

LAPAROSCOPIC ENDOMETRIOSIS SURGERY

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Types of Endometriosis

- Superficial Endometriosis:
 1. Peritoneal endometriosis
 2. Ovarian superficial endometriosis
- Ovarian Endometriomas
- Deeply Infiltrating Endometriosis (DIE)
(Extragenitale Endometriosis)

Why we do the surgery?

Arguments in favor of surgery

1. Create spontaneous pregnancy (40-70%)
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 surgery

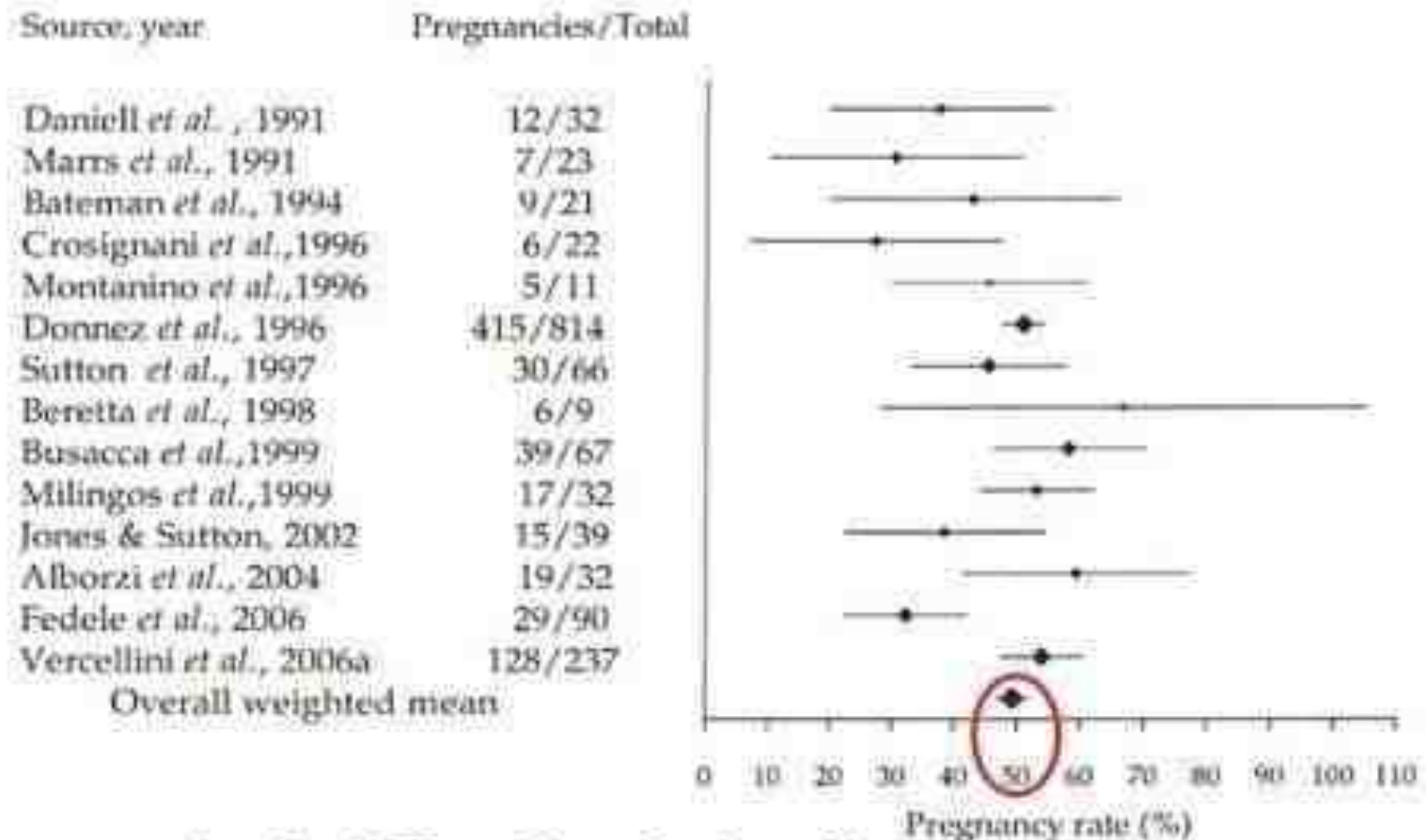
1. Decreased ovarian reserve, especially in repeated and bilateral surgery
2. Recurrence
3. Complexity of the endometriosis surgery

Surgery for endometriosis associated infertility

Surgery for endometriosis-associated infertility: a pragmatic approach

Paolo Vercellini^{1,3,4}, Edgardo Somigliana^{2,3}, Paola Viganò¹, Annalisa Abbiati^{1,2}, Giusy Barbara¹, and Pier Giorgio Crosignani¹

188, 2009



Pregnancy rates after LPS excision of endometriomas

Evidence-based medicine

- Which attempts to apply the best available evidence gained from scientific methods, tends to consider everything that is not proven as untrue, thus disregarding valuable observational information.

Endometriosis and RCTs

- Because endometriosis is a **highly variable** disease
- May manifest with **different clinical** scenarios
- It often may **not be incorporated** in inclusion and exclusion criteria of most RCTs

Management of the Endometrioma

- Because of lack of RCTs, there is no consensus about the proper management of an endometrioma in women who intends to conceive
- Once other potential infertility factors have been ruled out, surgery should be offered early, because the primary benefit of surgery to have naturel conception is higher shortly after surgery

Damage to the ovary: Bias

- Different **surgeon**, different **surgical techniques**, different **patient populations**, different **duration of follow-up** may account for the inconsistent results reported on post-op ovarian reserve.
- **Quality of the surgery**, **thickness of removed specimen** and of **ovarian tissue inadvertently removed**, **aggressive coagulation** ect..

All infertile patients with endometrioma have to be operated **except :**

- Advanced age and infertility
- Diminished ovarian reserve
- Severe male factor
- Bilateral endometriomas (optional)
- Recurrent endometrioma (optional)
- Bilateral recurrent endometriomas
- Lack of surgical skill and experience

Endometriosis may lead to Infertility by:

- Distorted pelvic anatomy
- Reduction of ovarian function
- Changed peritoneal environment
- Poor oocyte quality and implantation rate

Endometriomas can be associated with:

- Pelvic adhesions
- Abnormal tubo-ovarian and douglas anatomy
- Hydrosalpinx or tubal phymosis
- DIE, frozen pelvis

Endometriosis: Anatomic distortion



Bilateral Big Endometriomas (sh)



Endometriosis: Anatomic distortion



Could we do the IVF for all patients with endometriosis?

- It has been estimated that **25% to 30%** of infertile women have endometriosis and
- **30% to 50%** of women with endometriosis demonstrate infertility
- But, endometriosis represents only **3.9% of 95625 IVF cycles** in USA in 2010

ASRM committee opin. Fertil Steril 2012

Surry et al Semin Reprod Med 2013

Types of Endometriomas

- Typical endometrioma

- Atypical endometrioma:

unilocular cyste with papillary projections inside and any flow inside the papillary projections

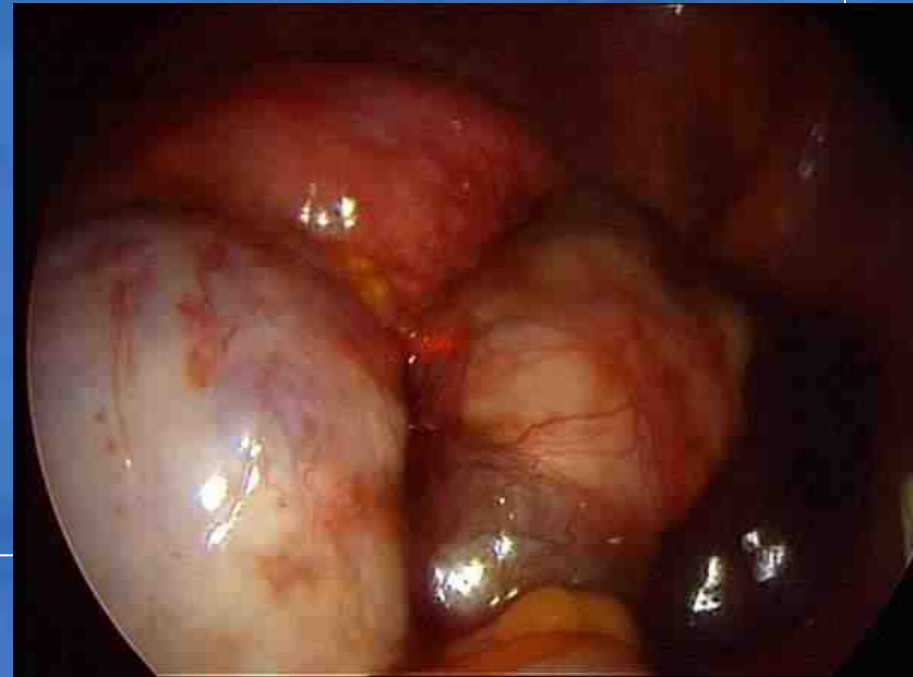
Misclassification of the Endometriomas

- Misclassify malignant lesions as endometriomas in 2% to 9% of cases
- **Borderline ovarian** tumors
- **Endometrioid** and **clear cell** ovarian carcinomas

Muzzi et al. JMIG 2014

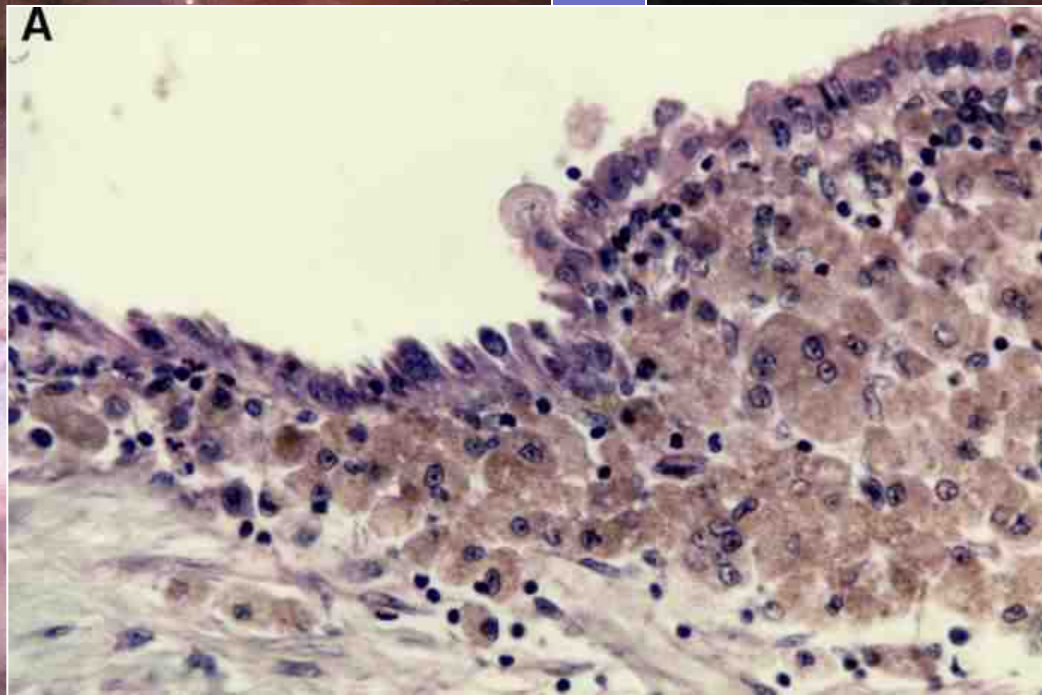
Ultrasound

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



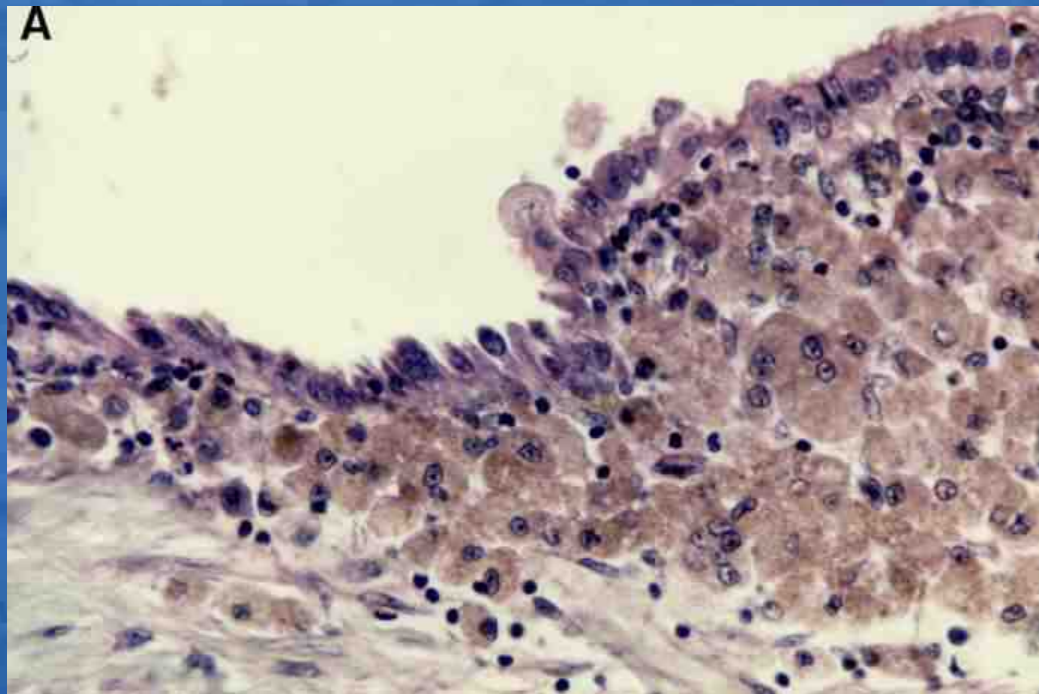
OVARIAN ENDOMETRIOSIS

Ovarian endometriosis is confirmed at laparoscopy and by histologic examination



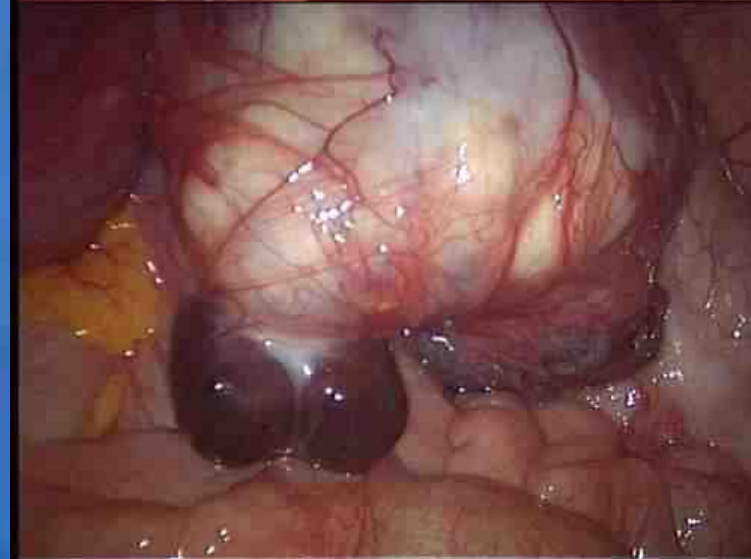
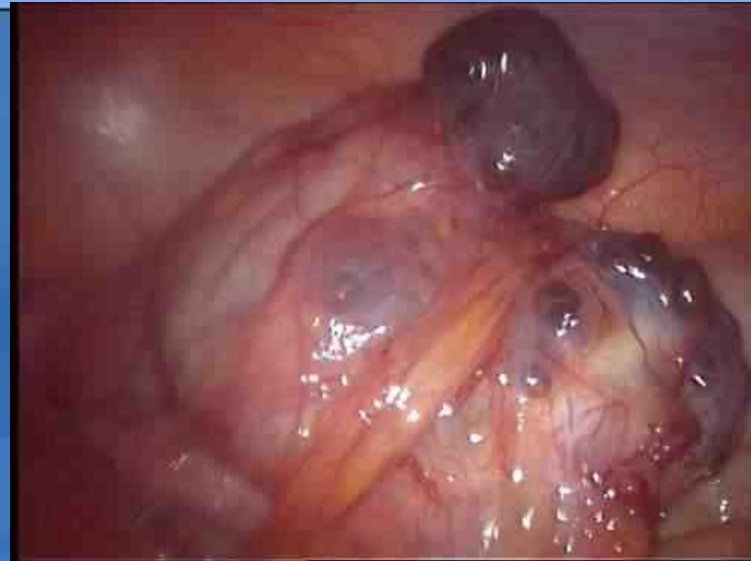
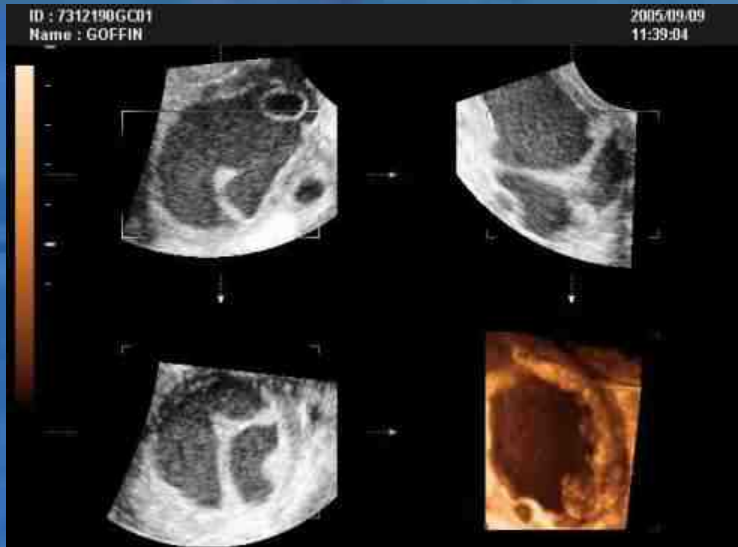
Endometriosis and cancer

Theoretical risk of malignancy by increasing the rate of dyskaryosis



(Blumenfeld Fertil Steril 2004 ; 81: 487-92)

Ovarian endometriosis mimicking malignancy



Key points of the Surgery

- When ?
- How ?
- To Whom ?



Management of women with endometriosis

Guideline of the European Society of Human
Reproduction and Embryology

ESHRE Endometriosis Guideline Development Group

September 2013

Recommendations

In infertile women with AFS/ASRM stage I/II endometriosis, clinicians should perform operative laparoscopy (excision or ablation of the endometriotic lesions) including adhesiolysis, rather than performing diagnostic laparoscopy only, to increase ongoing pregnancy rates (Jacobson, et al., 2010, Nowroozi, et al., 1987).

A

In infertile women with AFS/ASRM stage I/II endometriosis, clinicians may consider CO2 laser vaporization of endometriosis, instead of monopolar electrocoagulation, since laser vaporisation is associated with higher cumulative spontaneous pregnancy rates (Chang, et al., 1997).

C

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).

A

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.

GPP

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., 2006a).

B

Before the surgery

- Patient age
- Pre-op AFC, AMH, D₃ hormones levels
- Ovarian volume and vascularisation
- Recurrence, bilaterality
- Additional pathologies
- Additional symptoms
- Patient's desire

Laparoscopic surgery for endometriomas (1092 cases)

- Age :

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

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

Karaman 2011

Endometrioma diameters

	Patients	
< 2 cm	204	19%
2-5 cm	601	55%
6-10 cm	210	19%
> 10 cm	77	6%
Total	1092	

Bilateral endometriomas: 164/1092 15%

Karaman 2011

Cumulatif pregnancy rate (640 patients)

- | | P.R. |
|---------------|-------|
| • Stage 1-2 | : 62% |
| • Stage 3-4 | : 48% |
| if r- AFS >70 | : 0% |

Karaman 2011

1. Surgeon's performance index

- **Ovarian reserve alteration** before and after surgery (AFC, AMH, D3 hormones, inhibine)
- **Reccurrence rate** with in 1 year
- **Persistance of pain** after surgery (incomplet surgery, DIE, ect)

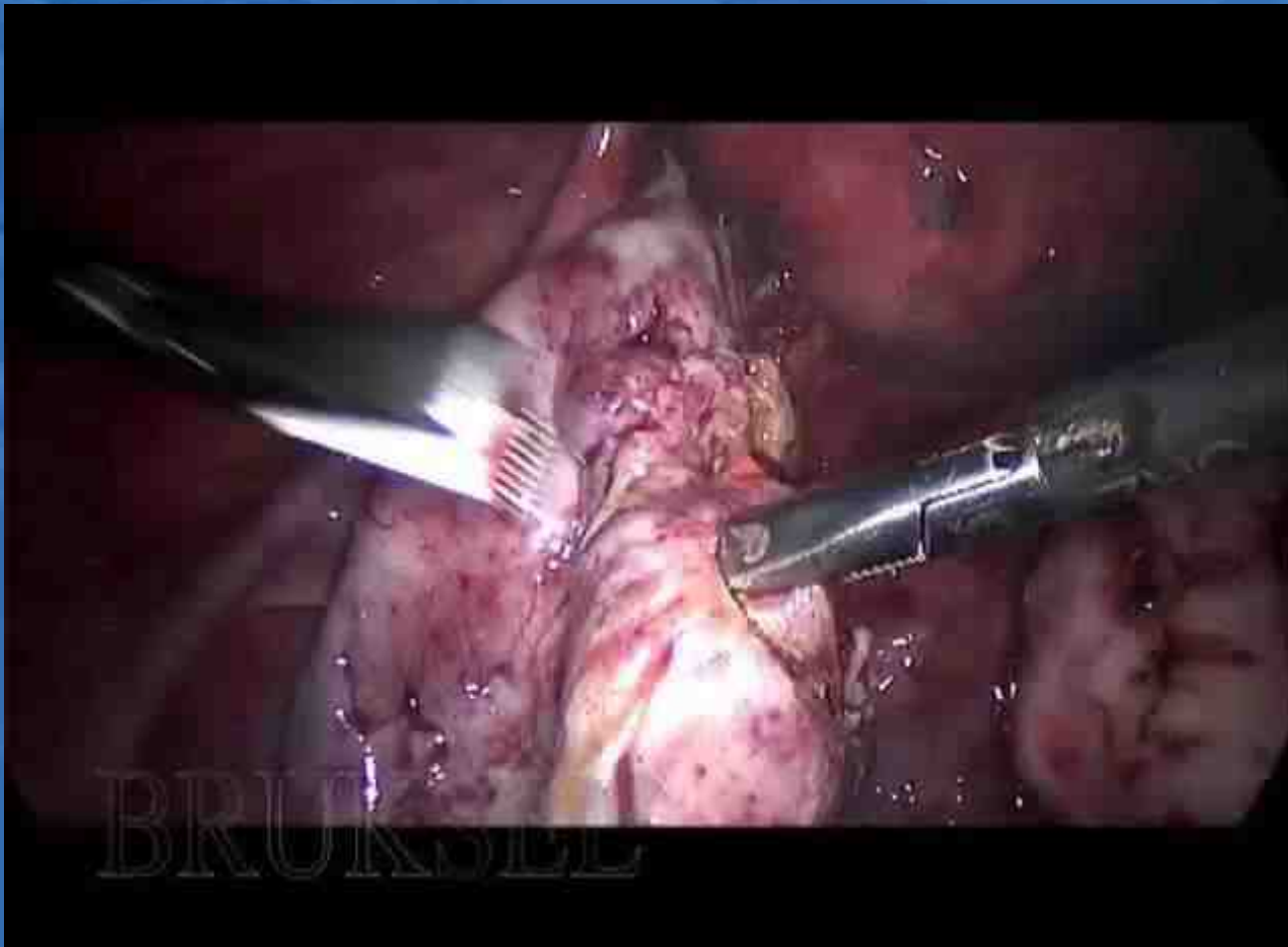
2. How can we protect better ovarian reserve during cystectomy?

- In an attempt to lower the ovarian damage, a **two step operative procedure** or **combination of techniques** has been proposed.

Endometrioma surgery



Endometrioma surgery



How to perform a good surgery

- The **thickness of the removed specimen** and the **thickness of the ovarian tissue** inadvertently removed together with the endometrioma wall
- Only **pinpoint bipolar coagulation** should be used step by step on small bleedings

Endometrioma surgery:stripping



Protection of ovarian blood supply

3. Protection of the hilus and utero-ovarian vessels

- **Non aggressive coagulation** (fine bipolar forceps), pin-point hemostasis
- Laser vaporisation of hilar part of the endometrioma (**combined treatment**)
- **Sutur of the hilus** for bleeding ??
- **Protection of utero-ovarian vessels**

Hemostasis by bipolar coagulation vs suture after surgical stripping of bilateral ovarian endometriomas: a randomised controlled trial
Ferrero S et al. J Minim Invasive Gyn. Nov 2012

- 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 groups at 3-6-12 months of follow up.
- Pregnancy rate, time to conception and rate of endometrioma recurrence was similar in the 2 groups.

Post-op Ovarian reserve evaluation

Post surgical ovarian trauma

- AFC
- AMH, D₃ hormones
- Residual post surgical ovarian volume
- Pulsality and resistance indexes

- The effect of surgery for endometrioma on ovarian reserve evaluated by AFC :a systematic review and meta-analysis.
L.Muzzi et al. Human Reprod 2014

- Ovarian reserve evaluated with AFC is not reduced after surgical treatment of an endometrioma
- A lower AFC is present for the affected ovary both before and after surgery
- Concerns have been raised as to the reliability of AMH as a marker of ovarian reserve
- Based on these findings, surgical treatment of an endometrioma may be considered safer for the ovarian reserve than previous thought .

Effect of Surgery for Endometrioma on Ovarian Function: A Different Point of View.

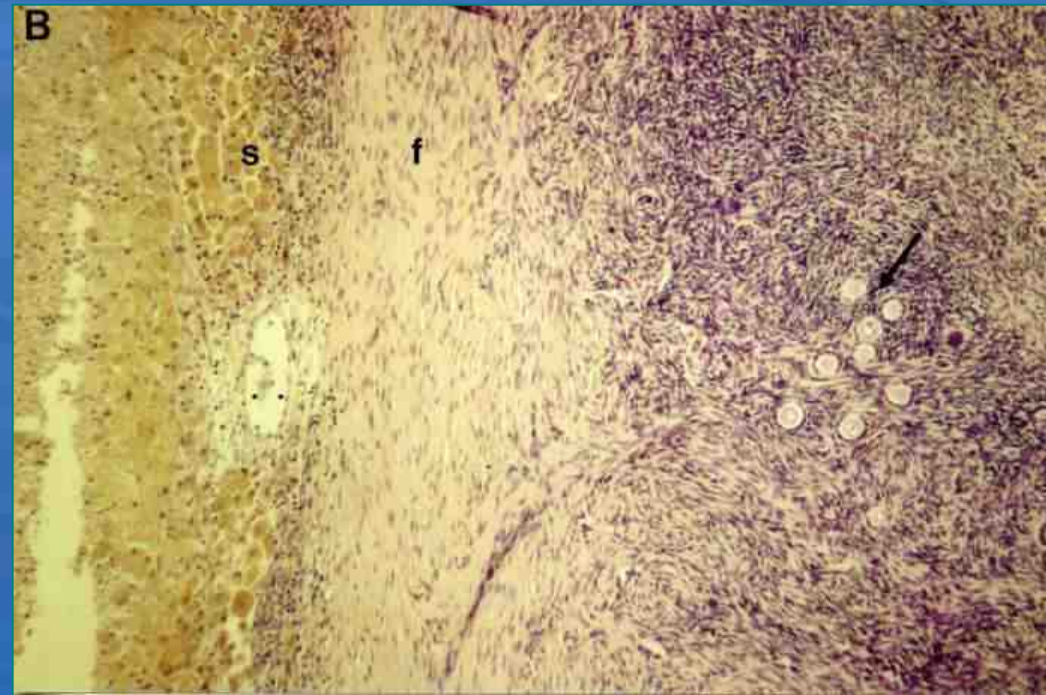
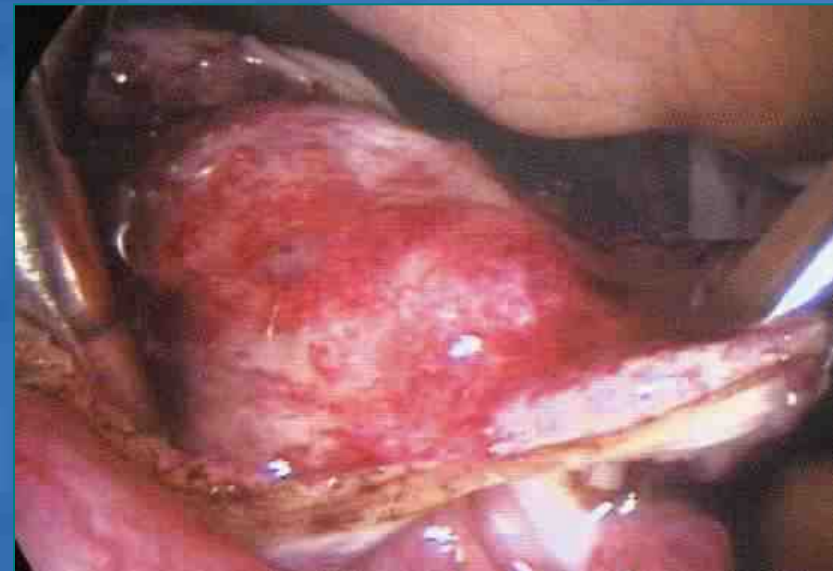
Muzzi et al. JMIG 2014

- Surgical excision may reduce ovarian reserve
- Because of inconsistent results and methodologic flaws of AMH as a marker of ovarian reserve, **AFC may be a more accurate noninvasive marker than AMH**
- And this **yield different conclusions** in so far as postsurgical damage to the ovary.

Ovarian Endometriomas

Cystectomy:

Risk of removal normal ovarian tissue and
ovocytes



Residual ovarian volume after surgery

Table IV Residual ovarian tissue before surgery and after surgery

	N	Mean ± SD
Endometriomas		
Ovarian tissue volume BEFORE to surgery (cm ³)	67	19.9 ± 17.8
Ovarian tissue volume AFTER surgery (cm ³)	67	5.1 ± 3.2*†
Dermoids		
Ovarian tissue volume BEFORE to surgery (cm ³)	62	10.1 ± 11.4‡
Ovarian tissue volume AFTER surgery (cm ³)	62	6.7 ± 3.3‡

* $P < .001$ ovarian volume before vs after surgical removal of endometriomas.

† $P < .05$ ovarian volume after surgical removal of endometriomas vs ovarian volume after surgical removal of dermoid cysts.

‡ NS ovarian volume before vs after surgical removal of dermoid cyst.

Table V Residual ovarian volume after surgery vs contralateral untreated ovaries

Ovaries after laparoscopic cystectomy	N	Mean ± SD
Endometriomas		
Normal treated ovary		
Ovarian tissue volume (cm ³)	40	4.3 ± 2.3*†
Contralateral untreated normal ovary		
Ovarian tissue volume (cm ³)	40	9.7 ± 3.9
Dermoids		
Normal treated ovary		
Ovarian tissue volume (cm ³)	46	7.1 ± 3.5‡
Contralateral untreated normal ovary		
Ovarian tissue volume (cm ³)	46	8.3 ± 3.1

* $P < .001$ volume treated vs contralateral untreated ovaries with endometriomas.

† $P < .001$ volume of treated ovaries with endometriomas vs treated with dermoids.

‡ NS volume treated vs contralateral untreated ovaries with dermoids.

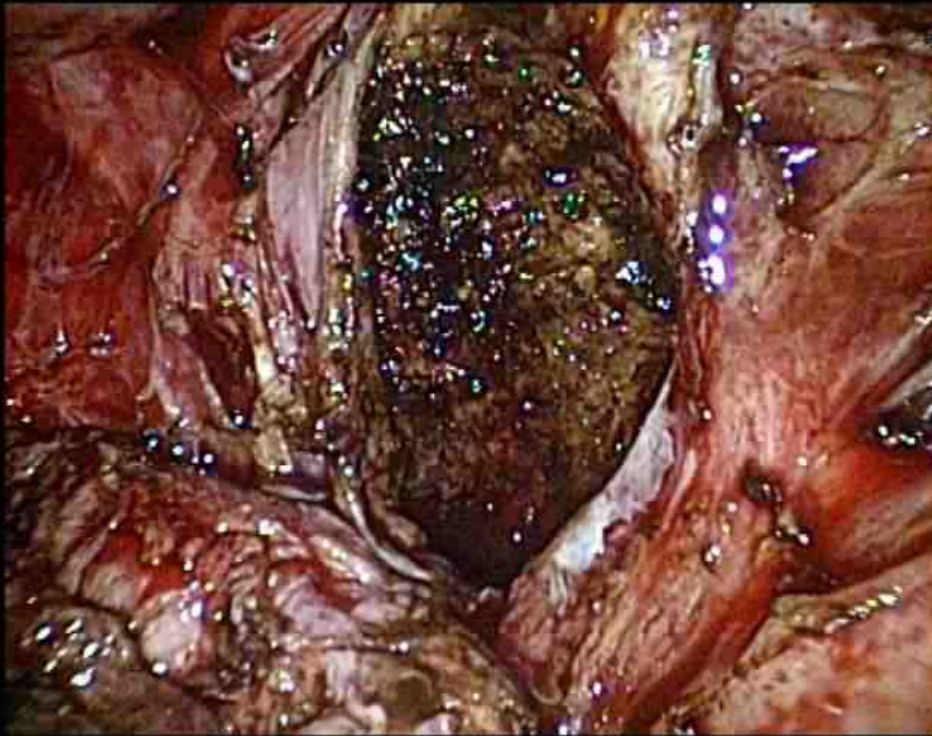
Exacoustos et al. Am J Obstet Gynec, 2004

Surgical Techniques

- Complete **excision** of the cyst wall
- **Ablation** (laser, bipolar energy, plasmajet)
- **Combined technique** (excisional and ablative surgery)
- **3 stage technique** (fenestration-GnRH 3 months-second laparoscopy with laser ablation of the cyst wall) but not cost-effective.

Ovarian Endometriosis

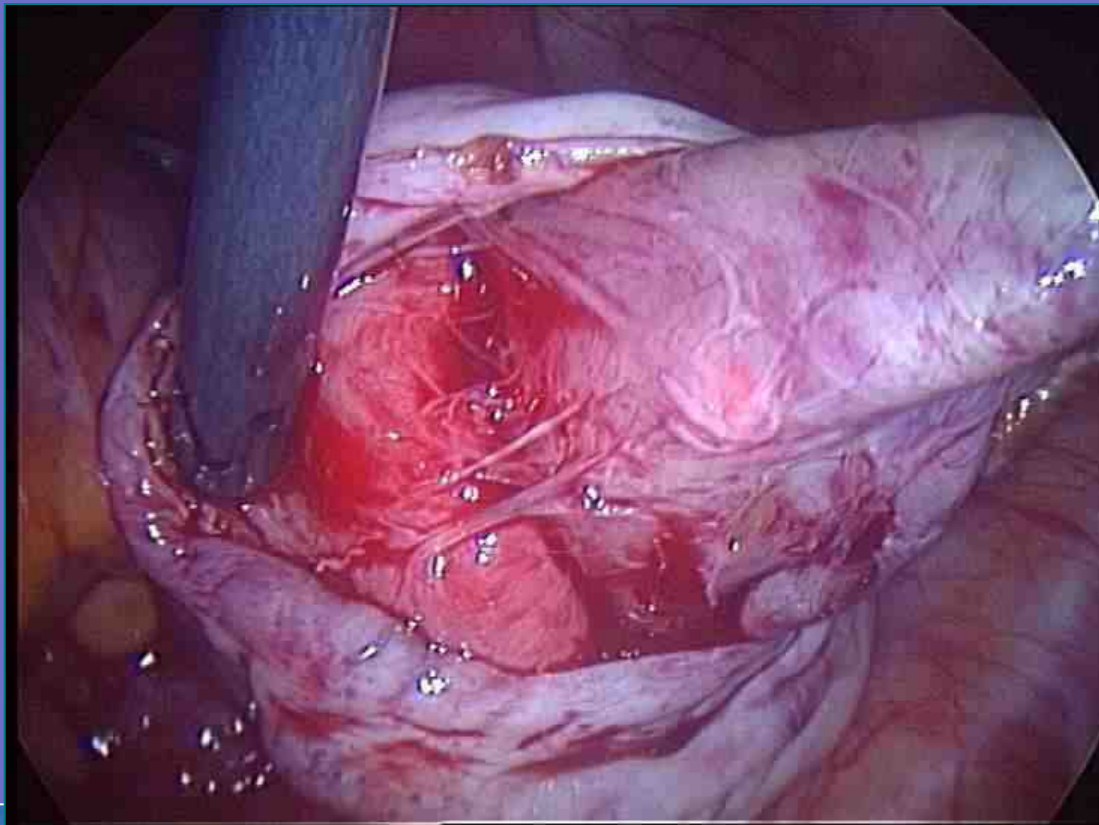
Ablation: Destruction of the cyst wall



Plasmajet
CO₂ Laser
KTP Laser
Bipolar coag.

Ovarian Endometriomas

Cystectomy: Dissection of the cyst wall from the ovarian cortex



Excisional surgery versus ablative surgery for ovarian endometriomata : 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 Rprod 2005 ; 11: 3000-7)

The Combined Technique

- Can be used in which the risk of the damage of the ovarian reserve is higher as :

Bilateral endometriomas

Recurrent endometriomas

But insufficient evidence (Donnez, Muzzi)
to recommend this technique

Combined technique



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 2

Ovarian volume and AFC 6 months after surgery in women with unilateral endometriomas and contralateral normal ovaries serving as controls.

	Ovarian volume (cm ³)	AFC
Combined technique (n = 20)	7.45 ± 2.93	5.5 ± 2.4
Contralateral normal ovaries (n = 20)	7.82 ± 3.91	5.7 ± 1.6

RECURRENCE

- 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

Surgery after recurrence or bilateral endometriomas

- **Possible damage** to the ovarian reserve due to disease or the surgery
- Surgical treatment **should be mandatory but when performed by experts** capable of preventing more damage from surgery than from the disease itself.
- A second surgery will have the paradoxical effect of ovarian reserve, than **ART should be considered the treatment of choice.**

Surgery for recurrent endometriosis

- **Repeated surgery** to treat recurrent endometriosis have the same limitations as primary surgery with **long term recurrence rate 20% to 40%**
- Only **25% of women conceive (half of the primary surgery)** after repeated surgery

Berlanda et al Curr Opin Obst Gyn 2010

Del Forno et al.J.Endometriosis 2013

Is endometrioma surgery necessary before IVF?

- **No**, 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.
- **Except**: pelvic pain, suspicion of malignancy, egg retrieval difficulties, IVF failure.

Conclusion

- The management of women with endometrioma before IVF should be individualized
- All the advantages and disadvantages should be fully discussed with the patient
- The risks of surgery with previous surgery or suboptimal ovarian reserve should be carefully considered and balanced

Conclusion

- Surgery in patients with endometrioma and infertility is a good option and gives 50% of PR.
- But surgery should be performed only by **experienced centers**.
- **Stripping technique** is still the only choice supported by strong scientific evidence
- The dual function of the surgery which improve fertility and reduce pain, can not be minimized or undervalued

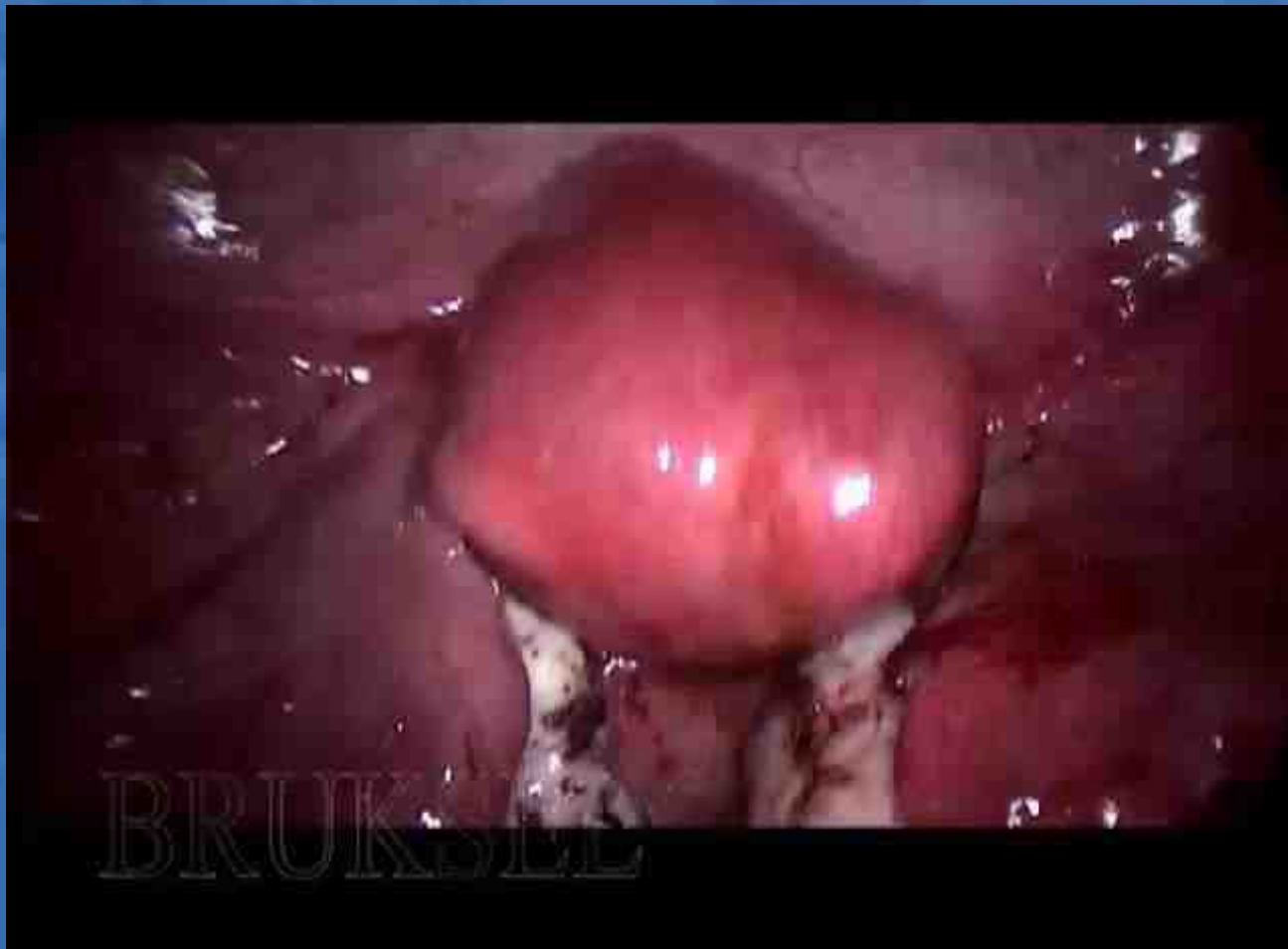
CONCLUSION

- **If infertility related endometriosis** 4 factors impact the decision: The age, whether other infertility factors (DOR, 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.

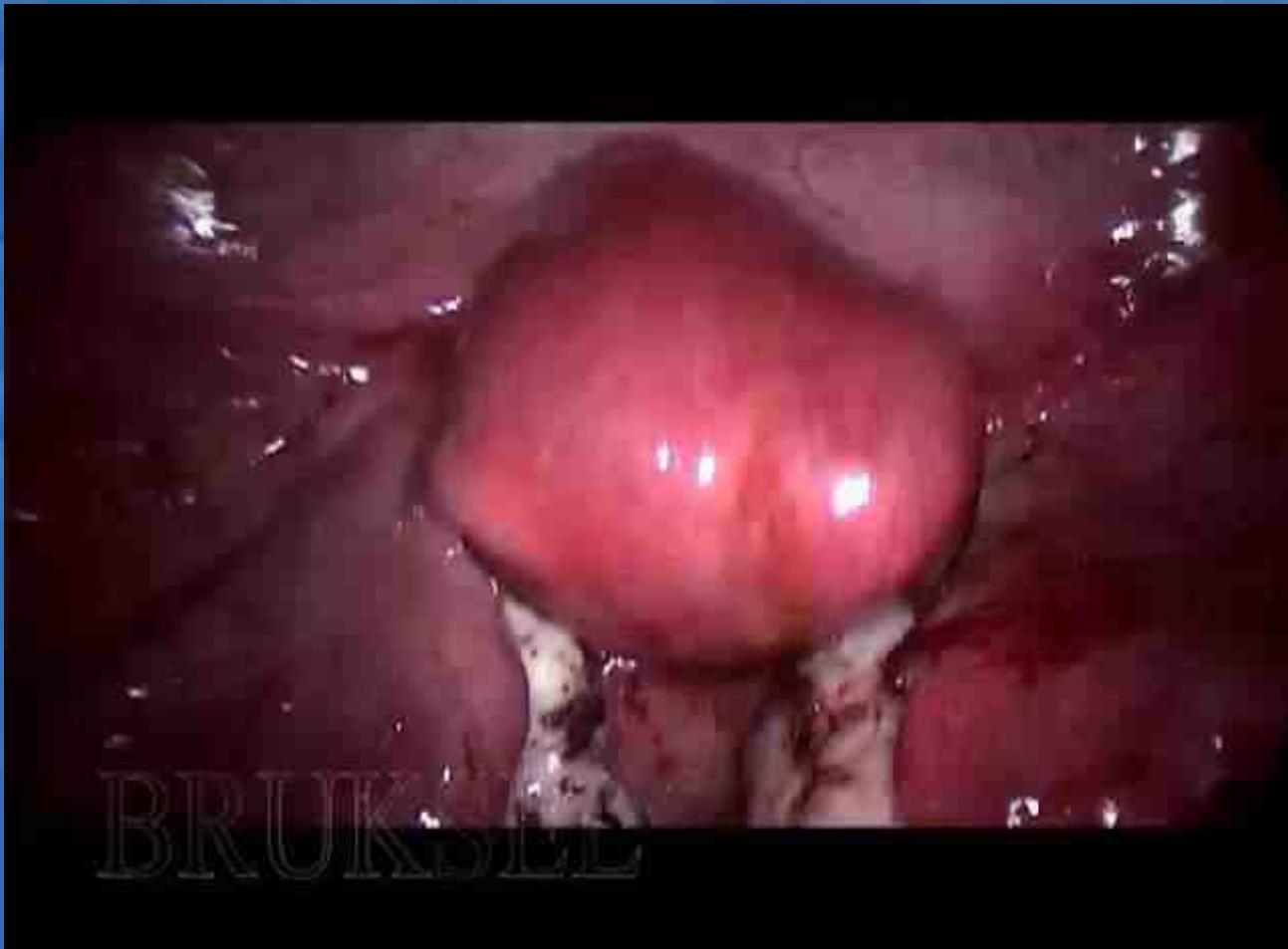
Bilateral Big Endometriomas (long)



Final view



Final view of bilat.cystectomy

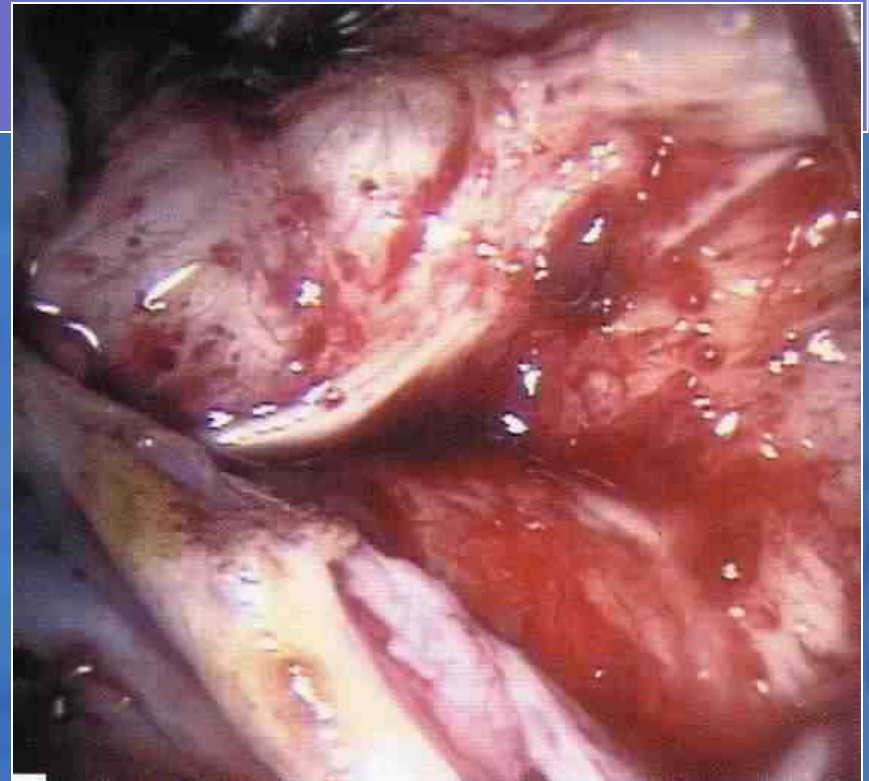
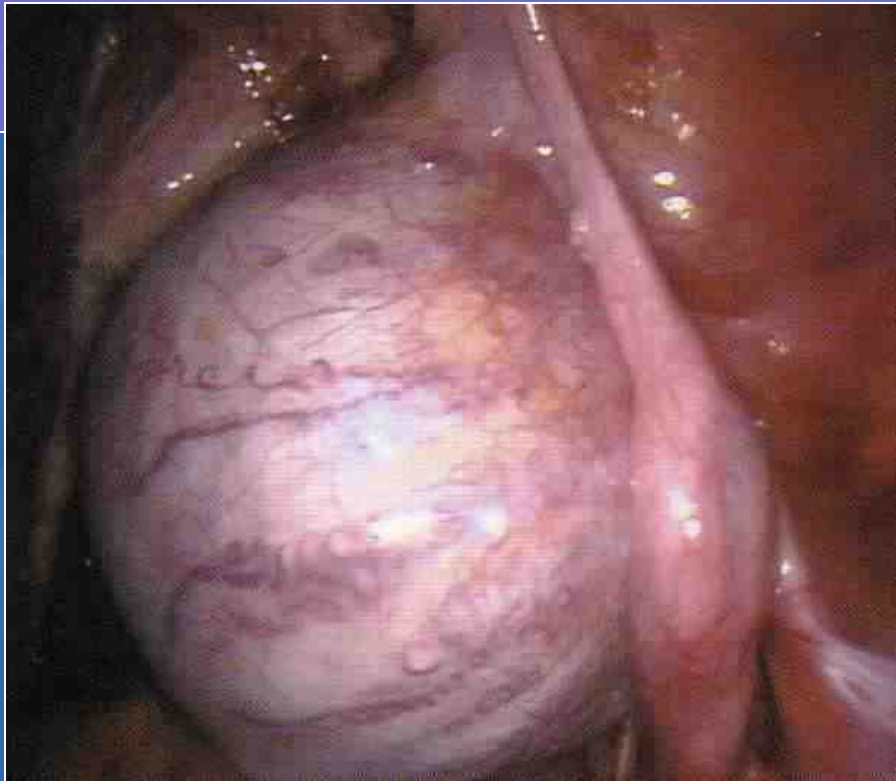


Protection of the hilus vessels



OVARIAN ENDOMETRIOSIS

Ovarian endometriosis is confirmed at laparoscopy and by histologic examination



Controversy in the treatment of Endometriomas

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

Surgery for Endometriosis

- How can we avoid ovarian **remnant syndrome** ?
- 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**?

Association of Ovarian Endometriomas and DIE

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

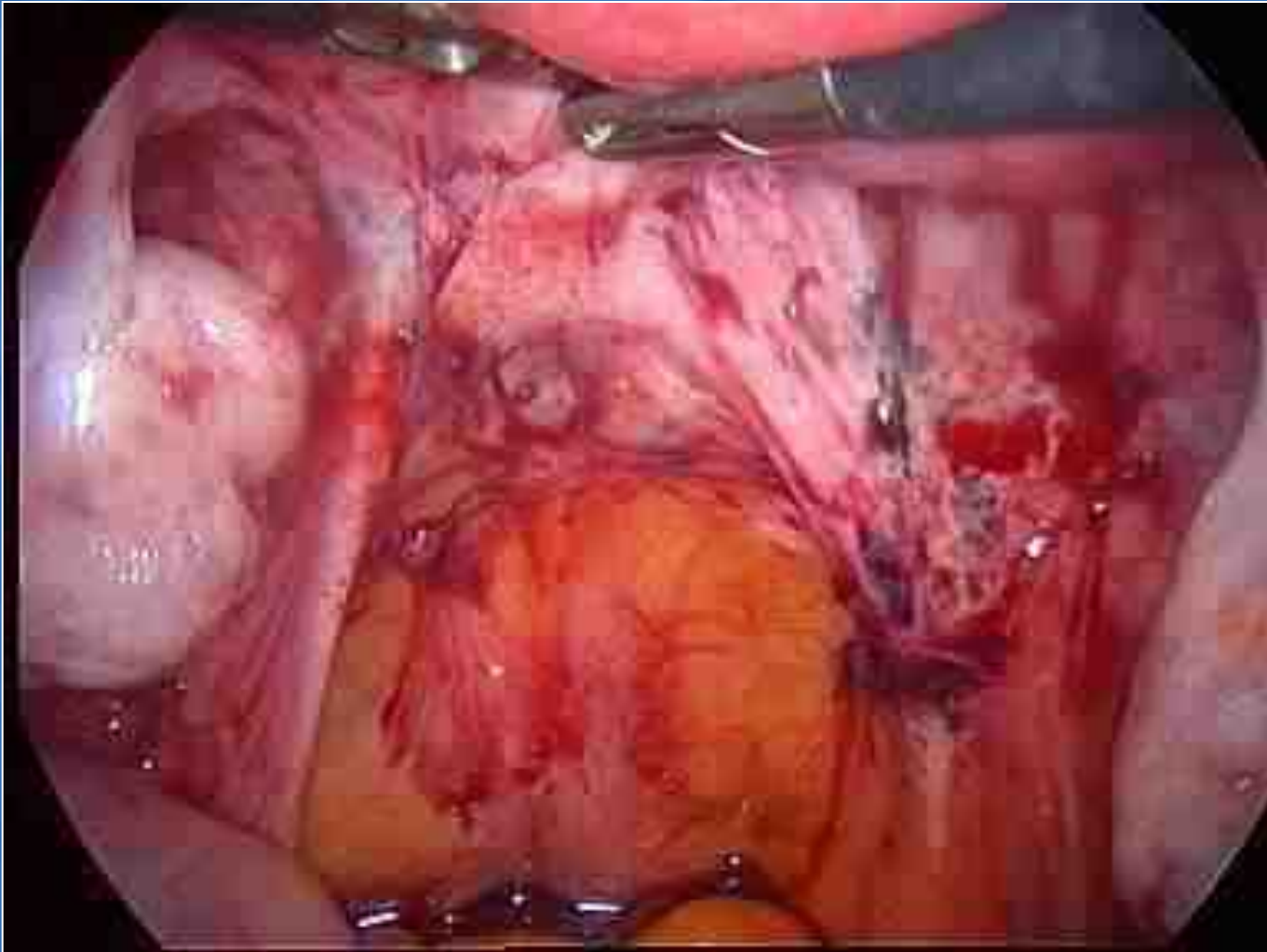
Associated ovarian endometrioma is a marker for greater severity of DIE

Surgical Indication of Ovarian Endometriomas :

If infertility related:

- AFC, D3 hormones,AMH,Inhibin*
- Age of patient*
- Other infertility factors*
- Uni/Bilaterale endometrioma*
- Re-surgery of endometrioma*
- Pre-IVF*

DIE and Peritoneal Endometriosis

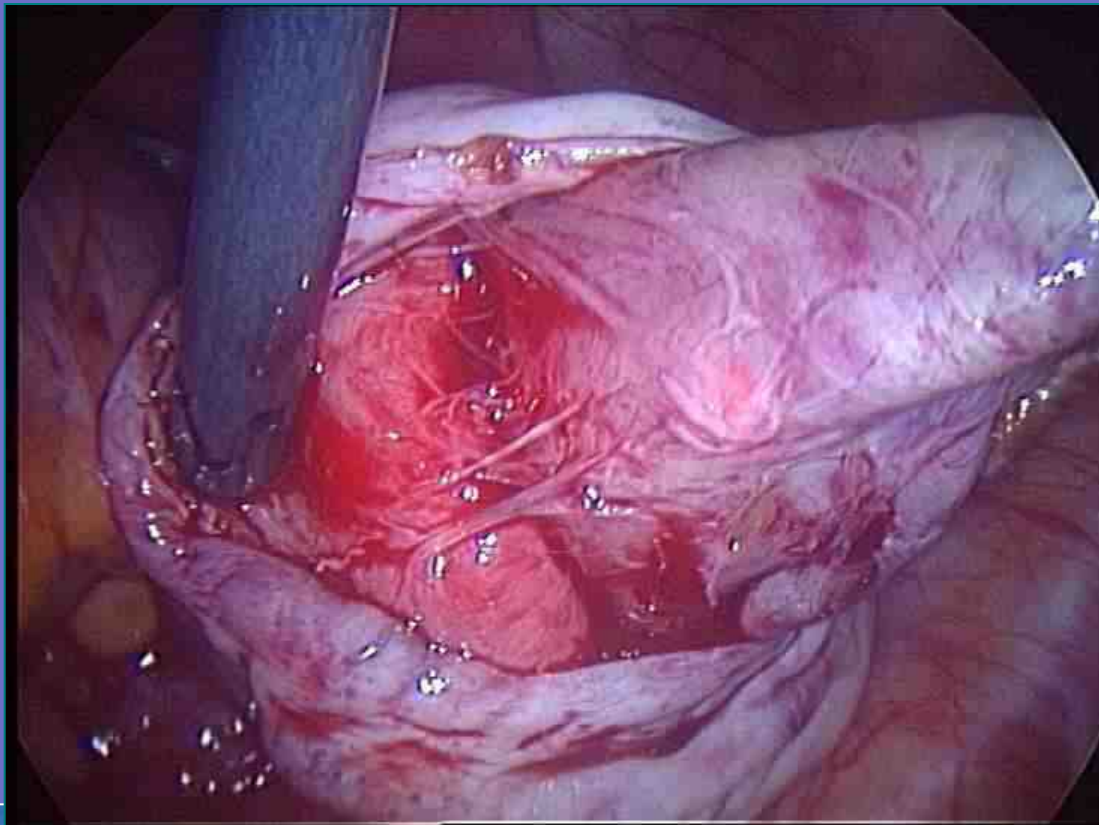


Surgery indication for endometriomas without infertility

- First line treatment is medical
- If persistence of pain after medical treatment than surgery is indicated
- Rapid growing of the endometrioma
- Suspicion of malignancy
- Size of the endometrioma ...

Ovarian Endometriomas

Cystectomy: Dissection of the cyst wall from the ovarian cortex



Ovarian Endometriomas

Cystectomy:

Risk of removal normal ovarian tissue and
ovocytes



Ovarian Endometriomas

- What is the impact of surgery on the ovarian tissue loss ?
- What kind of surgery has to be proposed ?
- What is the impact of ovarian endometriomas on IVF outcomes?



Management of endometriomas

- Ovarian response during IVF-ET after endometriomas removal : Retrospective studies

No decrease in the number of oocytes and embryos

Cystectomy

Canis et al. (2001)
Geber et al. (2002)
Marconi et al. (2002)

Cyst wall vaporization -
Cystectomy

Donnez et al.(2001)

Decrease in the number of oocytes

Cystectomy

Al -Azemi et al (2000)
Somigliana et al.(2003)

Management of endometriomas

In favor of surgery

- A cumulative Pregnancy Rate of 40 - 50 % at 1 year
- Risk of developing ovarian abscess during IVF procedure
- Risk of rupture of an ovarian endometrioma during first trimester of pregnancy.

(Garcia-Velasco Europ J Obst Gynec Reprod Biol 1998 ; 76: 41- 43)

- Theoretical risk of malignancy by increasing the rate of dyskaryosis

(Blumenfeld Fertil Steril 2004 ; 81: 487-92)



Surgical treatment of endometriosis associated infertility

Table II International guidelines on surgical treatment of endometriosis-associated infertility in asymptomatic women

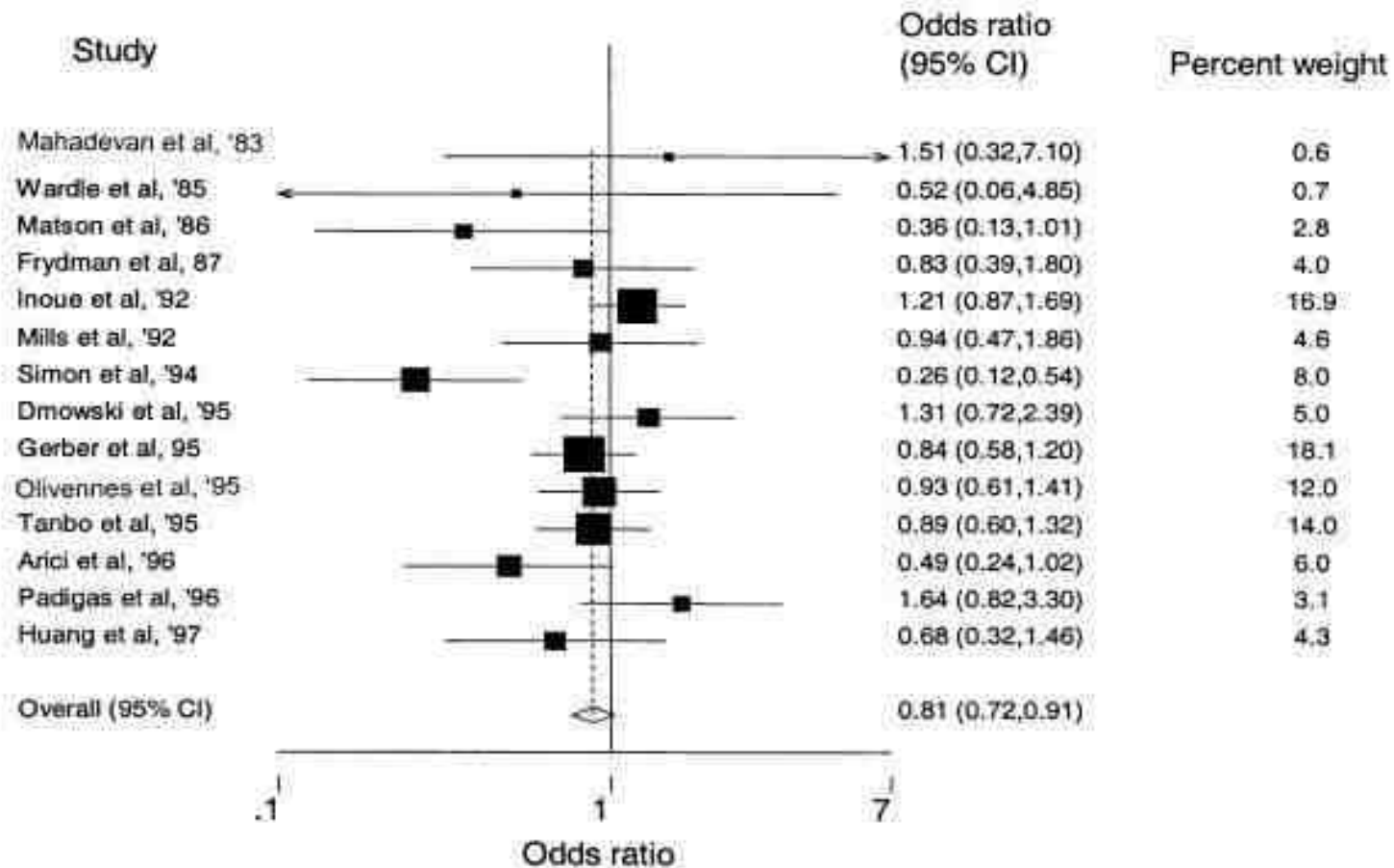
Clinical condition	Recommendation		
	ESHRE 2005	ASRM 2006	RCOG 2006
Normal-mild endometriosis (stage I-II disease)	Limited benefit: surgery recommended	Small benefit: surgery recommended	Demonstrated benefit: surgery recommended
Moderate-severe endometriosis (stage III-IV disease)	Possible but unproven benefit: surgery recommended	Possible benefit: surgery recommended	Possible benefit: recommendation uncertain
Best available medical treatment	No benefit: not recommended	No benefit: not recommended	No benefit: not recommended
Surgery before IVF	Recommended if endometrioma ≥ 4 cm	Doubtful benefit: no recommendation	Recommended if endometrioma ≥ 4 cm
Recurrent endometriosis	No recommendation	Second-line surgery: not recommended	No recommendation

Vercellini et al. *Hum an Reprod* 2008



Endometriosis and IVF

Decreased IVF success rate for patients with endometriosis



(Barnhart et al. Fertil Steril 2002 ; 77: 1148-55)

Correct timing for the surgery

- Medical therapy proposed until desire to conceive for preserving as much as possible ovarian reserve
- Surgery should be done at this time
- Indeed, delaying conception after surgery is associated with lower PR and higher recurrence rate

Somigliana et al. Reprod Biomed Online 2010

www.istanbulvf.com



- Hum rep Muzi 2014 p:2195 diagram koy
- P:2196 diagram koy

Fecundity rate

- In endometriosis stage 3-4 group is 2% to 10%
- In control group is 15% to 25%

Halis et al Ann N Y Acad Sci 2004

- JMİG 2014 P 513 teki diagram koy

Ovarian endometrioma and IVF

Results of retrospective studies

- Tinkanen and Kujansuu (2000)
- Wong et al (2004)
- Garcia-Velasco et al (2004)
- Suzuki et al (2005)

**IVF outcomes are not reduced
by the presence of endometrioma**

Is there still a place for surgery?

Ovarian Endometriosis and IVF

Canis et al. (Hum Reprod 2001;16:2583-6)

« *No difference between the group of patients who underwent laparoscopic ovarian cystectomy for **endometriomas >3 cm** and the **control** group in terms of the number of oocytes and embryos »*

Endometriosis and IVF

Effect of the presence of endometriomas on IVF outcomes

IVF outcomes were not impaired when compared with patients who had undergone removal of the endometriomas previously

- any adverse effect of chocolate fluid
- no need to perform surgery or repeated surgery

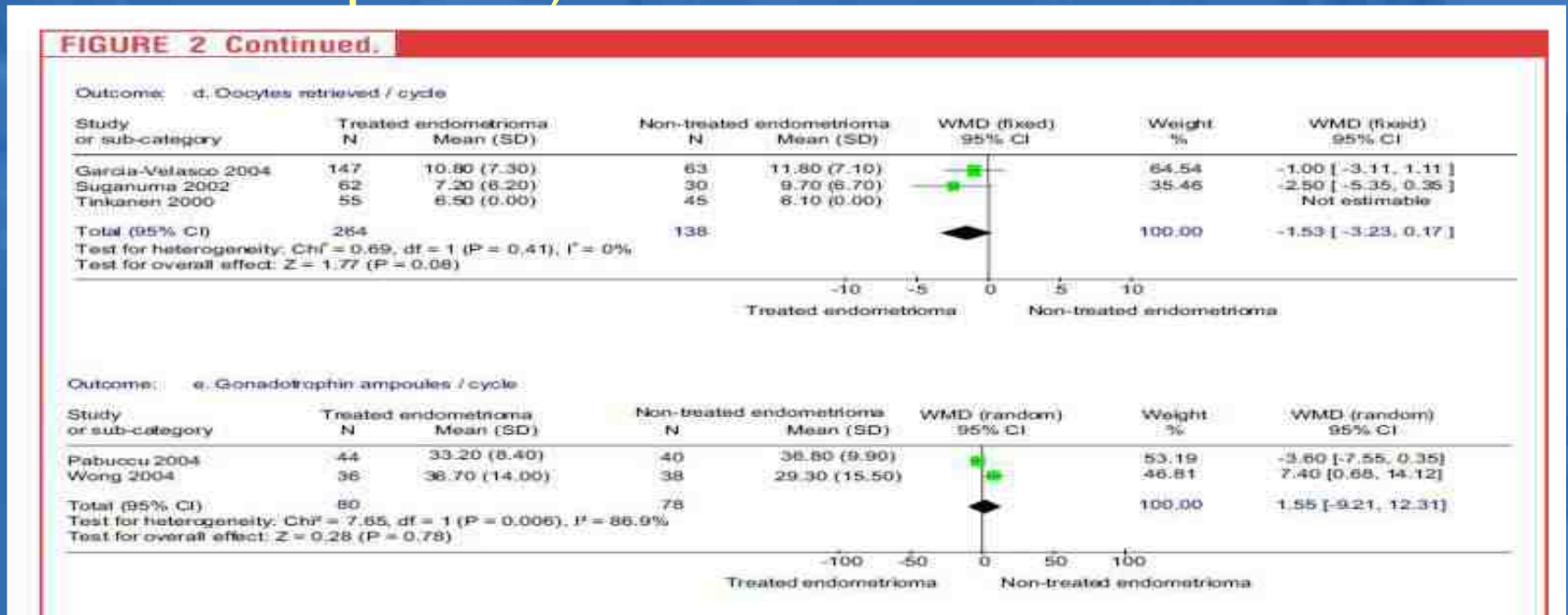
IVF outcomes **were impaired** when compared with **tubal infertility**

- possible other mechanism (peritoneal fluid ?)

Garcia-Velasco et al 2004

Ovarian endometrioma and IVF

- Systematic review and meta-analysis
Surgical vs non surgical treatment (No significant effect on IVF -PR and ovarian response)



(Tsoumpou et al 2009)

Ovarian Endometrioma and IVF

- Unilateral endometrioma
- Never operated
- Cyst diameter : 28.4 ± 3.9 mm

TABLE 1

Number of antral follicles and retrieved oocytes from endometrioma-containing ovaries and from the contralateral ovaries.

	Ovary with endometrioma	Ovary with no endometrioma	P value	95% Confidence interval
No. of antral follicles	7.7 ± 1.0	8.5 ± 0.9	.3	-1.0 to 3.0
No. of retrieved oocytes	6.0 ± 0.4	6.1 ± 0.5	.8	-1.0 to 1.0
No. of retrieved oocytes when endometrioma size >25 mm	5.8 ± 1.4	6.6 ± 1.1	.5	-4.0 to 2.0

(Almog et al Fertil Steril, 2010)

Ovarian Endometrioma and IVF

- Unilateral endometrioma
- Never operated
- Cyst diameter : 28.4 ± 3.9 mm

No significant difference
IVF without prior surgery?

Endometriosis and Ovarian reserve

	Endometriosis n = 825	Control n = 334
FSH U/L (d3): 3	8.8 ± 6.3	7.5 ±

Table 3 IVF outcomes in patients with endometriosis or male factor infertility after IVF treatment.

	Endometriosis (n = 317)	Male factor infertility (n = 334)	P-value
HCG on day of oestradiol (pg/ml)	1843.2 ± 1368	1889 ± 981	NS
Follicles	8.3 ± 5.8	11.2 ± 3.1	<0.001
MII oocytes	6.7 ± 5.2	10.3 ± 6	<0.001
Total embryos	4.0 ± 3.4	4.5 ± 3.8	<0.001
Embryos frozen	1.9 ± 3	2.7 ± 1	<0.001
Live births per patient	97/317 (30.6)	112/334 (33.5)	NS

(Barri et al 2010)

Endometriosis and Ovarian reserve

	Endometriosis	Control
	n = 825	n = 334
FSH U/L (d3):	8.8 ± 6.3	7.5 ± 3
Antral follicle count :	7.3 ± 4	10.2 ± 5.1

(Barri et al 2010)

Residual ovarian volume after surgery

Table IV Residual ovarian tissue before surgery and after surgery

	N	Mean \pm SD
Endometriomas		
Ovarian tissue volume BEFORE to surgery (cm ³)	67	19.9 \pm 17.8
Ovarian tissue volume AFTER surgery (cm ³)	67	5.1 \pm 3.2 [*]
Dermoids		
Ovarian tissue volume BEFORE to surgery (cm ³)	62	10.1 \pm 11.4 [†]
Ovarian tissue volume AFTER surgery (cm ³)	62	6.7 \pm 3.3 [‡]

* $P < .001$ ovarian volume before vs after surgical removal of endometriomas.

† $P < .05$ ovarian volume after surgical removal of endometriomas vs ovarian volume after surgical removal of dermoid cysts.

‡ NS ovarian volume before vs after surgical removal of dermoid cyst.

Residual ovarian volume after surgery

Table V Residual ovarian volume after surgery vs contralateral untreated ovaries

Ovaries after laparoscopic cystectomy	N	Mean \pm SD
Endometriomas		
Normal treated ovary		
Ovarian tissue volume (cm ³)	40	4.3 \pm 2.3 [*] †
Contralateral untreated normal ovary		
Ovarian tissue volume (cm ³)	40	9.7 \pm 3.9
Dermoids		
Normal treated ovary		
Ovarian tissue volume (cm ³)	46	7.1 \pm 3.5 [‡]
Contralateral untreated normal ovary		
Ovarian tissue volume (cm ³)	46	8.3 \pm 3.1

* $P < .001$ volume treated vs contralateral untreated ovaries with endometriomas.

† $P < .001$ volume of treated ovaries with endometriomas vs treated with dermoids.

‡ NS volume treated vs contralateral untreated ovaries with dermoids.

Residual ovarian volume after surgery

Table V Residual ovarian volume after surgery vs contralateral untreated ovaries

- Lack of correlation between residual ovarian volume and cyst diameter...
- Resection of even small endometrioma :significant loss of ovarian volume.

[†] $P < .001$ volume of treated ovaries with endometriomas vs treated with dermoids.

[‡] NS volume treated vs contralateral untreated ovaries with dermoids.

Exacoustos et al. Am J Obstet Gynec, 2004

IVF and bilateral endometriomas

- ↗ Cancelled cycles
- ↘ Number
 - Follicles
 - Oocytes
- Embryos

Table III. Characteristics of the IVF–ICSI cycles in patients operated for bilateral endometriomas (cases) and controls.

Characteristics	Cases (n = 68)	Controls (n = 136)	p
Cancelled cycle			<0.001
Hyper-response	1 (2%)	20 (15%)	
Poor response	17 (28%)	8 (6%)	
Dosage of rFSH/die	333 ± 133	212 ± 112	<0.001
Duration of stimulation (day) ^a	11.5 ± 2.3	11.8 ± 2.4	0.58
Number of follicles 11–15 mm ^a	3.2 ± 2.8	4.6 ± 3.3	0.009
Number of follicles > 15 mm ^a	5.2 ± 2.8	6.5 ± 2.7	0.006
Number of oocyte retrieved ^d	5.7 ± 4.0	7.2 ± 3.6	0.024
Number of oocyte used ^{a,b}	2.8 ± 2.3	3.8 ± 2.7	0.034
Number of embryos obtained ^{a,b}	2.0 ± 1.9	2.8 ± 2.0	0.024
Number of transfers not performed ^a	14 (28%)	16 (15%)	0.08
Number of embryos transferred ^e	2.0 ± 0.6	2.2 ± 0.7	0.20
Clinical pregnancy rate (PR)			
Number of pregnancies	5	26	
PR per starting cycle	7%	19%	0.027
PR per oocyte retrieval	10%	24%	0.051
PR per embryo transfer	14%	28%	0.11
Implantation rate	5 (7%)	33 (16%)	0.048
Delivery rate (DR)			
Number of deliveries	3	23	
DR per starting cycle	4%	17%	0.018
DR per oocyte retrieval	6%	21%	0.02
DR per embryo transfer	8%	25%	0.049

(Somigliana et al Hum Reprod 2008)

IVF and bilateral endometriomas

- ↗ Cancelled cycles
- ↘ Number
 - Follicles
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IVF outcome significantly impaired

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(Somigliana et al Hum Reprod 2008)

Ovarian endometrioma and IVF

Results of retrospective studies

- Tinkanen and Kujansuu (2000)
- Wong et al (2004)
- Garcia-Velasco et al (2004)
- Suzuki et al (2005)

**IVF outcomes are not reduced
by the presence of endometrioma**

Endometriosis and AMH

Mean serum
AMH level
surgery

Before surgery

After

- Ercan et al. 2010 (n=47) 1.62 ± 1.009 ng/ml 1.39 ± 1.16 ng/ml
NS

With endometriosis (306) Without

endometriosis(153)

- Shebl et al. 2009 (n=459) 2.75 ± 2.0 ng/ml 3.46 ± 2.30 ng/ml

(p<0.001)

Shebl et al Gynecol Endocrinol 2009

Endometriosis and Anti-müllerian hormone

Mean serum

AMH level
surgery

Before surgery

After

- **No damage in the AMH secreting healthy ovarian tissue after laparoscopic stripping surgery**

- Shebl et al. 2010 (n=459) 2.75 ± 2.0 mg/ml 3.46 ± 2.30 mg/ml (p<0.001)

Ercan et al Gynecol Endocrinol 2010

Endometriosis and ovarian reserve

	AMH ng/ml
Controls	3.44 ± 2.06
Mild endometriosis	3.28 ± 1.93
Severe endometriosis	2.38 ± 1.83*

* Significantly different from controls $p < 0.001$

Laparoscopic Laser Surgery for Endometriosis -Fev 2011

<u>r-AFS score</u>	<u>N</u>	<u>DIE Nodules</u>
Stage I-II	1153	-
Stage III-IV	1092	128
Total	2245	(5,7%)

Karaman 2011

Brüksel Kadın Sağlığı ve Tüp Bebek Merkezi, Istanbul
Hopital Français Reine Elizabeth, Brussels
Institut Medical Edith Cavell, Brussels

Type of the surgery (1092)

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

Karaman 2011

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.

4 Types of Endometriosis

- Superficial Endometriosis:
 1. Peritoneal endometriosis
 2. Ovarian superficial endometriosis
- Ovarian Endometriomas
- Deeply Infiltrating Endometriosis (DIE)
- Extragenitale Endometriosis

Endometrioma recurrence

- 125 to 30% after 2 to 5 years follow-up
- Recurrence of pain 7% to 30% within 3 years of surgery increasing 40% to 50% after 5 years

Valle et al. Ann N Y Acad Sci 2003

Gou et al Human Reprod Update 2009

Pathogenesis of Ovarian Endometriosis : Controversy

Ovarian cortex invagination

- **Transplantation Theory** : presence of active implants at the site of inversion ; shedding and bleeding

(Brosens et al. Fertil. Steril. 1994; 61:1034-1038)

- **Metaplasia Theory** : invagination of the ovarian cortex and metaplasia in typical glandular epithelium and stroma

(Nisolle and Donnez ,Fertil. Steril.1997; 68:585-596)

Surgical Approach of Ovarian Endometriomas

According to these theories, the surgical approach has to be chosen:

- 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.)

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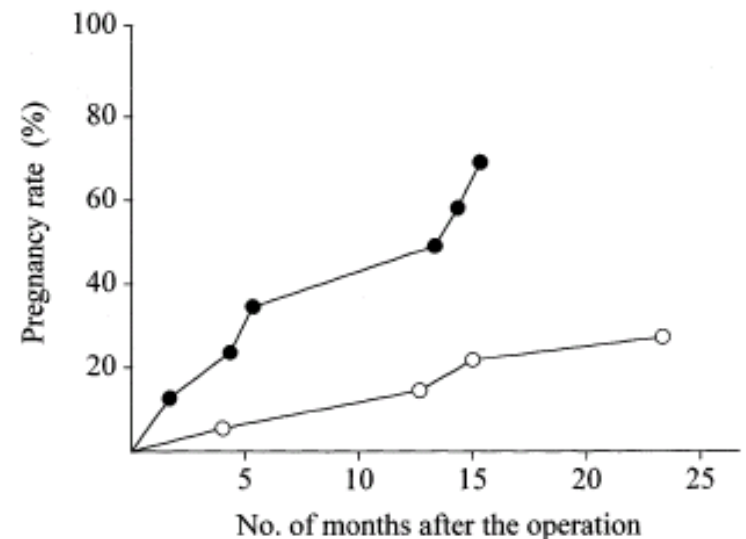


Risk of Recurrence of Ovarian Endometriosis at 1 year

	EXCISION	COAGULATION
Hemmings et al (Retro; 1998)	8%	12%
Beretta et al (RCT; 1998)	6%	18%
Salehand Tulandi (Retro; 1999)	6.1%	21.9%
Alborzi et al (RCT; 2004)	5.8%	22.9%

Management of endometriomas

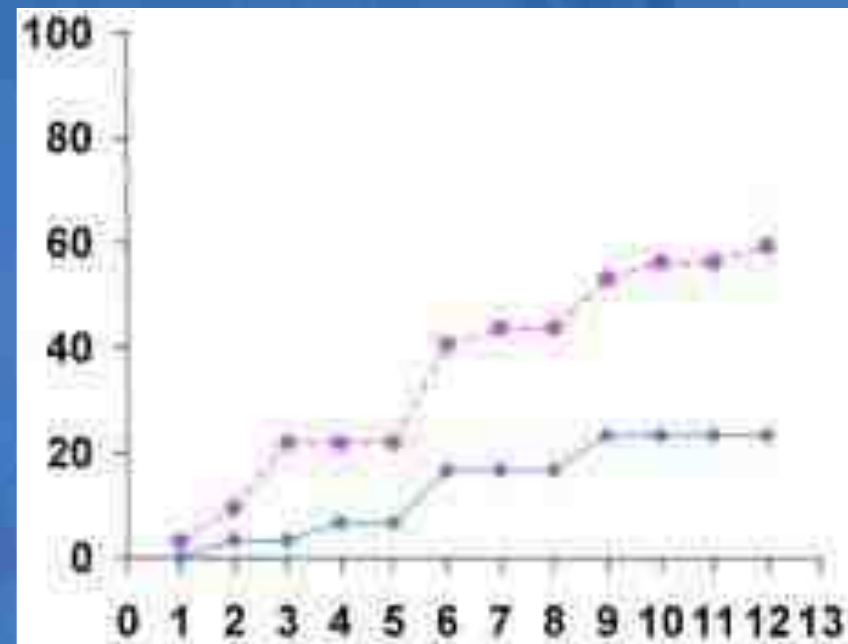
- RCT : Cystectomy vs drainage and coagulation
- - 64 patients with advanced stages of endometriosis
- Randomization at the time of laparoscopy
- The 24 - month cumulative PR was significantly higher
- in the cystectomy group
- (66.7 %, 6 / 9) than
- in the coagulation group
- (23.5 %, 4 / 17)



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 %)



(Alborzi et al Fertil Steril 2004 ; 82 : 1633-37)

Endometriosis and IVF



Endometriosis and IVF

**IVF results in presence
of ovarian endometrioma?**

Ovarian Endometriomas and IVF

1/ Should endometriomas be removed before IVF?

2/ What kind of surgery should we propose?

3/ What is the ovarian response during IVF-ET cycles after endometrioma surgery?

Ovarian Endometriosis and IVF

- Two retrospective studies

*1/ Donnez et al. Fertil Steril
2001;76:662-5*

*2/ Canis et al. Hum Reprod
2001;16:2583-6*

Ovarian Endometriosis and IVF



Donnez et al. Fertil. Steril. 2001;76:662-665

Ovarian Endometriosis and IVF



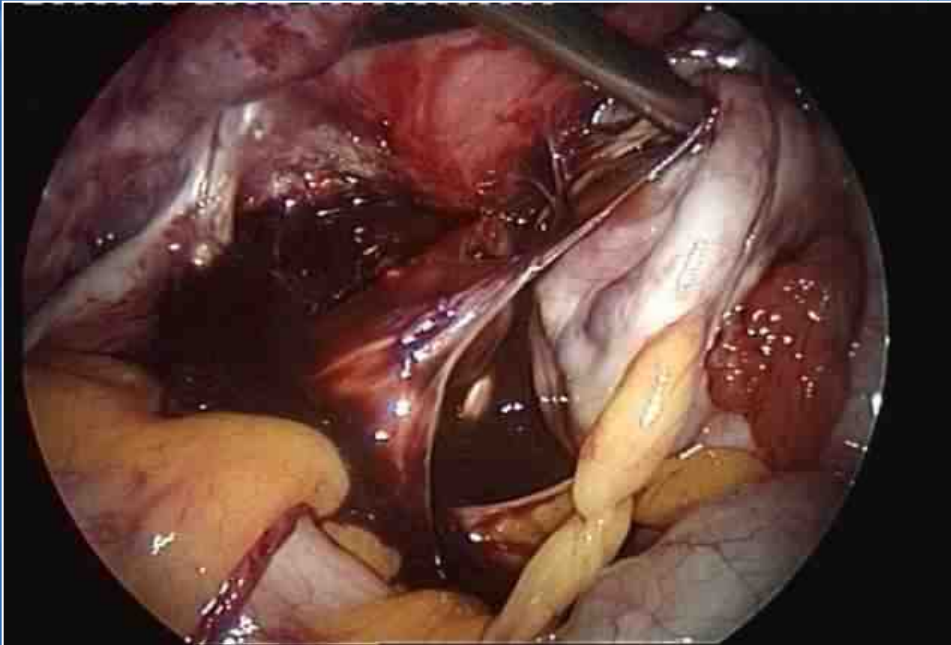
Donnez et al. Fertil. Steril. 2001;76:662-665

Ovarian Endometriosis and IVF



Donnez et al. Fertil. Steril. 2001;76:662-665

Impact of IVF on endometriosis



- Impact of IVF on endometriosis
 - Recurrence
 - Activation
 - Complications
 - Absces
 - Rupture
 - Neoplasia

IVF and endometriosis recurrence

- At 21 months, CERR : 31% (Histology-Cytology)
 - IVF: 7%
 - IVF and IUI : 43%
 - IUI : 70%
- At 36 months, CERR : 63%

Temporary exposure to high E² levels
is not a major risk factor

(D'Hooghe et al 2006)

IVF and Endometrioma increase

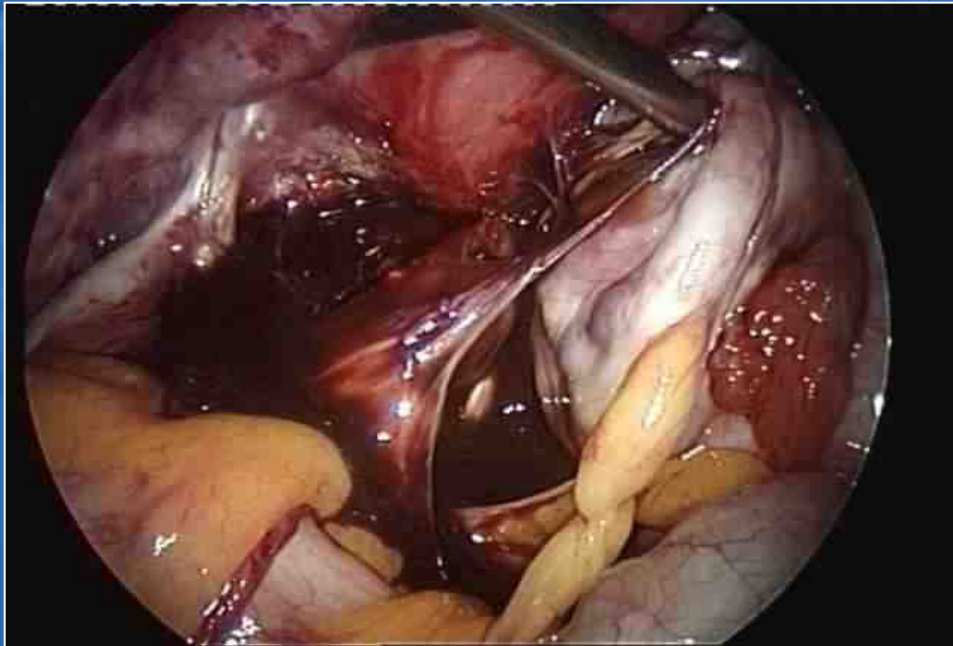
- 48 women
- Ovarian endometrioma (mainly < 3cm)
- No significant volumetric increase

Table 4. Influence of IVF on the modification of the volume of the endometriomas in relation to the dimension of the cysts and responsiveness to ovarian stimulation.

Characteristic	Number of cysts	Pre-IVF volume (ml)	Post-IVF volume (ml)
Basal dimension of the endometriomas			
<20 mm (volume <4.2 ml)	36	2.1 (1.3–3.1)	2.5 (1.1–3.0)
20–30 mm (volume = 4.2–14.1 ml)	24	6.1 (5.3–9.8)	7.5 (5.0–10.5)
>30 mm (volume >14.1 ml)	10	21.5 (19.9–26.0)	13.8 (11.2–47.1)
Responsiveness to ovarian stimulation			
Low	24	4.8 (1.5–7.0)	5.2 (2.5–7.1)
Moderate	22	5.7 (3.1–16.7)	7.9 (2.8–12.9)
High	24	3.2 (2.0–5.6)	2.9 (1.8–8.8)

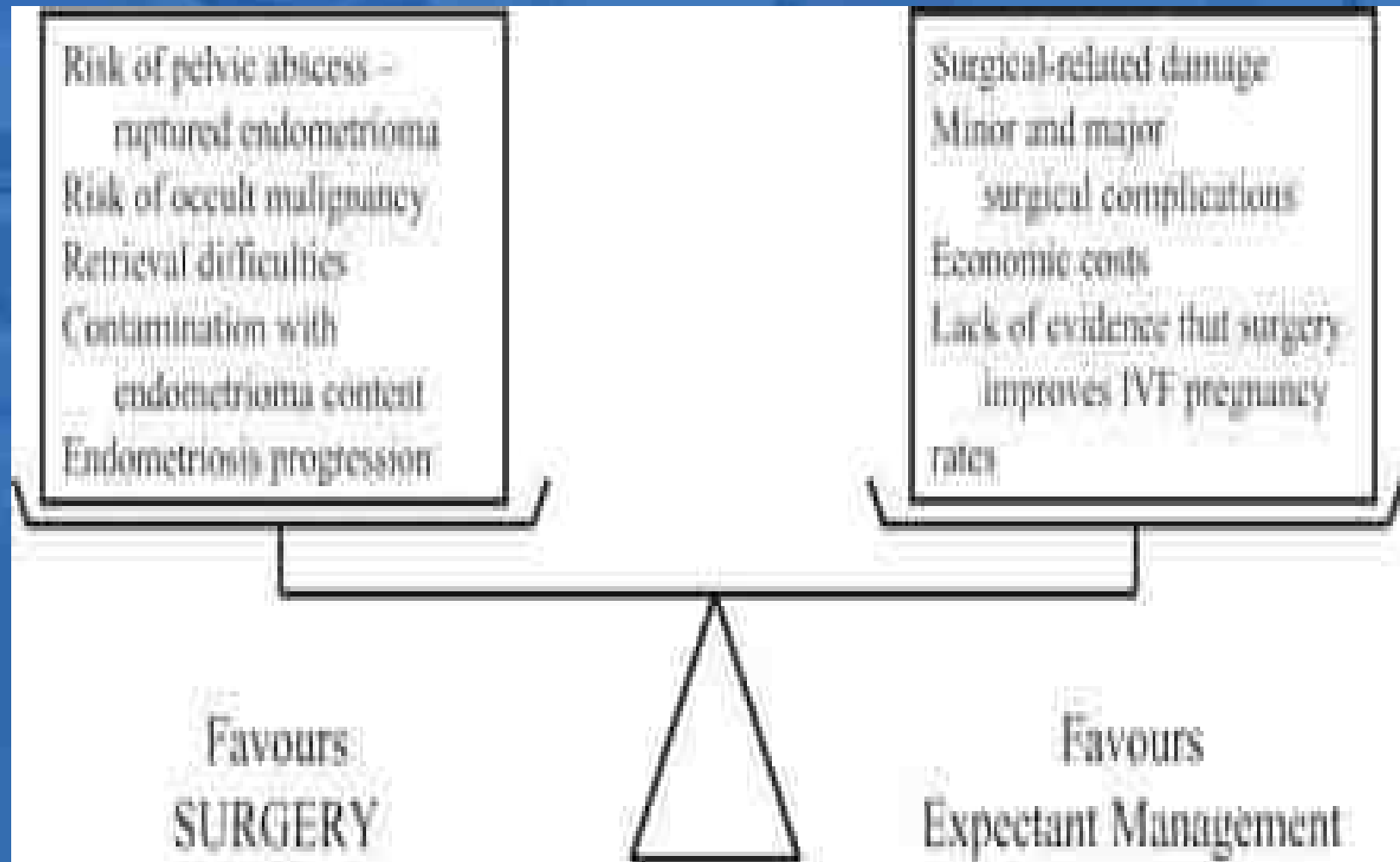
The analysis focussed on endometriomas. Data are medians (interquartile range). Differences were analysed using non-parametric Wilcoxon test for paired data. There were no statistically significant differences before and after IVF treatment. Responsiveness to ovarian stimulation was categorized as follows: (i) Low response: cancelled cycle due to poor response (six women) or retrieval of less than four oocytes (18 women). (ii) Moderate response: retrieval of 4–6 oocytes (22 women). (iii) High response: cancelled cycle for hyper response (one woman) or retrieval of more than six oocytes (23 women).

Impact of IVF on endometriosis



- Impact of IVF on endometriosis
 - Recurrence
 - Activation
 - Complications
 - Abces : case-report
 - Rupture: case-report
 - Neoplasia

Surgery vs Expectant Management



Risk of Recurrence of Ovarian Endometriosis

Saleh and Tulandi (1999)

- Laparoscopic ovarian ablation: 21.9%-57.8%
- Laparoscopic excision: 6.1%-23.6%



RECURRENCE

- 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

Risk of Recurrence: Impact of the side affected?

1/ Ghezzi et al (2001)

Lower risk of recurrence if endometriosis is located on the right side

2/ Chapron et al (2001)

Ovarian endometriosis involves the left hemipelvis more frequently than the right one and the risk of postoperative adhesions is also higher on the left side.

Role of the rectosigmoid loop?

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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

PREVANTION

- In fact, **ovulation** seems crucial in the of **development ovarian endometriotic** cysts and supression should substantially decrease cyst recurrence after laparoscopic treatment

Jaina, Dalton 1999;Seracchioli 2009

Practice Committee of ASRM 2008

‘ Endometriosis should be viewed as a **chronic disease** that requires a **life-long management** plan with goal of maximizing the use of **medical treatment** and avoiding repeated surgical procedures’.

Conclusion

- Laparoscopic ovarian cystectomy can be done 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 spontan pregnancy rate(50%).

Conclusion

- But, laparoscopic endometrioma cystectomy before IVF does not give any advantages in term of PR after IVF.

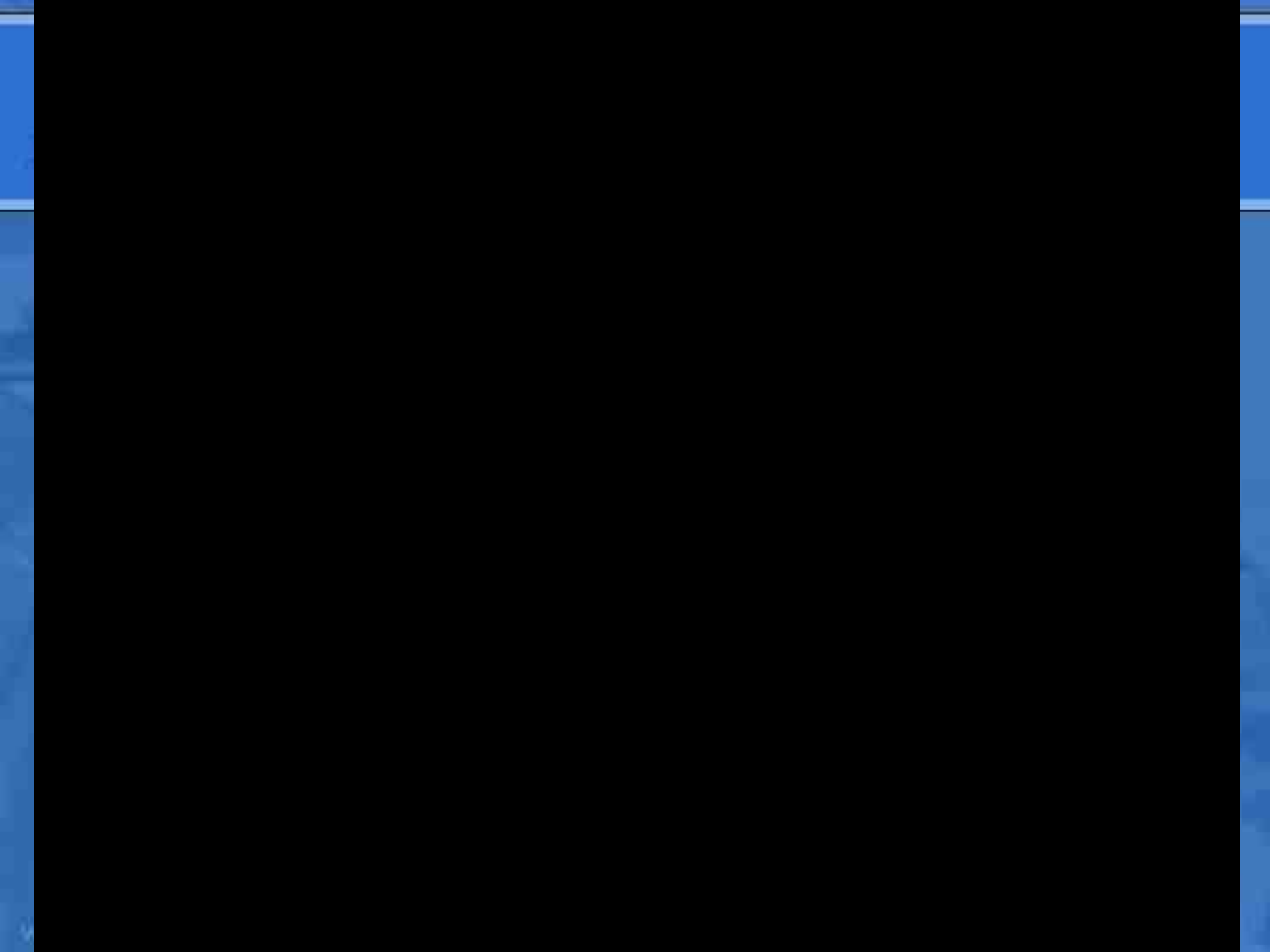
Conclusion

- 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**

ENDOMETRİOMA KİSTEKTOMİ



PROF. DR. YÜCEL KARAMAN





Surgical treatment of endometriosis associated infertility

Table II International guidelines on surgical treatment of endometriosis-associated infertility in asymptomatic women

Clinical condition	Recommendation		
	ESHRE 2005	ASRM 2006	RCOG 2006
Minimal-mild endometriosis (stage I-II disease)	Limited benefit: surgery recommended	Small benefit: surgery recommended	Demonstrated benefit: surgery recommended
Moderate-severe endometriosis (stage III-IV disease)	Possible but unproven benefit: surgery recommended	Possible benefit: surgery recommended	Possible benefit: recommendation uncertain
Best available medical treatment	No benefit: not recommended	No benefit: not recommended	No benefit: not recommended
Surgery before IVF	Recommended if endometriosis ≥ 4 cm	Doubtful benefit: no recommendation	Recommended if endometriosis ≥ 4 cm
Recurrent endometriosis	No recommendation	Second line surgery: not recommended	No recommendation

Vercellini et al. *Hum an Reprod* 2008



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 spontan pregnancy rate(50%).

Laparoscopic Laser Surgery for Endometriosis 1990-Oct 2009

<u>r-AFS score</u>	<u>N</u>	<u>DIE Nodules</u>
Stage I-II	1153(56%)	-
Stage III-IV	892 (44%)	107
Total	2045	(5,2%)

Karaman 2009

Brüksel Kadın Sağlığı ve Tüp Bebek Merkezi, Istanbul
Hopital Français Reine Elizabeth, Brussels
Institut Medical Edith Cavell, Brussels

Endometrioma diameters

	Patients	
< 2 cm	168	19%
2-5 cm	493	55%
6-10 cm	172	19%
> 10 cm	59	6%
Total	892	

Bilateral endometriomas: 128/892 14%

Karaman 2009

Type of the surgery (892)

- Cystectomy : 785
- Ovariectomy : 91
- LH-LAVH : 16

Karaman 2009

Cumulatif pregnancy rate (524 patients)

	P.R.
• Stage 1-2	: 62%
• Stage 3-4	: 48%
if r- AFS >70	: 0%

Karaman 2009

Major risk factors of recurrence

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- Less aggressive surgery
- Inadequate previous surgery
(44% Chapron 2004)
- Younger age of patient
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- In fact, **ovulation** seems crucial in the of **development ovarian endometriotic** cysts and supression should substantially decrease cyst recurrence after laparoscopic treatment

Jaina, Dalton 1999;Seracchioli 2009

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.

Conclusion

- 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**
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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

Ferrero 2010, Panay 2008, Guo 2008, Fedele 2008, Hompes 2007, Mihalyi 2006, Attar 2006 Olive 2004, D'Hooge 2003

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

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

MEDLINE search CT in progestin or OCs vs other hormonal compound

- The result consistently confirmed that progestin and OCs are effective in relieving pain, generally well-tolerated and not inferior to danazol, GnRH agonists and aromatase inhibitors,

Vercellini 1993, Prentice 2004, Cosson 2002, Peyya 2005, Schlaff 2006, Crognani 2006, Davis 2007, Selak 2007, Harada 2009, Ferrero 2009, Strowitzki 2010

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PREVENTION of RECURRENCE

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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 impair responsiveness to progesterone
- In breast and endometrial cancers such alterations in the PR-B/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 pathogenesis** 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 extra cellular acidosis and deposit of reactive substance)



Reactive hallogen 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

Annual cost of medicale 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

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.

DIE has Two Major Specificities

- DIE is a multifocal pathology:
USL, vagina, bladder, intestine, ureter
- DIE is very often associated with other endometriotic lesions:

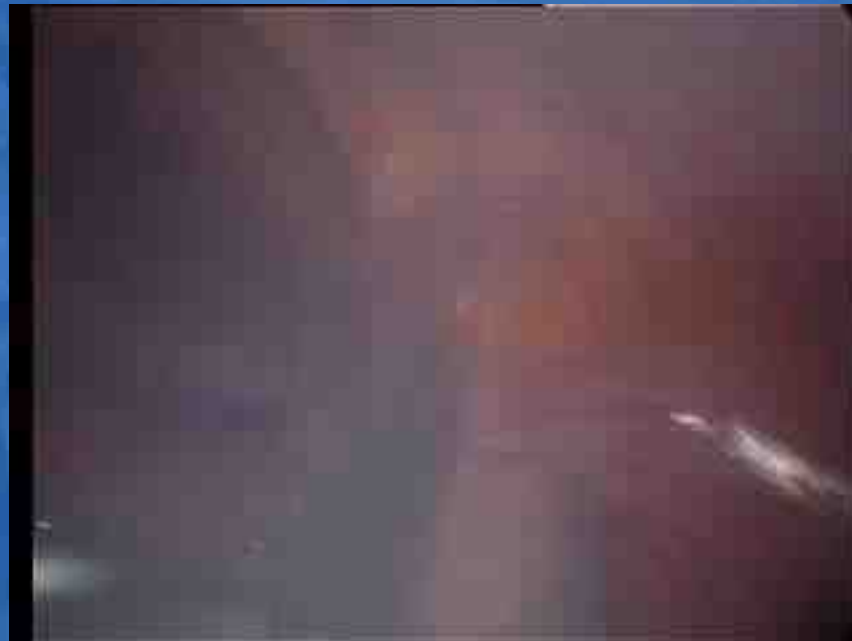
Unique lesion	10 %
Superficial lesions	61.3%
Endometriomas	50.5%
Adhesions	74.2%

Association of Ovarian Endometriomas and DIE

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

Associated ovarian endometrioma is a marker for greater severity of DIE

Anatomic Reconstruction







Prof. Dr. Yücel Karaman

Endometriosis

Conclusion

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

Endometrial biopsy for diagnosis of endometriosis

A pilot study to evaluate the relative efficacy of endometrial biopsy and full curettage in making a diagnosis of endometriosis by the detection of endometrial nerve fibres (small unmyelinated sensory C – nerve fibres).

- 37 women:
 - 20 women with endometriosis
 - 17 women without endometriosis
- Immunohistochemistry: PGP 9.5 (Dako, Australia) pan-neuronal marker protein gene product 9.5
 - positive in all women with endometriosis
 - negative in all women without endometriosis

« Al-Jefout et al. Am J Obstet Gynecol. 2007 »

Diagnosis of endometriosis by detection of nerve fibres in an endometrial biopsy: a double blind study

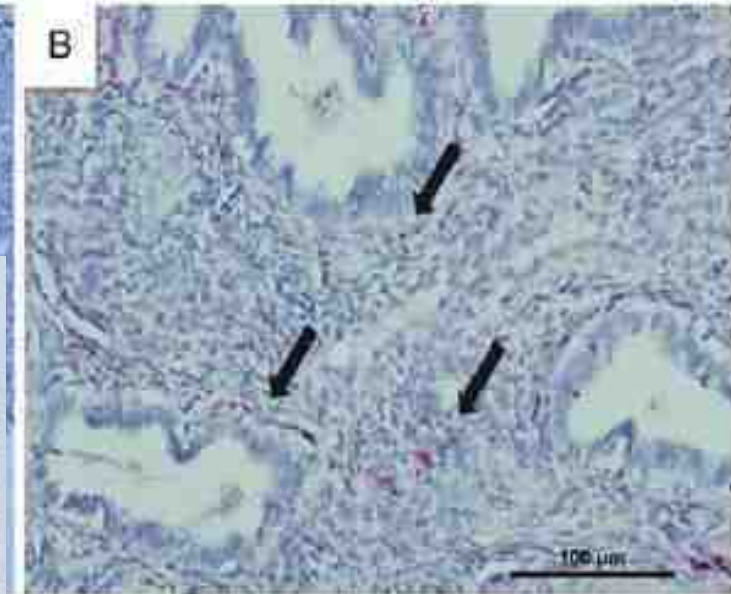


Table III Presence of nerve fibres in endometrial biopsy in women with and without endometriosis, as diagnosed at laparoscopy

	Endometriosis diagnosis at laparoscopy		Total
	Yes	No	
Endometrial Nerve fibres present	Yes	63	69
	No	1	30
Total	64	35	99
Specificity*	83% (66–93%)		
Sensitivity*	98% (90–99%)		
PPV*	91% (81–96%)		
NPV*	96% (81–99%)		



« Al-Jefout et al. Hum Reprod. 2009 »

ENDOMETRIOSIS and IVF

- **Prospective matched case-control study**
- **Objective :** To analyze the impact of severe endometriosis on IVF outcome in women oocytes receiving from the same donor
- **Results:** Implantation in recipients of sibling oocytes was not affected by stage III-IV endometriosis (14.8%) when compared to controls (16 %)
- **Conclusion:** Endometriosis does not alter the endometrial receptivity

Endometriosis and IVF

The calculated Ors for fertilization rate, implantation rate and peak E concentrations were significantly lower in women with endometriosis compared with women without endometriosis

Negative association with endometriosis and IVF outcomes:
35% reduction in the possibility of achieving pregnancy with IVF in women with endometriosis compared with women without it (OR,0.63; CI,0.51-0.77)

Endometriosis and IVF

Worse outcome for patients with stages III to IV vs stages I to II (observational data)

Outcome	Endo III-IV	Endo I-II	P	Crude OR (95% CI)	Adjusted OR* (95% CI)
Pregnancy rate	13.84	21.12	<0.001	0.60 (.42–.87)	0.64 (.35–1.17)
Fertilization rate	74.47	58.35	<0.001	1.11 (1.09–1.13)	not interpretable
Implantation rate	10.23	11.31	0.003	0.93 (.89–.98)	0.21 (.15–.32)
Mean oocyte count	6.70	8.19	<0.001	0.83 (.78–.87)	0.31 (.24–.39)
Peak E ₂	1447.74	5813.38	<0.001	N/A	N/A

Note: Total no. of observations: 669. N/A = not applicable
 * Adjusted for publication date and age.

(Barnhart et al Fertil Steril 2002; 77:1148-55)

Ovarian surgery for bilateral endometriomas influences age at menopause

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

	All patients	Peritoneal endometriosis, no ovarian endometrioma	Ovarian surgery	Monolateral endometrioma	Bilateral endometrioma
Menopause, n (%)	302 43 (14.2%)	63 11 (17.5%)	239 32 (13.4%)	155 21 (13.5%)	84 11 (13.1%)
Mean age at menopause (years)	45.3 ± 4.3	45.1 ± 3 ^{a,b}	45.7 ± 4.5	47.1 ± 3.5 ^{a,c}	42.1 ± 5.1 ^{b,c}
POF (n)	7 (7/43, 16.3%)	2 ^{d,e} (2/11, 18.2%)	5 (5/32, 14.3%)	1 ^{d,f} (1/21, 4.8%)	4 ^{e,f} (4/11, 36.4%)
Menopausal symptoms (hot flushes, night sweats and vaginal dryness)	18 (18/259, 6.9%)	2 ^{g,h} (2/52, 3.8%)	16 (16/207, 7.7%)	7 ^{g,i} (7/134, 5.2%)	9 ^{h,i} (9/73, 12.3%)

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

^{a,b,c}Student t-test.

$P^a = 0.102$; $P^b = 0.117$; $P^c = 0.003$.

^{d,e,f,g,h,i} χ^2 test.

$P^d = 0.266$; $P^e = 0.635$; $P^f = 0.037$; $P^g = 0.990$; $P^h = 0.184$; $P^i = 0.120$.

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