
  - 14 studies; approximately 1500 patients; overall weighted mean was 50%
  - Assume ½ of this observation: NNT = 4

NNT = number needed to treat
Systematic Reviews, Meta-analysis & Cochrane review: Intervention for Women with endometrioma prior to ART

• Meta-analysis: Tsoumpou et al. Fertil Steril 2009
  - 5 studies: No treatment versus surgery before IVF
    • No difference in clinical pregnancy rate
    • No significant difference in outcome (PR/oocytes retrieved/ embryos/gonadotropins/estradiol)

• Cochrane database Syst Rev 2010: Benschop et al
  - 4 trials-
    - Ovarian cystectomy or aspiration does not yield improved clinical PR
ESHRE consensus

• In infertile women with endometrioma less than 3 cm there is no evidence that cystectomy prior to treatment with assisted reproductive technologies improves pregnancy rates. (Benschop, et al., 2010, Donnez, et al., 2001, Hart, et al., 2008).
ESHRE consensus

- In women with endometrioma larger than 3 cm, the GDG recommends clinicians only to consider cystectomy prior to assisted reproductive technologies to improve endometriosis-associated pain or the accessibility of follicles.
ESHRE consensus

• The GDG recommends that clinicians counsel women with endometrioma regarding the risks of reduced ovarian function after surgery and the possible loss of the ovary. The decision to proceed with surgery should be considered carefully if the woman has had previous ovarian surgery.
How do you decide: Chance of spontaneous pregnancy vs. need for IVF
Long Term suppression: 18-24 months

- Recurrence
  - 2-year follow-up (Seracchioli R et al. Fertil Steril 2010)
    - No suppressive therapy: 29 %
    - Cyclic oral contraceptives (OCs): 15 %
    - Continuous: 8 %
  - Porpora MG et al F&S 2010
    - 9.6 % after 3 years with suppressive therapy
  - Vercellini et al meta analysis 2012
    - Endometrioma recurrence
    - 8 % with OC and 34 % control group
  - Chen et al AJOG June 2017-RCT post cystectomy- Mirena vs. control- recurrence at 30 months –pain much better with Mirena but recurrent cyst same (25%vs.37%)