Optimal Approaches of Laparoscopic Endometriosis Surgery to Protect Ovarian Reserve

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Factors favoring surgery

- Relieve the pain and return of normal sexual life
- Increase the fertility after surgery and offers couples the possibility for a spontaneous conception with reported PR between 40-60% most of them occurring in a mean delay of 10 months.
- To avoid risk of infection and abscess at the time of oocyte pick-up during IVF.
Why we do the surgery?

Arguments in favor of the surgery
1. Create spontaneous pregnancy (40-60%)
2. Relieve pain, return of normal daily and sexual life
3. Possible association between endometriosis and increase risk of ovarian carcinoma (clear cell ca., endometrioid ca.)

Arguments in against of the surgery
1. Decreased ovarian reserve, especially in repeated surgery
2. Recurrence
3. Complexity of the surgery in DIE
Surgical Indication of Ovarian Endometriomas:

1. Severe Symptoms (pelvic pain, pelvic mass)
2. Symptoms persistace under medical treatment
3. Presence of advanced disease (anatomic distortion of pelvic organs, obstruction of bowel or urether)
4. Exclusion of malignancy (suspected adnexal mass, rapid growth)
5. Contraindication of hormonal treatment
6. Infertility
Surgical Indication of Ovarian Endometriomas depend on:

1. Uni or bilateral
2. If association with dens adhesion (obliterated douglas)
3. If associated with adenomyosis
4. If associated with DIE
5. If association with infertility
6. If pre-IVF
Surgical Indication of Ovarian Endometriomas:

*If infertility related:*

- AFC, D3 hormones, AMH, İnhibin
- Age of patient
- Other infertility factors
- Uni/Bilaterale endometrioma
- Re-surgery of endometrioma
Treatment Objectives

- Restore normal anatomy
- Remove or ablate all endometriotic tissues
- Prevent or delay recurrence rate
- With better protection of ovarian reserve
Ovarian Endometriomas

- Are present in 17-44% of patients with endometriosis (Chapron et al 2002)

- In 1/3 of the cases, endometriomas are bilateral (Guo et al 2008)
But before surgery

- AMH, AFC, inhibin, D3 hormones
- Previous endometriomas surgery
- Bilateral endometriomas
- DIE association and pain
- Medical treatment failure
- Cyste diameter, quick growing
- Quality of life
Association of Ovarian Endometriomas and DIE

- Somigliana 2004: 50%
- Chapron 2009: 23%

Associated ovarian endometrioma is a marker for greater severity of DIE
The surgical approach has to be chosen:

**ABLATION** or **EXCISION**

- Coagulation of the site of eversion
  
  *(Brosens et al.)*

- Endometrioma fenestration and vaporization
  
  *(Donnez et al.; Hemmings et al.; Saleh and Tulandi)*

- Ovarian Cystectomy
  
  *(Canis et al.)*
Endometrioma Surgery

- Ablation
- Excision
- Combined Technique
- 3 Steps Therapy
- US Guided ponction and ethanol injection
OPTIMAL APPROACHES of the ENDOMETRIOMA SURGERY
3 Steps Therapy

- First Laparoscopy with fenestration and drainage
- GnRH Agonist treatment for 2-3 months
- Second-Look Laparoscopy and cystectomy or ablation
US Guided Punction

• Is not recommended because of high recurrence rate
• Infection risk
• With ethanol injection in endometriomas or in recurrent endometriomas cases (not too much data)
Ovarian Endometriosis

**Ablation**: Destruction of the cyst wall

- Plasmajet
- CO$_2$ Laser
- KTP Laser
- Bipolar coag.
<table>
<thead>
<tr>
<th>Study</th>
<th>Excision</th>
<th>Ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemmings et al (Retro; 1998)</td>
<td>8%</td>
<td>12%</td>
</tr>
<tr>
<td>Beretta et al (RCT; 1998)</td>
<td>6%</td>
<td>18%</td>
</tr>
<tr>
<td>Salehand Tulandi (Retro; 1999)</td>
<td>6.1%</td>
<td>21.9%</td>
</tr>
<tr>
<td>Alborzi et al (RCT; 2004)</td>
<td>5.8%</td>
<td>22.9%</td>
</tr>
</tbody>
</table>
Excisional surgery versus Ablative surgery for ovarian endometriomas: a Cochrane Review

There is some evidence that **excisional surgery for endometriomata** provides a **more favourable** outcome than drainage and ablation with regard to the

- recurrence of the endometrioma
- recurrence of symptoms
- subsequent spontaneous pregnancy

*(Hart et al. Hum Reprod 2005)*
Ablation Techniques

- Electrocoagulation by uni or bipolar energy
- Plasma-jet
- KTP laser
- CO\(_2\) Laser
Ovarian Endometriomas

**Excision**: Dissection of the cyst wall from the ovarian cortex
Surgery of Large Endometrioma

1/Adhesiolysis, reconstruction of anatomy and incision on the posterior wall of the ovary
2/Aspiration of chocolat
3/Vaporization of peritoneal lesions
4/Cystectomy or,
5/Partial cystectomy + vaporization of the cyst wall on the ovarian hilus
Big Bilateral Endometriomas
The impact of excision of ovarian endometrioma on ovarian reserve: a systematic review and meta-analysis

• 38% reduction in AMH after stripping technique

Raffi et al. J Clin Endocrinol Metab. 2012
Surgical Indication of Ovarian Endometriomas pre-IVF

1. Loss of small follicles adjacent to cyst wall, leading reduced oocyte pool.

2. However, a meta-analysis of 5 studies comparing surgery to no surgery before IVF found no significant difference in clinical PR (Tsoumpou. Fert Ster 2009)

3. No consensus between ESHRE, ASRM, RCOG
COLLATERAL DAMAGE

- By heat transmission and thermal damage during uni-bipolar coagulation,
- By hypoxia-anoxia during hemostatic suturing
- By removing healthy ovarian tissue (false cleavage plane)
- By increased ovarian tissue destruction during the excision if the endometrioma wall is severely fibrotic and densely attached to ovarian stroma.
Heat Conduction

• Two ways heat can occur

1. Absorption
   - Energy used instantly heats tissue to absorption depth
   - PRECISE, UNMATCHED, DEPTH CONTROL!!!
Heat Conduction

- Two ways heat can occur

2. Conduction
   - Heat flows from region heated by energy into adjacent tissue
• Conduction of heat takes time

Heat Conduction (2)

Hot object

Time

Thermal damage
Thermal damage

**Electrosurgery**
Considerable coagulation and inflammatory infiltrate

**CO₂ Laser**
Superficial vacuolar degeneration, minor coagulation, less inflammatory infiltrate.
“Crater” of ablation

1. Vaporization zone
2. Carbonization
3. Coagulation due to light
4. Coagulation due to diffusion of heat

P. Total area of involved tissue

The depth of zone 1 is related to the energy density, the depth of zone 3 is constant, and depth of zone 4 is related to the time of exposition.
Ablation by CO$_2$ laser vs bipolar coagulation

- CO$_2$ laser allows an adequate dept of vaporisation with limited surrounding thermal damage (just 0.1 mm in dept) than uncontrolled destruction by bipolar electrocoagulation.
Tissue penetration

- Erbium
- CO
- KTP
- Pulse Dye
- Alexandrite
- Diode

Depth of Penetration
Combined Technique (Excision + Hilus Vaporisation)
• By heat transmission and thermal damage during uni-bipolar coagulation,
• By hypoxia-anoxia during hemostatic suturing
• By removing healthy ovarian tissue (false cleavage plane)
• By increased ovarian tissue destruction during the excision if the endometrioma wall is severely fibrotic and densely attached to ovarian stroma.
Risk of Endometrioma Surgery

Cystectomy:
Risk of removal normal ovarian tissue and ovocytes
Easy Stripping
Difficult Stripping + Clivage Plane
Residual ovarian volume after surgery

**Table IV**
Residual ovarian tissue before surgery and after surgery

<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endometriomas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian tissue volume</td>
<td>67</td>
<td>19.9 ± 17.8</td>
</tr>
<tr>
<td><strong>BEFORE to surgery (cm³)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian tissue volume</td>
<td>67</td>
<td>5.1 ± 3.2*</td>
</tr>
<tr>
<td><strong>AFTER surgery (cm³)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dermoids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian tissue volume</td>
<td>62</td>
<td>10.1 ± 11.4*</td>
</tr>
<tr>
<td><strong>BEFORE to surgery (cm³)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian tissue volume</td>
<td>62</td>
<td>6.7 ± 3.3*</td>
</tr>
<tr>
<td><strong>AFTER surgery (cm³)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* P < .001 ovarian volume before vs after surgical removal of endometriomas.
\[ P < .05 \text{ ovarian volume after surgical removal of endometriomas vs ovarian volume after surgical removal of dermoid cysts.} \]

**Table V**
Residual ovarian volume after surgery vs contralateral untreated ovaries

<table>
<thead>
<tr>
<th>Ovaries after laparoscopic cystectomy</th>
<th>N</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endometriomas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal treated ovary</td>
<td>40</td>
<td>4.3 ± 2.3*</td>
</tr>
<tr>
<td>Ovarian tissue volume (cm³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contralateral untreated normal ovary</td>
<td>40</td>
<td>9.7 ± 3.9</td>
</tr>
<tr>
<td>Ovarian tissue volume (cm³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dermoids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal treated ovary</td>
<td>46</td>
<td>7.1 ± 3.5*</td>
</tr>
<tr>
<td>Ovarian tissue volume (cm³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contralateral untreated normal ovary</td>
<td>46</td>
<td>8.3 ± 3.1</td>
</tr>
<tr>
<td>Ovarian tissue volume (cm³)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* P < .001 volume treated vs contralateral untreated ovaries with endometriomas.
\[ P < .001 \text{ volume of treated ovaries with endometriomas vs treated with dermoids.} \]

\[ NS \text{ volume treated vs contralateral untreated ovaries with dermoids.} \]
AMH trend evaluation after laparoscopic surgery of monolateral endometrioma using a new Dual Wavelenghts Laser System (DWLS) for hemostasis.

- Monolateral endometrioma cyst by stripping without using a BP coagulation and hemostasis with DWLS (45 patientes)
- AMH before surgery, 1-1,5-6-9 months after surgery
- With this technique, no significant reduction of ovarian reserve

Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery

Jacques Donnez, M.D., Ph.D., Jean-Christophe Lousse, M.D., Pascale Jadoul, M.D., Olivier Donnez, M.D., and Jean Squifflet, M.D.

Department of Gynecology, Université Catholique de Louvain, Brussels, Belgium

**TABLE 1**

Ovarian volume and AFC 6 months after surgery in women treated for endometriomas by the combined technique and in women of similar age with normal ovaries and regular ovulatory cycles presenting for IVF because of male factor infertility.

<table>
<thead>
<tr>
<th></th>
<th>Ovarian volume (cm³)</th>
<th>AFC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined technique (n = 31)</td>
<td>7.64 ± 2.95</td>
<td>6.1 ± 3.2</td>
</tr>
<tr>
<td>Women without endometriosis (n = 20)</td>
<td>7.99 ± 5.33</td>
<td>6.2 ± 4.8</td>
</tr>
</tbody>
</table>

Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery

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### TABLE 2

<table>
<thead>
<tr>
<th>Ovarian volume and AFC 6 months after surgery in women with unilateral endometriomas and contralateral normal ovaries serving as controls.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ovarian volume (cm³)</strong></td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>Combined technique (n = 20)</td>
</tr>
<tr>
<td>Contralateral normal ovaries (n = 20)</td>
</tr>
</tbody>
</table>

Comparison between the **stripping technique** and **combined (by BD) technique** for the treatment of bilateral endometriomas: a multicenter RCT

### Table I Characteristics of patients ($n = 51$) in a comparison between the stripping and combined excisional/ablative techniques for treatment of bilateral ovarian endometriomas.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Stripping technique</th>
<th>Combined technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean ± SD)</td>
<td>32.9 ± 5.7</td>
<td></td>
</tr>
<tr>
<td>Cyst diameter (cm; mean ± SD)</td>
<td>4.0 ± 1.7</td>
<td>4.2 ± 1.7</td>
</tr>
<tr>
<td>Main indication for surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>31 (61%)</td>
<td></td>
</tr>
<tr>
<td>Infertility</td>
<td>20 (39%)</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>39 (76%)</td>
<td></td>
</tr>
<tr>
<td>1 or more</td>
<td>12 (24%)</td>
<td></td>
</tr>
<tr>
<td>Procedure performed on left versus right ovary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stripping ($n/n$)</td>
<td>26/25</td>
<td></td>
</tr>
<tr>
<td>Combined ($n/n$)</td>
<td>25/26</td>
<td></td>
</tr>
</tbody>
</table>

Muzzi et al. Human Repro 2016
Comparison between the *stripping technique* and the *combined excisional (BD) technique* for the treatment of bilateral ovarian endometriomas: a multicenter RCT

### Table II AFC, and OV, for the stripping technique and the combined technique at 1, 3 and 6-month follow-up.

<table>
<thead>
<tr>
<th></th>
<th>1 month (n = 51)</th>
<th></th>
<th>3 months (n = 47)</th>
<th></th>
<th>6 months (n = 40)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AFC</td>
<td>OV (mL)</td>
<td>AFC</td>
<td>OV (mL)</td>
<td>AFC</td>
<td>OV (mL)</td>
</tr>
<tr>
<td>Stripping side</td>
<td>4.5 ± 2.1</td>
<td>8.4 ± 5.1</td>
<td>5.0 ± 2.9</td>
<td>7.7 ± 4.6</td>
<td>4.8 ± 2.9</td>
<td>8.4 ± 5.0</td>
</tr>
<tr>
<td>Combined side</td>
<td>4.8 ± 2.4</td>
<td>7.3 ± 4.0</td>
<td>4.6 ± 2.3</td>
<td>7.0 ± 3.7</td>
<td>4.4 ± 2.3</td>
<td>6.5 ± 3.3</td>
</tr>
<tr>
<td>( P ) value*</td>
<td>0.42</td>
<td>0.24</td>
<td>0.43</td>
<td>0.42</td>
<td>0.57</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.

*Paired Student’s t-test.
Is the combined excisional/ablative technique (BD) for the treatment of ovarian endometriomas better than the traditional stripping technique in terms of recurrence rate?

A prospective, multicentre, randomized blinded clinical trial was carried out on 51 patients with bilateral endometriomas larger than 3 cm. For each patient, serving as her own control, one ovary was randomized to the stripping technique and the contralateral to the combined excisional/ablative technique.

PARTICIPANTS/MATERIALS, SETTING, METHODS:
Patients of reproductive age with pelvic pain and/or infertility affected by bilateral endometriomas larger than 3 cm were included (n = 51). The patients underwent laparoscopic removal of endometriomas with two different surgical techniques performed at either side after random assignment: complete removal by stripping on one side versus the combined technique, consisting of partial excisional cystectomy followed by completion with ablative surgery using bipolar coagulation, on the other side. Post-operative follow-up was performed at 1, 3 and 6 months after surgery for the evaluation of endometrioma recurrence and of AFC and ovarian volumes to assess ovarian reserve (secondary outcome).
Is the combined excisional/ablative technique (BD) for the treatment of ovarian endometriomas better than the traditional stripping technique in terms of recurrence rate?

**MAIN RESULTS AND THE ROLE OF CHANCE:**

Recurrence rates were 5.9% for the stripping technique versus 2.0% for the combined technique (odds ratio 3.00; 95% confidence interval: 0.24-157.5; P = 0.62). AFC in the ovaries treated with the stripping technique did not differ significantly from AFC in ovaries treated with the combined technique at all follow-up visits, whereas OV was significantly lower after the combined technique at the 6-month follow-up visit (P = 0.04).
Impact of hemostasis methods, electrocoagulation vs suture in laparoscopic endometriotic cystectomy on the ovarian reserve: a randomised controlled trial

• 50 patientes. AMH (pre-op): 2.90±2.26 vs 2.52±2.37
• No significant differences of AMH decline between two groups at 1 week, 1 month, 3 and 6 months

Tanprasertkul et al. J. Med Assoc Thai 2014
Effects of bipolar coagulation vs suture after laparoscopic endometrioma cystectomy on the ovarian reserve and outcome of IVF: retrospective study

(44 patientes with unilateral endometrioma cystectomy)

- No significant differences in serum levels of AMH, FSH, E2, AFC between pre-post operative samples in both groups
- But there was no differences in the outcome of IVF between the 2 different methods of hemostasis

Takashima A et al J Obst Gyn Res 2013
Impact of hemostasis methods, electrocoagulation vs suture in laparoscopic endometriotic cystectomy on the ovarian reserve: prospective comparative study

- 125 patients
- Significant differences of AMH decline between two groups (p<.001).
- Decline rate of AMH was significantly greater in the bipolar group (42.2%) than in the suture group (24.6%)

Song T et al JMIG 2015
Hemostasis by bipolar coagulation vs suture after surgical stripping of bilateral ovarian endometriomas: a randomised controlled trial

- 100 patients with bilateral endometriomas
- Randomised to undergo hemostasis by laparoscopic suturing (LS) or bipolar coagulation (BC)
- At 3-6-12 months follow-up in both groups, postsurgical AMH levels were significantly lower and basal FSH levels were significantly higher than before surgery.
- There was no significant difference in the mean % decrease of AMH in both group at 3-6-12 months of follow up.
- Pregnancy rate, time to conception and rate of endometrioma recurrence was similar in the 2 groups.
Effect of vasopressin injection technique in laparoscopic excision of bilateral ovarian endometriomas on ovarian reserve: prospective randomized study

- 86 women with bilateral endometriomas
- 3 groups: Cystectomy group without injection (1), with saline solution injection (2), with vasopressin injection (3)
- Basal FSH levels were significantly different before and after surgery in group 1 and 2 but not in the group 3 (p > .05)

Qiong-Zhen et al. JMIG 2014
Hemostatic Sealant

- Bowin-derivated gelatin matrix component and a human or bowin-derivated thrombin powder in calcium chloride solution
- They are in two separate syringes and are mixed just before application to the bleeding site
- A minority patients (5/65) need additional intervention (suturing or BD)
- Same complications (viral transmission, pulmonary embolism, DIC, small bowel obstruction, allergic reaction)
Impact of bipolar coagulation vs hemostatic sealant for laparoscopic endometriotic cystectomy in preserving ovarian reserve: multicenter randomized controlled trial

- 100 patients
- Significant differences of AMH decline between two groups (p=0.004).
- Decline rate of AMH was significantly greater in the bipolar group (41.2%) than in hemostatic sealant group (16.1%)

Song T et al Hum Repro 2014
Effect of Hemostatic Method on Ovarian Reserve Following Laparoscopic Endometrioma Excision; Comparison of Suture, Hemostatic Sealant and Bipolar Desiccation. A Systemic Review and Meta-Analysis

Barıs Ata et al. JMIG 2015

### Fig. 2

Mean difference in the rate of decline in serum AMH levels between different hemostatic methods.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Non-electrosurgical</th>
<th>Bipolar desiccation</th>
<th>Mean Difference</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>3.1.1 Bipolar vs hemostatic sealant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sonmez 2013</td>
<td>19.3</td>
<td>16.6</td>
<td>13</td>
<td>23.5</td>
</tr>
<tr>
<td>Song 2014</td>
<td>26.1</td>
<td>22.8</td>
<td>28</td>
<td>33.5</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: $\chi^2 = 0.14$, df = 1 ($P = 0.71$); $I^2 = 0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 1.36$ ($P = 0.17$)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3.1.2 Bipolar vs suture</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kumakiri 2012</td>
<td>44</td>
<td>28</td>
<td>20</td>
<td>58</td>
</tr>
<tr>
<td>Ferrero 2012</td>
<td>13</td>
<td>28.2</td>
<td>45</td>
<td>19</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>65</td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: $\chi^2 = 0.64$, df = 1 ($P = 0.42$); $I^2 = 0%$</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect: $Z = 1.84$ ($P = 0.07$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>106</td>
<td></td>
<td></td>
<td>107</td>
</tr>
</tbody>
</table>
We reviewed the literature to determine whether different hemostatic methods used following laparoscopic endometrioma excision have differing effects on ovarian reserve. We performed a systematic literature search to identify studies comparing the rate of change in levels of serum anti-Müllerian hormone (AMH) at 3 months after laparoscopic endometrioma excision using bipolar dessication (BD) or suturing/application of a hemostatic sealant (HS) for hemostasis. A total of 712 articles were identified, of which 6 were included in the qualitative analysis. Four studies involving 213 women were included in the meta-analysis. Our qualitative analysis suggested that BD is more detrimental to ovarian reserve than alternative hemostatic methods. There is moderate-quality evidence favoring HS and low-quality evidence favoring sutures over BD. The meta-analysis also showed that alternative hemostatic methods are associated with significantly less decline in ovarian reserve compared with BD. The mean decline in serum AMH levels was 6.95% less with alternative hemostatic methods than with BD (95% CI, −13.0% to −0.9%; p = .02) at 3 months after surgery. According to the best available evidence, the use of BD should be cautiously limited, even avoided when possible, during endometrioma excision in women who desire to have children.
Our qualitative analysis suggested that BD is more detrimental to ovarian reserve than alternative hemostatic methods. There is moderate-quality evidence favoring Hemostatic Sealant and low-quality evidence favoring sutures over BD. The use of BD should be cautiously limited, even avoided when possible, during endometrioma excision.
Excision + Ablation + DIE
Bilateral Endometrioma+DIE
• Endometriosis recurrence rate is 20% at 2 years, 40-50% at 5 years.

• Post-operative endometrioma recurrence rate is 30-50% after 2-5 year follow-up

Guo et al., 2009; Kikuchi et al., 2006; Koga et al., 2006; Vercellini et al., 2008
Prevention of Recurrence after surgery

1. OC
2. Progestins (MPA, Norethindron acetate 5 mg/day, Dienogest 3mg/day)
3. Lng IUD
4. GnRH agonists
5. Aromatase inhibitors (significant bone loss with prolonged use)
6. Others.
Key point: Better Protection of the Hilus Vascularisation

1. Non aggressive coagulation but in case we need (use fine bipolar forceps or pin point hemostasis by laser but under irrigation)
2. Combined technique by Laser vaporisation
3. Hemostatic sealant(?), vasopressin injection before excision
4. Homostatic sutures > BD?
Don’t do the Extensive Coagulation and Aggressive Hemostatic Sutures
Don’t be a Happy Surgeon with a Harmed Ovary
Controversy in the treatment of Endometriomas

- Etiopathogenesis of endometriomas?
- Ablation or excision?
- Decreased ovarian reserve after surgery?
- Is surgery necessary before or after IVF?
- Association between endometriomas and increased risk of ovarian carcinoma?
- Is oocyt quality impaired by endometriosis?
- Underdiagnosis of associated endometriosis (uterine adenomyosis, DIE) when we treat ovarian endometriomas.
- How can we diminish the recurrence after surgery?
Excision of Endometriomas

- How can we protect better ovarian reserve?
- How can we diminish de-novo adhesions?
- How can we treat associated endometriosis (DIE, peritoneal, uterine adenomyosis ect.)?
- How can we treat pain and infertility?
- How can we diminish recurrence after surgery?
Management of Ovarian Endometriomas:

1. Initial surgery as the preferred therapeutic approach for women with symptomatic or enlarging endometriomas.

2. Cyclic/continuous use of OC to prevent recurrence post surgery (RR after 36 months 6% vs 49% in non-user, Vercellini 2008).
Management of endometriomas

- **RCT : Cystectomy vs drainage and coagulation**

- 64 patients with advanced stages of endometriosis
  
  Randomization at the time of laparoscopy

- The **24-month cumulative PR** was significantly higher
  
  in the cystectomy group
  
  (66.7%, 6/9) than

  in the coagulation group
  
  (23.5%, 4/17)

(Beretta et al Fertil Steril 1998; 70: 1176-80)
Management of endometriomas

- RCT: Cystectomy vs drainage and coagulation

- 100 patients with advanced stages of endometriosis
  Randomization before laparoscopy

- The 12-month cumulative PR was significantly higher
  in the cystectomy group (59.4%) than
  in the coagulation group (23.3%)

Surgery for endometriosis-associated infertility

Source, year

<table>
<thead>
<tr>
<th>Study</th>
<th>Cases/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daniell et al., 1991</td>
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</tr>
<tr>
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<tr>
<td>Busacca et al., 1999</td>
<td>39/67</td>
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<td>Milingos et al., 1999</td>
<td>17/32</td>
</tr>
<tr>
<td>Jones &amp; Sutton, 2002</td>
<td>15/39</td>
</tr>
<tr>
<td>Alborzi et al., 2004</td>
<td>19/32</td>
</tr>
<tr>
<td>Fedele et al., 2006</td>
<td>29/90</td>
</tr>
<tr>
<td>Vercellini et al., 2006a</td>
<td>128/237</td>
</tr>
</tbody>
</table>

Overall weighted mean

Pregnancy rates after LPS excision of endometriomas

Pregnancy rate (%)
Risk of Recurrence of Ovarian Endometriomas at 2-5 year

High risk of recurrence:
- Younger women
- Severe disease
- History of endometriosis related medical therapy in adolescence

Recurrence rate: 15-30% (5 years)

Prevention of Recurrence after surgery

1. OC vs no treatment (277 women):
   6% vs 49% (3 years)  
   (Vercellini AJOG 2008)

2. Randomised trial, 239 patients (2 years):
   - Cyclic OC : 15%
   - Continuous : 8%
   - No treatment: 29%

(Seracchioli et al. Fert. Steril. 2010)
Major risk factors of recurrence

• ↑ duration of exposure retrograde menstruation
• Less aggressive surgery
• Inadequate previous surgery (44% Chapron 2004)
• Younger age of patient
• Stage III-IV
DIE has Two Major Specificities

- DIE is a multifocal pathology:
  USL, vagina, bladder, intestine, ureter
- DIE is very often associated with other endometriotic lesions:
  Unique lesion 10%
  Superficial lesions 61.3%
  Endometriomas 50.5%
  Adhesions 74.2%

Somigliana et al Hum Reprod 2004
Association of Ovarian Endometriomomas and DIE

- Somigliana 2004: 50%
- Chapron 2009: 23%

Associated ovarian endometrioma is a marker for greater severity of DIE
Laser-Tissue Interaction

- Reflection - not relevant
- Scattering - usually leads to absorption
- Transmission - not relevant
- Absorption - major factor of laser surgery
Surgeon’s performance index

- Ovarian reserve alteration before and after surgery (AMH, AFS, D3 hormones, inhibine)
- Recurrence rate within 1-5 years
- Persistence of pain after surgery (incomplete surgery, DIE, ect)
CONCLUSION

- Complexity of the pathology renders conclusion from prospective randomised studies difficult.
- The results may be biased by selection of patients from groups with major differences in pathology.
- Presence of adenomyosis within the uterus or in the pelvis should be incorporated in the analysis of the post surgical treatment.
CONCLUSION

• Treatment should be individualized taking into account different factors as:
  - Age of patient
  - Size, number and localisation of the endometriomas
  - Presence of pain
  - Associated lesions
  - Recurrence
  - Wish to conceive
CONCLUSION

• If infertility related endometriosis 4 factors impact the decision: The age, whether other infertility factors (eg male factor), the stage of endometriosis, patient preference

• For women with minimal/mild endometriosis at diagnostic laparoscopy, recommendation ablation or excision of endometriotic implants (Grade 1A)

• For young women with moderate/severe endometriosis at laparoscopy, recommendation to resect endometriosis and adhesions (Grade 2C)

• Repeated surgical procedures do not enhance fertility

• Endometrioma resection before IVF only, if pelvic pain, suspicion of ovarian malignancy, endometrioma interfere egg retrieval or IVF failure.
Effect of Hemostatic Method on Ovarian Reserve Following Laparoscopic Endometrioma Excision; Comparison of Suture, Hemostatic Sealant, and Bipolar Dessication. A Systematic Review and Meta-Analysis

Baris Ata, MD, MCT, Engin Turkgeldi, MD, Ayse Seyhan, MD, Bulent Urman MD
JMIG.2015
Comparison between the stripping technique and the combined excisional/ablative technique for the treatment of bilateral ovarian endometriomas: a multicentre RCT.

Muzii L1, Achilli C2, Bergamini V3, Candiani M4, Garavaglia E4, Lazzeri L5, Lecce F2, Maiorana A6, Maneschi F7, Marana R8, Perandini A3, Porpora MG2, Seracchioli R9, Spagnolo E9, Vignali M10, Benedetti Panici P2.
Association of different types of endometriosis:

- Endometriomas, DIE and uterine adenomyosis
- Imaging techniques like 3-D ultrasound, MRI give us all information about the presence, localisation and extend of extra-uterine and uterine adenomyosis.
Ethiopathogenesis:

- **Sampson** was the first to suggest that ovarian endometriotic cysts originate from the outside of the ovary and was caused by adhesions and bleeding of surrounding peritoneal implants.
Donnez and Nisolle suggested that mesothelial metaplasia is at the origine, but also causing an invagination of ovarian cortex.

That’s why ovarian endometriomas differs from other benign ovarian cysts by his extra ovarian localisation and why ovarian volume and AFC decreased after cystectomy.
Ovarian volume and AFC after other cystectomy:

- For example dermoid cyste where there is no intrinsic demage, the ovarian volume and AFC can not be too much altered post cystectomy.
Ovarian reserve alteration after surgery for endometriomas

- Both ablative and excisional surgery diminish ovarian reserve.
- But in hands of experienced surgeon there will probably be no difference in final ovulatory function between the two techniques.
- However in the hands of inexperienced surgeon it is likely that the damage of ovarian function will be greater after cystectomy.
How can we protect better ovarian reserve during cystectomy?

• In an attempt to lower the ovarian damage, a two step operative procedure or combination of techniques has been proposed.
Is endometrioma surgery necessary before IVF?

- Recent *meta-analysis* could *not* identify statistically significant differences in PR and clinical PR per cycle after IVF between women undergoing surgery for endometriomas and woman with endometriomas without surgery.

Tsoumpou I et al Fert.Ster.2009
• Since several decades basically the treatment of ovarian endometriosis remained unchanged.
• It is hardly questionable if we are performing better now.
• Why treat endometriosis?
Why to treat Endometriosis?

- Endometriosis can disrupt environment in peritoneal cavity
  - anatomical
  - hormonal and
  - immunological

- Then endometriosis may cause
  Pelvic Pain, Infertility, and Pelvic Mass
Endometriosis is an estrogen-dependent chronic inflammatory disease.

It can be effectively cured by radical surgery.

Also prolonged medical therapies, after conservative surgery may be needed, as for most chronic inflammatory disorders in general.

Vercellini et al 2011
Endometriosis should be viewed as a chronic disease that requires a life-long management plan with a goal of maximizing the use of medical treatment and avoiding repeated surgical procedures.
ENDOMETRIOSIS: A CHALLENGING SYNDROME

• 15-30% INFERTILITY
• 30-50% PELVIC PAIN
• 4% ASYMPTOMATIC
OBJECTIVES of THE SURGICAL APPROACH

• PAIN
• INFERTILITY
• DIAGNOSIS
• RECURRENCE
Cause of infertility: minimal, mild endometriosis

- Over production of prostaglandins, macrophages, metalloproteinases, cytokines and chemokins: inhibits sperm function and ciliary function.

- These resulting inflammatory process, impairs ovarian, peritoneal, tubal and endometrial function, leading to defective folliculogenesis, fertilization and/or implantation.

4 Types of Endometriosis

- Superficial Endometriosis:
  1. Peritoneal endometriosis
  2. Ovarian superficial endometriosis

- Ovarian Endometriomas

- Deeply Infiltrating Endometriosis (DIE)

- Extragenital Endometriosis
Histological classification

A. well-differentiated glandular pattern
B. Pure stromal pattern
C. Glandular pattern of mixed differentiation
D. Undifferentiated glandular pattern

- Type D was more frequently associated with stages III/IV than A and B patterns.
- B and C patterns were more frequently associated with rectovaginal endometriosis.
- Patients presenting A and B patterns responded better to therapeutic treatment than those who presented D pattern.
- No significant differences in cases related to sterility.

(Abraho, 2003)
Diagnosis: Ultrasound

- Characteristic feature of endometriomas
  - Presence of diffuse, low-level internal echoes
  - Hyperechogenic foci in the wall

Image of ultrasound and visual inspection of the organ.
Diagnosis: Ca125

- It is an important tumor marker
- But it is not a sensitive indicator of endometriosis
- The best correlation is seen in stage 3 or 4
- In such women Ca 125 > 100 extensive peritoneal disease adhesions or ruptured endometriomas are primarily associated with (Cheng et al Obst Gyn 2002)
Ovarian endometriosis is confirmed at laparoscopy and by histologic examination.
Ovarian endometriosis is confirmed at laparoscopy and by histologic examination.
Pathogenesis of Endometriomas is not clear: *Controversy*

1. Mesothelial metaplasia
2. Invaginating of the ovarian cortex
Pathogenesis of Endometriomas: *Consensus*

Typical endometrioma is formed by accumulation of menstrual debris from the shedding and bleeding of active implants.

The *invagination theory* is accepted.
Surgical treatment of endometriosis associated infertility

<table>
<thead>
<tr>
<th>Clinical condition</th>
<th>Recommendation ESHRE 2005</th>
<th>ASRM 2006</th>
<th>RCOG 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal-mild endometriosis (stage I-II)</td>
<td>Limited benefit; surgery recommended</td>
<td>Small benefit; surgery recommended</td>
<td>Demonstrated benefit; surgery recommended</td>
</tr>
<tr>
<td>Moderate-severe endometriosis (stage III-IV)</td>
<td>Possible but unproven benefit; surgery recommended</td>
<td>Possible benefit; surgery recommended</td>
<td>Possible benefit; recommendation uncertain</td>
</tr>
<tr>
<td>Fallopian tube adhesions</td>
<td>No benefit not recommended</td>
<td>No benefit; not recommended</td>
<td>No benefit; not recommended</td>
</tr>
<tr>
<td>Surgery before IVF</td>
<td><strong>Recommended if endometriosis ≥4 cm</strong></td>
<td>Doubtful benefit; no recommendation</td>
<td>Recommended if endometriosis ≥4 cm</td>
</tr>
<tr>
<td>Recurrent endometriosis</td>
<td>No recommendation</td>
<td>Second-line surgery not recommended</td>
<td>No recommendation</td>
</tr>
</tbody>
</table>

Vercellis et al. Human Reprod 2008
Reconstruction of anatomy
- Lack of correlation between residual ovarian volume and cyst diameter...

- Resection of even small endometrioma: significant loss of ovarian volume.
### Surgery and Ovarian reserve

**IVF-ET outcome after endometriomas removal: Retrospective studies**

<table>
<thead>
<tr>
<th>No decrease in the IVF-ET outcome</th>
<th>Decrease in the IVF-ET outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystectomy</td>
<td>Cystectomy</td>
</tr>
<tr>
<td>Canis et al (2001)</td>
<td></td>
</tr>
<tr>
<td>Garcia-Velasco (2004)</td>
<td></td>
</tr>
<tr>
<td>Cyst wall vaporization - Cystectomy</td>
<td></td>
</tr>
<tr>
<td>Donnez et al (2001)</td>
<td></td>
</tr>
</tbody>
</table>
Post-operative cumulative pregnancy rate
Ovarian surgery for bilateral endometriomas influences age at menopause

Maria Elisabetta Coccia¹,*, Francesca Rizzello², Giulia Mariani¹, Carlo Bulletti³, Antonio Palagiano⁴, and Gianfranco Scarselli¹

¹Department of Science for the Health of Woman and Child, University of Florence; Via Ippolito Nievo 2, 50129 Florence, Italy ²Department of Experimental Medicine, Section of Medical Physiopathology, University of Rome 'La Sapienza', Rome, Italy ³Unit of Physiopathology of Reproduction, Cattolica General Hospital and University of Bologna, Bologna, Italy ⁴Department of Obstetrics, Gynecology, and Reproductive Sciences, Second University of Naples, Naples, Italy

Table III Frequency of patients with menopause, POF or lamenting menopausal symptoms (hot flushes, night sweats and vaginal dryness) after surgery for endometriosis.

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Peritoneal endometriosis, no ovarian endometrioma</th>
<th>Ovarian surgery</th>
<th>Monolateral endometrioma</th>
<th>Bilateral endometrioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menopause, n (%)</td>
<td>302</td>
<td>63</td>
<td>239</td>
<td>155</td>
<td>84</td>
</tr>
<tr>
<td>Mean age at menopause (years)</td>
<td>45.3 ± 4.3</td>
<td>45.1 ± 3.3abc</td>
<td>45.7 ± 4.5</td>
<td>47.1 ± 3.5abc</td>
<td>42.1 ± 5.1abc</td>
</tr>
<tr>
<td>POF (n)</td>
<td>7 (7/43, 16.3%)</td>
<td>2 (2/11, 18.2%)c</td>
<td>5 (5/32, 14.3%)</td>
<td>1 (1/21, 4.8%)</td>
<td>4 (4/11, 36.4%)</td>
</tr>
<tr>
<td>Menopausal symptoms (hot flushes, night sweats and vaginal dryness)</td>
<td>18 (18/259, 6.9%)</td>
<td>2 (2/52, 3.8%)abc</td>
<td>16 (16/207, 7.7%)</td>
<td>7 (7/134, 5.2%)</td>
<td>9 (9/73, 12.3%)</td>
</tr>
</tbody>
</table>

Results are stratified according to the groups 'peritoneal endometriosis', 'monolateral endometrioma', 'bilateral endometriomas'. The mean age of menopause onset was calculated for each group.

abc Student t-test.

P = 0.102; P = 0.117; P = 0.003.

def Χ² test.

P = 0.266; P = 0.635; P = 0.037; P = 0.990; P = 0.184; P = 0.120.
# Endometriosis and Infertility: Recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Evidence</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Laparoscopic cystectomy for the treatment of endometrioma &gt;4cm improves pregnancy rate in comparison to drainage and coagulation</td>
<td>1b</td>
</tr>
<tr>
<td>B</td>
<td>Vaporization of the endometrioma capsule without excision increases the recurrence rate</td>
<td>1b</td>
</tr>
<tr>
<td>A</td>
<td>Pregnancy rate after IVF in endometriosis is lower than in tubal factor with independency of the presence of an ovarian endometrioma (Suzuki 05)</td>
<td>1a</td>
</tr>
<tr>
<td>A</td>
<td>Postoperative treatment in stages III-IV might increase the pregnancy rates after IVF</td>
<td>1b</td>
</tr>
<tr>
<td>A</td>
<td>In patients with isolated endometrioma measuring less than 4 cm, surgery may reduce ovarian response to stimulation without increasing the IVF results.</td>
<td>1b</td>
</tr>
<tr>
<td>GPP</td>
<td>Endometriomas over 4 cm may be treated by laparoscopic cystectomy but the ovarian reserve and previous ovarian surgery should be taken into account (RCT Beretta 98, Alborzi 04)</td>
<td></td>
</tr>
</tbody>
</table>
Endometrioma without surgery befor IVF

- Treatment with a GnRH agonist for 3-6 months before IVF or ICSI should be considered in women with endometriosis as it increases the odds of clinical pregnancy fourfold.

- However the authors of the Cochrane review stressed that the recommendation is based on only one properly randomised study and called for further research, particularly on the mechanism of action.

Sallam et al., 2006
Endometrioma and surgery

- Laparoscopic ovarian cystectomy in patients with unilateral endometriomas between 3 and 6 cm in diameter before IVF/ICSI can decrease ovarian response without improving cycle outcome.

- In the prospective randomized trial 49 patients underwent conservative ovarian surgery before the ICSI cycle and 50 patients underwent the ICSI cycle directly.

- Ovarian stimulation parameters for those who underwent ovarian endometrioma cystectomy were significantly reduced and fewer mature oocytes were retrieved in the cystectomy group.

- No difference in implantation and clinical pregnancy rates were detected

Demirol et al., 2006
Endometrioma and surgery

- Studies evaluating the response to ovarian stimulation in patients previously operated for endometriomas have led to controversial results in terms of ovarian response and cycle outcome.

- In patients with unilateral disease a significantly reduced number of follicles in the operated ovary compared to the intact side were reported in several but not all studies. The authors of one systematic review conclude that overall evidence suggests that surgery does not benefit asymptomatic women preparing to undergo IVF-ICSI who are found to have an endometrioma

..................Somigliana et al.,2006
Endometrioma and surgery

- The observation of an impaired ovarian response in women with endometriomas does not clarify whether the damage is consequent to surgery or antecedent to the intervention.

- An observational study in women with unilateral endometriomas who did not undergo previous ovarian surgery showed a significant mean reduction in follicles in the affected ovaries, suggesting that the presence of ovarian endometriomas is associated with a reduced responsiveness to gonadotrophins.


Somigliana et al., 2006
Endometrioma and surgery

- The other meta analysis indicates that ovarian endometrioma have adverse effects on follicle number and oocytes retrieved but not on embryo quality or pregnancy outcomes.

- Surgery may decrease the number of retrieved oocytes, but the overall fertility outcome is not affected

Gupta et al., 2006
Effects of ovarian endometrioma on the oocytes number in IVF

- Approximately 1/3 of women with endometriosis have an ovarian endometrioma
- 81 women with unilateral endometrioma underwent their first IVF cycle at McGill Univ.
- Endometrioma diameter : 28.4+-3.9mm
- No significant difference in the number of oocytes retrieval between endometrioma containing ovary and in the opposite ovary (7.7 vs 8.5 oocytes)
- CC: they recommend IVF treatment without prior removal of ovarian endometrioma.

Almog and Tulandi et al., Fertil. Steril. 2011
In Summary

- Laparoscopic ovarian cystectomy can be considered if an ovarian endometrioma >4 cm in diameter is present to:
  - confirm the diagnosis histologically;
  - reduce the risk of infection;
  - improve access to follicles and
  - possibly increase spontaneous pregnancy rate (50%).
Surgery for endometriosis associated infertility

Surgery for endometriosis-associated infertility: a pragmatic approach

Paolo Vercellini, Edgardo Somigliana, Paola Viganò, Annalisa Abbiati, Giussy Barbara, and Pier Giorgio Crosignani

<table>
<thead>
<tr>
<th>Source, year</th>
<th>Pregnancies/Total</th>
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<tbody>
<tr>
<td>Daniell et al., 1991</td>
<td>12/32</td>
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</table>

Overall weighted mean

Pregnancy rates after LPS excision of endometriomas
Laparoscopic Laser Surgery for Endometriosis - Fev 2011

<table>
<thead>
<tr>
<th>r-AFS score</th>
<th>N</th>
<th>DIE Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I-II</td>
<td>1153</td>
<td>-</td>
</tr>
<tr>
<td>Stage III-IV</td>
<td>1092</td>
<td>128</td>
</tr>
<tr>
<td>Total</td>
<td>2245</td>
<td>(5.7%)</td>
</tr>
</tbody>
</table>

Karaman 2011
Brüksel Kadın Sağlığı ve Tüp Bebek Merkezi, İstanbul
Hopital Français Reine Elizabeth, Brussels
Institut Medical Edith Cavell, Brussels
Laparoscopic surgery for DI Endometriosis (128 cases)

- Laparoscopic removal of the rectovaginal nodule 83
  - with resection of posterior vaginal fornix 54
  - Only nodule excision 29
- Laparoscopy assisted sigmoidectomy 31
- Laparoscopic discoid resection of sigmoid 9
- Laparoscopic partial bladder excision for vesical nodules 5

KARAMAN 2011
Laparoscopic surgery for endometriomas (1092 cases)

- **Age:**
  - 20-29: 388
  - 30-39: 510
  - 40-49: 152
  - 50-55: 42

- **Symptoms:**
  - Infertility: 41%
  - Pelvic pain: 24%
  - Pelvic pain + infertility: 23%
  - Asymptomatic: 12%

Karaman 2011
## Endometrioma diameters

<table>
<thead>
<tr>
<th>Diameter Range</th>
<th>Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 cm</td>
<td>204</td>
<td>19%</td>
</tr>
<tr>
<td>2-5 cm</td>
<td>601</td>
<td>55%</td>
</tr>
<tr>
<td>6-10 cm</td>
<td>210</td>
<td>19%</td>
</tr>
<tr>
<td>&gt; 10 cm</td>
<td>77</td>
<td>6%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1092</strong></td>
<td></td>
</tr>
</tbody>
</table>

Bilateral endometriomas: 164/1092  15%

Karaman 2011
Type of the surgery (1092)

- Cystectomy: 958
- Ovariectomy: 102
- LH-LAVH: 32

Karaman 2011
Cumulative pregnancy rate (640 patients)

- Stage 1-2: 62%
- Stage 3-4: 48%
- If r- AFS >70: 0%

Karaman 2011
In fact, ovulation seems crucial in the development of ovarian endometriotic cysts and suppression should substantially decrease cyst recurrence after laparoscopic treatment.

Jaina, Dalton 1999; Seracchioli 2009
Table III  Results of studies comparing the endometrioma recurrence rate in women undergoing laparoscopic excision of ovarian cysts followed by a long-term post-operative OC use versus EM (literature data, 2000–2010).

<table>
<thead>
<tr>
<th>Source</th>
<th>Study design</th>
<th>Patients enrolled (n)</th>
<th>Follow-up (months)</th>
<th>Number of recurrence in OC group (%)</th>
<th>Number of recurrence in EM group (%)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vercellini et al. (2008b)</td>
<td>Cohort</td>
<td>277</td>
<td>28</td>
<td>9/102a (9)</td>
<td>26/46 (56)</td>
<td>0.07</td>
<td>0.03–0.18</td>
</tr>
<tr>
<td>Takamura et al. (2009)</td>
<td>Cohort</td>
<td>87</td>
<td>24</td>
<td>1/34a (3)</td>
<td>17/39 (44)</td>
<td>0.04</td>
<td>0.00–0.32</td>
</tr>
<tr>
<td>Seracchioli et al. (2010a)</td>
<td>RCT</td>
<td>239</td>
<td>24</td>
<td>17/148b (11)</td>
<td>20/69 (29)</td>
<td>0.32</td>
<td>0.15–0.66</td>
</tr>
</tbody>
</table>

EM, expectant management; OR, odds ratio; CI, confidence interval.

aOnly ‘always OC users’ are considered.
bCyclic and continuous OC users are considered together.

Table IV  Results of RCTs comparing the dysmenorrhoea recurrence rate in women undergoing laparoscopic treatment of endometriosis followed by post-operative progestin or OC use versus expectant management (literature data, 2000–2010).

<table>
<thead>
<tr>
<th>Source</th>
<th>Patients enrolled (n)</th>
<th>Post-operative intervention</th>
<th>Follow-up (months)</th>
<th>DYSM recurrence in progestin/OC group [n (%)]</th>
<th>DYSM recurrence in EM group [n (%)]</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vercellini et al. (2003c)</td>
<td>40</td>
<td>LNG-IUD</td>
<td>12</td>
<td>2/20 (10)</td>
<td>9/20 (45)</td>
<td>0.14</td>
<td>0.02–0.75</td>
</tr>
<tr>
<td>Seracchioli et al. (2010b)</td>
<td>311</td>
<td>Continuous/cyclic OC</td>
<td>18</td>
<td>33/187ab (18)</td>
<td>35/87 (40)</td>
<td>0.32</td>
<td>0.18–0.56</td>
</tr>
</tbody>
</table>

aCyclic and continuous OC users are considered together.
bOnly subjects who completed the study are considered.
CONCLUSION

- **Complexity of the pathology** renders conclusion from prospective randomised studies difficult.
- The results may be biased by selection of patients from groups with **major differences in pathology**
- **Presence of adenomyosis** within the uterus or in the pelvis should be incorporated in the analysis of the post surgical treatment.
• Treatment should be individualized taking into account different factors as:
  - Age of patient
  - Size, number and localisation of the endometriomas
  - Presence of pain
  - Associated lesions
  - Recurrence
  - Wish to conceive
CONCLUSION

- If infertility related endometriosis 4 factors impact the decision: The age, whether other infertility factors (eg male factor), the stage of endometriosis, patient preference.
- For women with minimal/mild endometriosis at diagnostic laparoscopy, recommendation ablation or excision of endometriotic implants (Grade 1A).
- For young women with moderate/severe endometriosis at laparoscopy, recommendation to resect endometriosis and adhesions (Grade 2C).
- Repeated surgical procedures do not enhance fertility.
- Endometrioma resection before IVF only, if pelvic pain, suspicion of ovarian malignancy, endometrioma interfere egg retrieval or IVF failure.
Medical Treatment for Endometriosis

- It must achieve 2 main objectives:
  - Relief of pain for prolonged periods
  - Prevention of disease progression between conservative surgery and conception seeking.

OCs for peritoneal and ovarian endometriosis and Progestins for DIE appears to be preferable compound, when these fails expensive therapies are indicated.
Medical Treatment for Endometriosis

- No optimal drug for endometriosis yet exists.
- In the past few years, many experts published reviews and concluded that we were entering a new therapeutic era which could act on etiological mechanisms and change the management prognosis of endometriosis.
- Regrettably, the situation appears considerably different.

Medical Treatment for Endometriosis

- Medical treatment should ideally eradicate endometriosis rather than merely relieving its symptoms.
- However, in case cytoreductive compound would be developed, which can eliminate endometriotic lesions, it is difficult to comprehend how this effect would be limited to ectopic but not eutopic endometrium and the receptor pattern and biological behaviour of the two mucosae are substantially similar.

Noel et al., 2010
<table>
<thead>
<tr>
<th>Table 1</th>
<th>Experimental drugs and proposed future therapeutic schemes for endometriosis (literature data 1987–2010).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-angiogenic agents</strong></td>
<td></td>
</tr>
<tr>
<td>Cabergoline</td>
<td></td>
</tr>
<tr>
<td>Endostatin</td>
<td></td>
</tr>
<tr>
<td>Sirolimus</td>
<td></td>
</tr>
<tr>
<td>Thalidomide</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular endothelial growth factor inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Antioxidants</strong></td>
<td></td>
</tr>
<tr>
<td>N-acetylcysteine</td>
<td></td>
</tr>
<tr>
<td>Vitamin E succinate</td>
<td></td>
</tr>
<tr>
<td><strong>Aromatase inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Anastrozole</td>
<td></td>
</tr>
<tr>
<td>Fadrozole</td>
<td></td>
</tr>
<tr>
<td>Formestane</td>
<td></td>
</tr>
<tr>
<td>Exemestane</td>
<td></td>
</tr>
<tr>
<td>Letrozole</td>
<td></td>
</tr>
<tr>
<td>Anastrozole plus oral contraceptive</td>
<td></td>
</tr>
<tr>
<td>Anastrozole plus GnRH analogue</td>
<td></td>
</tr>
<tr>
<td>Anastrozole plus progesterone, calcitriol and rofecoxib</td>
<td></td>
</tr>
<tr>
<td>Letrozole plus norethindrone acetate, calcium citrate and vitamin D</td>
<td></td>
</tr>
</tbody>
</table>
COX-2 inhibitor
  Celecoxib
  Indomethacin
  Nimesulide
  Rofecoxib
  Valdecoxib

GnRH antagonists
  Abarelix
  Cetrorelix

Histone deacetylase inhibitors
  Trichostatin A
  Valproic acid
  Valproic acid plus retinoic acid
Immunomodulators

- Acetylcholine nicotinic receptor analogue—Levamisole
- Cytokines interleukin-12
- Guanosine analogue—Loxoribine
- Interferon-α2β
- Rapamycin
- Xantine analogue—Pentoxifylline

Mitogen-activated protein kinase inhibitors

- FR167653
- p38 inhibitor

Matrix metalloproteinases inhibitors

- ONO-4817

Nuclear factor kappa B inhibitors

- Caffeic acid phenethyl ester
Capsaicin
SN-50

Perossisome proliferator-activated receptor-γ (Thiazolidinediones)
  Rosiglitazone
  Troglitazone

Progesterone antagonists
  Mifepristone (RU 486)
  Onapristone

Selective PR modulators
  Asoprisnil
  J-956 (asoprisnil ecamate)
  J-1042 (megestrone)
Selective estrogen receptor β agonists

ERB-041

Selective estrogen receptor modulators

Fulvestrant
Raloxifene
Tamoxifen

Statins

Atorvastatin
Lovastatin

TNF blockers

Chimeric anti-TNF-α monoclonal immunoglobulin—Infliximab
TNF-α receptor-immunoglobulin fusion protein—Etanercept
Aromatase Inhibitors

- Aromatase is expressed in several tissues (breast, ovary, endometrium, placenta, testis, skin, bone, fat and brain)
- Aromatase mediates in situ conversion of androstenedione to estrone and of testosterone to estradiol.
- Aromatase expression is higher in endometriosis implants than in normal endometrium, thus providing the ectopic mucosa with excessive proliferative stimulus.

Attar and Bulun et al., 2006-2009
Aromatase Inhibitors

- **Side effects:** mainly joint pain, myalgia, potential reduction in bone mineral density
- **Histologic examination of endometriotic lesions excised after treatment** shows preservation of endometrial glands and high stromal proliferative activity
- **Thus, aromatase inhibitors are neither cytoreductive nor curative**

Remorgida et al., 2007
The result consistently confirmed that progestin and OCs are effective in relieving pain, generally well-tolerated and not inferior to danasol, GnRH agonists and aromatase inhibitors.

<table>
<thead>
<tr>
<th>Source</th>
<th>Study design</th>
<th>Number of patients enrolled</th>
<th>Study drug</th>
<th>Comparator</th>
<th>Treatment period</th>
<th>Follow-up period</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vercellini et al.</td>
<td>RCT open</td>
<td>57</td>
<td>EE 0.02 mg + DSG 0.15 mg/day per os (n = 28)</td>
<td>Goserelin 3.6 mg depot s.c. injections/28 days (n = 29)</td>
<td>6 months</td>
<td>6 months</td>
<td>Significant reduction in dysm and CPP; goserelin better for dysm pain at follow-up</td>
</tr>
<tr>
<td>Vercellini et al.</td>
<td>RCT open</td>
<td>80</td>
<td>DMPA 150 mg i.m. injections/3 months (n = 40)</td>
<td>Danazol 50 mg/day per os + low-dose monophasic OC (n = 40)</td>
<td>12 months</td>
<td>No follow-up</td>
<td>Similar pain relief and degree of satisfaction</td>
</tr>
<tr>
<td>Casson et al.</td>
<td>RCT multicentre open</td>
<td>142</td>
<td>Dienogest 2 mg/day per os (n = 74)</td>
<td>Triptorelin 3.75 mg depot i.m. injections/28 days (n = 68)</td>
<td>4 months</td>
<td>12 months (reproductive outcome only)</td>
<td>Similar pain relief after LPS; no pain evaluation at follow-up</td>
</tr>
<tr>
<td>Pettet et al.</td>
<td>RCT multicentre open</td>
<td>82</td>
<td>LNG-IUD (n = 39)</td>
<td>Leuprolide 3.75 mg depot i.m. injections/28 days (n = 43)</td>
<td>6 months</td>
<td>No follow-up</td>
<td>Similar pain relief and psychological well-being; More bleeding with IUD</td>
</tr>
<tr>
<td>Crosignani et al.</td>
<td>RCT multicentre evaluator-blinded</td>
<td>299</td>
<td>DMPA 104 mg s.c. injections/3 months (n = 183)</td>
<td>Leuprolide 3.75 or 11.25 mg depot s.c. or i.m. injections/28-90 days (n = 146)</td>
<td>6 months</td>
<td>12 months</td>
<td>Similar pain relief and improvement in QoL and productivity. Less BMD decline with DMPA</td>
</tr>
<tr>
<td>Schlaff et al.</td>
<td>RCT multicentre evaluator-blinded</td>
<td>274</td>
<td>DMPA 104 mg s.c. injections/3 months (n = 136)</td>
<td>Leuprolide 11.25 mg depot i.m. injection/3 months (n = 138)</td>
<td>12 months</td>
<td>12 months</td>
<td>Similar pain relief and improvement in QoL and productivity. More bleeding but less hypo-estrogenic side effects and BMD loss with DMPA</td>
</tr>
<tr>
<td>Harada et al.</td>
<td>RCT double-dummy</td>
<td>271</td>
<td>Dienogest 2 mg/day per os (n = 137)</td>
<td>Buserelin 900 mg/day (n = 134)</td>
<td>No follow-up</td>
<td></td>
<td>Similar pain relief and improvement in QoL. More bleeding, but less hypo-estrogenic side effects and BMD loss with DMPA</td>
</tr>
<tr>
<td>Ferrero et al.</td>
<td>PPT</td>
<td>82</td>
<td>Letrozole 2.5 mg + NETA 2.5 mg/day per os (n = 41)</td>
<td>NETA 2.5 mg/day per os (n = 41)</td>
<td>6 months</td>
<td>12 months</td>
<td>Greater pain relief with letrozole + NETA, but fewer side effects and higher patients' satisfaction with NETA only. Similar pain at follow-up</td>
</tr>
<tr>
<td>Strowitzki et al.</td>
<td>RCT multicentre open</td>
<td>252</td>
<td>Dienogest 2 mg/day per os (n = 124)</td>
<td>Leuprolide 3.75 mg Depot IM injections/28 days (n = 128)</td>
<td>6 months</td>
<td>No follow-up</td>
<td>Similar pain relief. Higher improvement in QoL with Dienogest. More bleeding, but less hypo-estrogenic side effects and BMD loss with Dienogest</td>
</tr>
</tbody>
</table>
PREVENTION of RECURRENCE

- OC used cyclically or continuously may constitute an adequate first-line option for PERITONEAL and OVARIAN ENDOMETRIOSIS, whereas low-dose oral norethisterone acetate is probably the best choice for RECTOVAGINAL ENDOMETRIOSIS.

- The extensive epidemiologic information available demonstrates that OCs and progestins are safest medical alternative for long-term treatments of endometriosis.

ACOG 2010, Cibula 2010, Hannaford 2010
OCs and Progestin treatment in Endometriosis

- Women who have used OCs for prolonged periods might be reassured that they will be protected from an increase in risk of endometriosis-associated ovarian cancer.

Missmer et al., 2004
Endometriosis lesions suppression with progestins

- 9% patients do not respond to progestin treatment
- Human PR is controlled by two promoters that direct the synthesis of mRNA transcripts encoding two receptor proteins, PR-A and PR-B.
- High level of PR-A may impaired responsiveness to progesterone
- In breast and endometrial cancers such alterations in the PR-A/PR-A ratio induced a marked effect on cell morphology and features of invasive behaviour
- A decrease PR-B/PR-A ratio has been demonstrated not only in ectopic but also in eutopic endometrium of women with endometriosis

Attia et al., 2000, Bukulmez et al., 2008, Guo et al., 2009, McGowan et al., 2003, Igarashi et al., 2005.
PR-A and PR-B in Endometrial Cells

- An alteration of the relative expression of PR-A and PR-B in endometrial cells may play a pivotal role in the patogenesis of endometriosis, leading to impaired stromal differentiation and a consequent relative resistance to progesterone action.

Attia et al., Igarashi et al., 2005
PR-A and PR-B in inducing Endometriosis

- Inflammatory environment
- Epigenetic reprogramming (through local extracellular acidosis and deposit of reactive substance)
- Reactive halogen compounds
- DNA methylation alteration
- Disruption of epigenetic code
- Disturbed methylation-binding proteins in both activating and silencing of genes
- Differential receptor expression pattern (total endometrial PR and PR-B increased, PR-A decreased)

Inducing Endometriosis

Backdahl et al., 2009, Lee et al., 2009
Endometriosis (including analgesics, hormonal therapies, gynecological consultations, hospital admissions, surgical procedures, days off-work and reduced productivity): 18.8-22 billion per year

Crohn’s disease: 865 million per year

Migraine: 13-17 billion per year

Gao et al., 2006 Simoens et al., 2007
Annual cost of medical treatment for endometriosis

- Low-dose (2.5mg) Norethisterone acetate: 18 €
- Aromatase inhibitors or GnRH agonist: 2100 €
- Combination of these two drugs: 4200 €

Vercellini et al. Human Repro 2011
Deep infiltrating endometriosis

- **Rectovaginal endometriosis**
  - Upper vagina
  - Rectum
  - Uterosacral ligaments, cervix corpus uteri

- **Aim of management of DIE**
  - Improve quality of life
  - Preserve fertility
  - Low recurrence rate
  - Low complication rate
Role of medical treatment

- Hormonal therapy has been designed to
  - suppress oestrogen synthesis
  - atrophy of ectopic endometrial implant
- Recurrence after cessation is high: 50%
- Relative ineffectiveness of medical therapy: fibrotic reaction

Surgery of symptomatic DIE is required
Role of conservative surgery

- Surgery is efficacious
  - 2RCT: pain is reduced by surgical removal of endometriotic lesions (Sutton et al 1994; Abbott et al 2004)
  - Pain reduction in > 70% of patients after surgical removal of DIE (Angioni et al 2006; Chapron et al 2001; Possover et al 2000; Donnez et al 2004)

- Hysterectomy is not needed for treatment of DIE
Role of conservative surgery

- Surgery is efficacious
  - 2RCT: pain is reduced by surgical removal of endometriotic lesions (Sutton et al 1994; Abbott et al 2004)
  - Pain reduction in > 70% of patients after surgical removal of DIE (Angioni et al 2006; Chapron et al 2001; Possover et al 2000; Donnez et al 2004)
- Hysterectomy is not needed for treatment of DIE

Complete excision is needed
Conservative surgery for DIE

• How to be sure that the resection is complete?
• How to avoid complications associated with complex surgery?

Preoperative assessment
Multidisciplinary approach in specialised centres
DIE: Clinical Examination

Is bowel infiltrated?
DIE: Clinical examination and laparoscopy
Inspection
DIE: Clinical examination and laparoscopy
Preoperative assessment of DIE

Is the bowel infiltrated?

Rectal endoscopic
Sonography
- Distinction between muscularis propria submucosa-mucosa

MRI
- Cartography

Bazot et al Hum Reprod 2007
Similar accuracy for diagnosis of rectal involvement when compared to MRI
Deep infiltrating endometriosis
Surgical Techniques

- Redwine (1991) : Laparoscopic resection
- Bailey (1994) : Laparotomy
- Donnez (1994) : Laparoscopy without bowel resection
- Possover (2000) : Vaginal dissection followed by laparoscopy and minilaparotomy
- Chapron (2003) : Laparotomy if positive EER
- Koninckx: Laparoscopy - discoid resection
- Keckstein, Wattiez, Canis, Darai, Anaf : Laparoscopy and minilaparotomy
- Possover (2005) : LANN technique
- Landi (2006) : Laparoscopic nerve-sparing complete excision of DIE
- Nezhat (2010) : Robotic-assisted laparoscopy
Deep infiltrating endometriosis

- Preoperative assessment
- Type of surgical treatment?
  - Exision of the nodular lesion
    - Without bowel resection: **shaving technique**
      - Uterosacral ligaments infiltration
      - Vaginal infiltration
    - With bowel resection:
      - discoid or segmental bowel resection
      - laparoscopy; laparotomy; laparoscopically assisted technique
Adhesiolyis
Deep Infiltrating Endometriosis

Without bowel resection

Section of both US ligaments
Rectal dissection
Rectal dissection
Rectal dissection
Vaginal exposure
Vaginal excision
RECTOVAGINAL ENDOMETRIOSIS

- Without bowel resection

Vaginal opening

Vaginal closure
Deep infiltrating endometriosis

- « Check list » at the end of the surgery
  - Treatment is complete
  - Haemostasis is achieved
  - Absence of rectal perforation
    (Methylene blue rectal injection)
  - Ureteral peristaltism
    is satisfactory
Posterior vaginal fornix excision?

- Systematic vaginal excision in cases of DIE
  - Macroscopic lesion preoperatively detected
  - Apparently normal vagina? \((\text{Angioni et al 2006})\)

Microscopic infiltration of the vaginal wall is diagnosed in 10% of cases even in absence of macroscopic lesions

Quality of life is improved
Deep infiltrating endometriosis

- Without bowel resection
  - Advantages:
    - Rate of intraoperative complications is minimal
    - Improved quality of life

Angioni et al 2006
Dubernard et al 2006
DIE with bowel infiltration:

- Preoperative assessment
- Type of surgical treatment?
  - Exision of the nodular lesion
    - Without bowel resection: *shaving technique*
      - Uterosacral ligaments infiltration
      - Vaginal infiltration
    - With bowel resection:
      - discoid or segmental bowel resection
      - laparoscopy; laparotomy; laparoscopically assisted technique
With bowel infiltration

- Baryum enema: irregularities of anterior rectal - sigmoid wall
With bowel infiltration
## Colorectal surgery for endometriosis

<table>
<thead>
<tr>
<th>Authors</th>
<th>Segment-resection</th>
<th>Full-thickness disc excision</th>
<th>Superficial thickness excision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nezhat et al. (1992)</td>
<td>10</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Redwine and Wright (2001)</td>
<td>6</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>Jerby et al. (1999)</td>
<td>7</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>Possover et al. (2000)</td>
<td>34</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Duepree et al. (2002)</td>
<td>18</td>
<td>5</td>
<td>26</td>
</tr>
<tr>
<td>Daraï et al. (2005)</td>
<td>40</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Campagnacci et al. (2005)</td>
<td>3</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Ribeiro et al. (2006)</td>
<td>115</td>
<td>2</td>
<td>8</td>
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<tr>
<td>Panel et al. (2006)</td>
<td>18</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Jatan et al. (2006)</td>
<td>14</td>
<td>20</td>
<td>61</td>
</tr>
<tr>
<td>Lyons et al. (2006)</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Brouwer and Woods (2007)</td>
<td>137</td>
<td>58</td>
<td>18</td>
</tr>
<tr>
<td>Wills et al. (2009)</td>
<td>85</td>
<td>82</td>
<td>0</td>
</tr>
<tr>
<td>Minelli et al. (2009)</td>
<td>357</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>855</strong></td>
<td><strong>205</strong></td>
<td><strong>154</strong></td>
</tr>
</tbody>
</table>

N=1214

- 70 %
- 17 %
- 13 %
Bowel endometriosis
Section of the distal part of the rectum (Endo GIA)
Minilaparotomy for exteriorisation of the bowel
BOWEL ENDOMETRIOSIS
BOWEL ENDOMETRIOSIS

- With bowel resection: II Step
BOWEL ENDOMETRIOSIS

- With bowel resection

End-to-end colorectal anastomosis (CCEA)
BOWEL ENDOMETRIOSIS

- With bowel resection

Final view
Bowel Endometriosis

Conversion rate to laparotomy during laparoscopic colorectal resection for endometriosis

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of patients</th>
<th>Conversion to laparotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nezhat et al. [38]</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Jerby et al. [14]</td>
<td>30</td>
<td>4 (13.3%)</td>
</tr>
<tr>
<td>Possover et al. [35]</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>Duepree et al. [36]</td>
<td>46</td>
<td>4 (8.7%)</td>
</tr>
<tr>
<td>Daraï et al. [37]</td>
<td>40</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Campagnacci et al. [39]</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Ribeiro et al. [40]</td>
<td>125</td>
<td>0</td>
</tr>
<tr>
<td>Panel et al. [41]</td>
<td>21</td>
<td>2 (9.5%)</td>
</tr>
<tr>
<td>Jatan et al. [42]</td>
<td>95</td>
<td>19 (20%)</td>
</tr>
<tr>
<td>Lyons et al. [43]</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>420</td>
<td>7.8%</td>
</tr>
</tbody>
</table>
## Digestive complications of colorectal surgery

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients</th>
<th>Rectovaginal fistula</th>
<th>Linkage of anastomosis</th>
<th>Secondary ileo-colost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nezhat et al. (1992)</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jerby et al. (1999)</td>
<td>26</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Possover et al. (2000)</td>
<td>34</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Daraï et al. (2005)</td>
<td>40</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Campagnacci et al. (2005)</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ribeiro et al. (2006)</td>
<td>125</td>
<td>2</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Panel et al. (2006)</td>
<td>21</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Lyons et al. (2006)</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Brouwer and Woods (2007)</td>
<td>213</td>
<td>2</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>Wills et al. (2009)</td>
<td>167</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Minelli et al. (2009)</td>
<td>357</td>
<td>14</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>1003</strong></td>
<td><strong>27 (2.7%)</strong></td>
<td><strong>10 (1%)</strong></td>
<td><strong>21 (2.1%)</strong></td>
</tr>
</tbody>
</table>
### DIE Excision and Recurrence

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Pain</th>
<th>Reoperation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fedele et al (2004)</td>
<td>28%</td>
<td>27%</td>
</tr>
<tr>
<td>Jatan et al (2006)</td>
<td>5.3%</td>
<td></td>
</tr>
<tr>
<td>Panel et al (2006)</td>
<td>4.8%</td>
<td></td>
</tr>
<tr>
<td>Daraï et al (2007)</td>
<td>16.4%</td>
<td></td>
</tr>
<tr>
<td>Vignali et al (2005)</td>
<td>24%</td>
<td>10%</td>
</tr>
<tr>
<td>Brouwers- Woods (2007)</td>
<td>4.6%</td>
<td></td>
</tr>
</tbody>
</table>

- **Rectal dissection** 22%
- **Anterior excision** 5.17%
- **Segmental rectal** 2.19%
Laparoscopic Laser Surgery for Endometriosis - Feb 2011

<table>
<thead>
<tr>
<th>r-AFS score</th>
<th>N</th>
<th>DIE Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I-II</td>
<td>1153</td>
<td>-</td>
</tr>
<tr>
<td>Stage III-IV</td>
<td>1092</td>
<td>128</td>
</tr>
<tr>
<td>Total</td>
<td>2245</td>
<td>(5.7%)</td>
</tr>
</tbody>
</table>

Karaman 2011
Brüksel Kadın Sağlığı ve Tüp Bebek Merkezi, Istanbul
Hopital Français Reine Elizabeth, Brussels
Institut Medical Edith Cavell, Brussels
Laparoscopic surgery for DI Endometriosis (128 cases)

- Laparoscopic removal of the rectovaginal nodule 83
  - with resection of posterior vaginal fornix 54
  - Only nodule excision 29
- Laparoscopy assisted sigmoidectomy 31
- Laparoscopic discoid resection of sigmoid 9
- Laparoscopic partial bladder excision for vesical nodules 5

KARAMAN 2011
Endometriomas: Conclusions

- If infertility related endometriosis, 4 factors impact the decision: The age, whether other infertility factors (e.g., male factor), the stage of endometriosis, patient preference.

- For women with minimal/mild endometriosis at diagnostic laparoscopy, recommendation of ablation or excision of endometriotic implants (Grade 1A).

- For young women with moderate/severe endometriosis at laparoscopy, recommendation to resect endometriosis and adhesions (Grade 2C).

- Repeated surgical procedures do not enhance fertility.

- Endometrioma resection before IVF only, if pelvic pain, suspicion of ovarian malignancy or endometrioma interfere egg retrieval.
DIE : Conclusions

- Surgery is needed
- Conservative surgery
- Preoperative assessment is required
- Several surgical approaches
  - Absence of bowel infiltration: shaving technique
  - Presence of bowel infiltration: segmental colorectal resection, discoid resection, stapled resection
- Postoperative results
  - QOL
  - Fertility
  - Recurrence
  - Complications
Deep Endometriosis: Conclusions

- Complete removal of the lesion is needed  
  - ↓ Risk of recurrence
- Appropriate surgical team  
  - ↓ Risk of complications
- Need for a multidisciplinary approach
  - Diagnosis
  - Surgery
Deep Endometriosis: Conclusions

- Complete removal of the lesion is needed
  -↓ Risk of recurrence
- Appropriate surgical team
  -↓ Risk of complications
- Need for a multidisciplinary approach
  - Diagnosis
  - Surgery

Need for Referral centres
Conclusion

- Laparoscopy has a major impact in diagnosis and management of all stages including retroperitoneal, rectovaginal, intestinal and vesical endometriosis.
Conclusion

• Medical treatment for endometriosis is crucial for prevention of recurrence.
• The latest pills are generally the most expensive, but not necessarily the most cost-effective; they can be used when OCs and progestin have failed.
• OC used cyclically or continuously, may constitute an adequate first-line option for PERITONEAL and OVARIAN ENDOMETRIOSIS, whereas low-dose oral norethisterone acetate is probably the best choice for RECTOVAGINAL ENDOMETRIOSIS

• The extensive epidemiologic information available demonstrates that OCs and progestins are safest medical alternative for long-term treatments of endometriosis
DIE has Two Major Specificities

- DIE is a multifocal pathology: USL, vagina, bladder, intestine, ureter
- DIE is very often associated with other endometriotic lesions:
  - Unique lesion 10%
  - Superficial lesions 61.3%
  - Endometriomas 50.5%
  - Adhesions 74.2%

Somigliana et al. Hum Reprod 2004
Association of Ovarian Endometriomas and DIE

- Somigliana 2004: 50%
- Chapron 2009: 23%

Associated ovarian endometrioma is a marker for greater severity of DIE

Deep Infiltrating Endometriosis

- Presence of Endometrial like Glands and Stroma > 5mm under the peritoneum

- These lesions are considered very active and are strongly associated with increasing pelvic pain, deep dysparenia, rectal pain, rectorrugia and urinary symptoms.

Anatomic Reconstruction
Prof. Dr. Yücel Karaman
Endometriosis
Conclusion

- Endometriosis is an estrogen-dependent chronic inflammatory disease.
- It can be effectively cured by definitive surgery.
- But, prolonged medical therapies after conservative surgery may be needed, as for most chronic inflammatory disorders in general.