



Endometriozis ve İnfertilite – Ne zaman IVF/ICSI ?

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Endometriozis- İnfertilite

Tedavi

- Gözlemsel
- Tıbbi
- Cerrahi
- ART
 - IUI
 - IVF/ICSI

***Endometriozis-İnfertilite &
Tıbbi Tedavi***

RCT's for conservative surgery with or without post-operative medical treatment

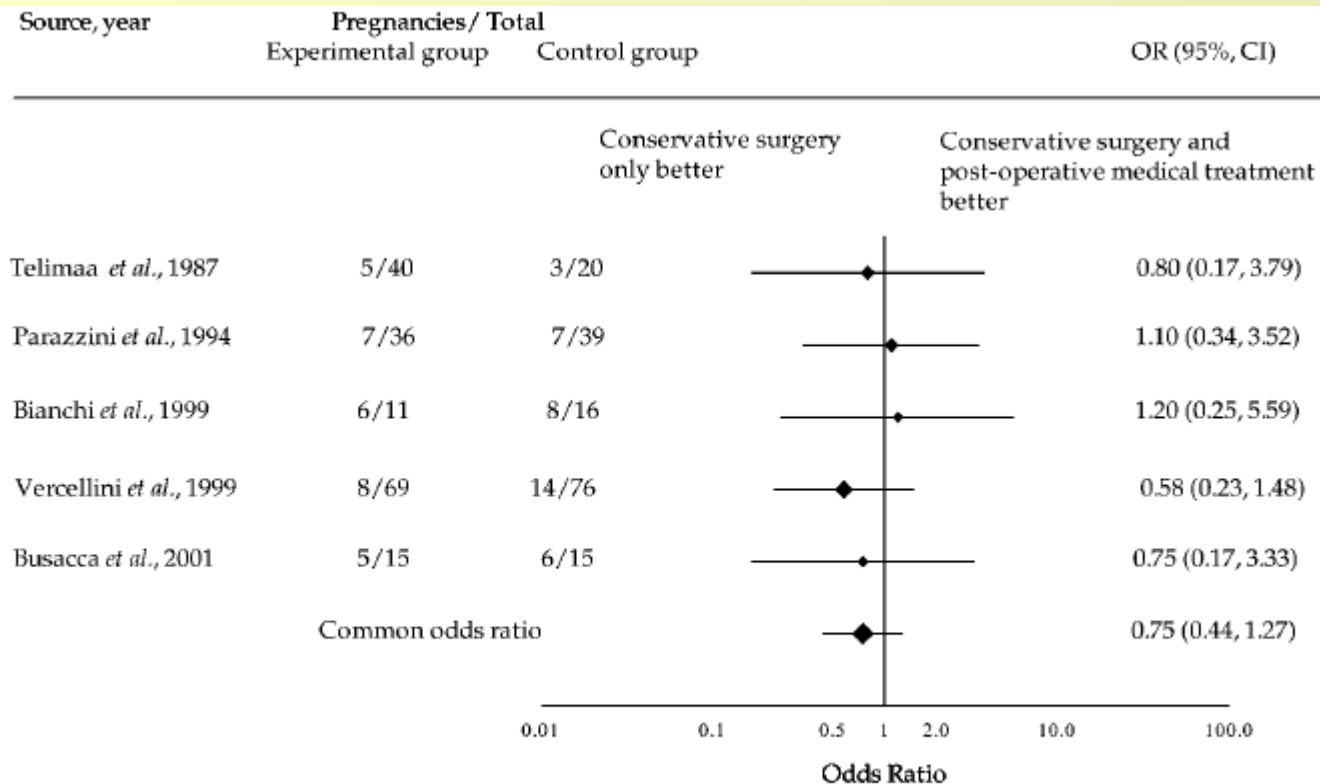


Figure 6: Overview of RCTs comparing conservative surgery for endometriosis with or without post-operative medical treatment. Diamonds represent odds ratio of conception, and horizontal lines are 95% CIs. Breslow-Day test for heterogeneity: $\chi^2_4 = 0.95$, $P = 0.91$. Modified from Vercellini *et al.* (2003b), with permission.

***Endometriozis-İnfertilite &
Cerrahi Tedavi***

Cumulative 36-month probability of pregnancy after conservativs surgery – *n=222 & No other infertility factor*

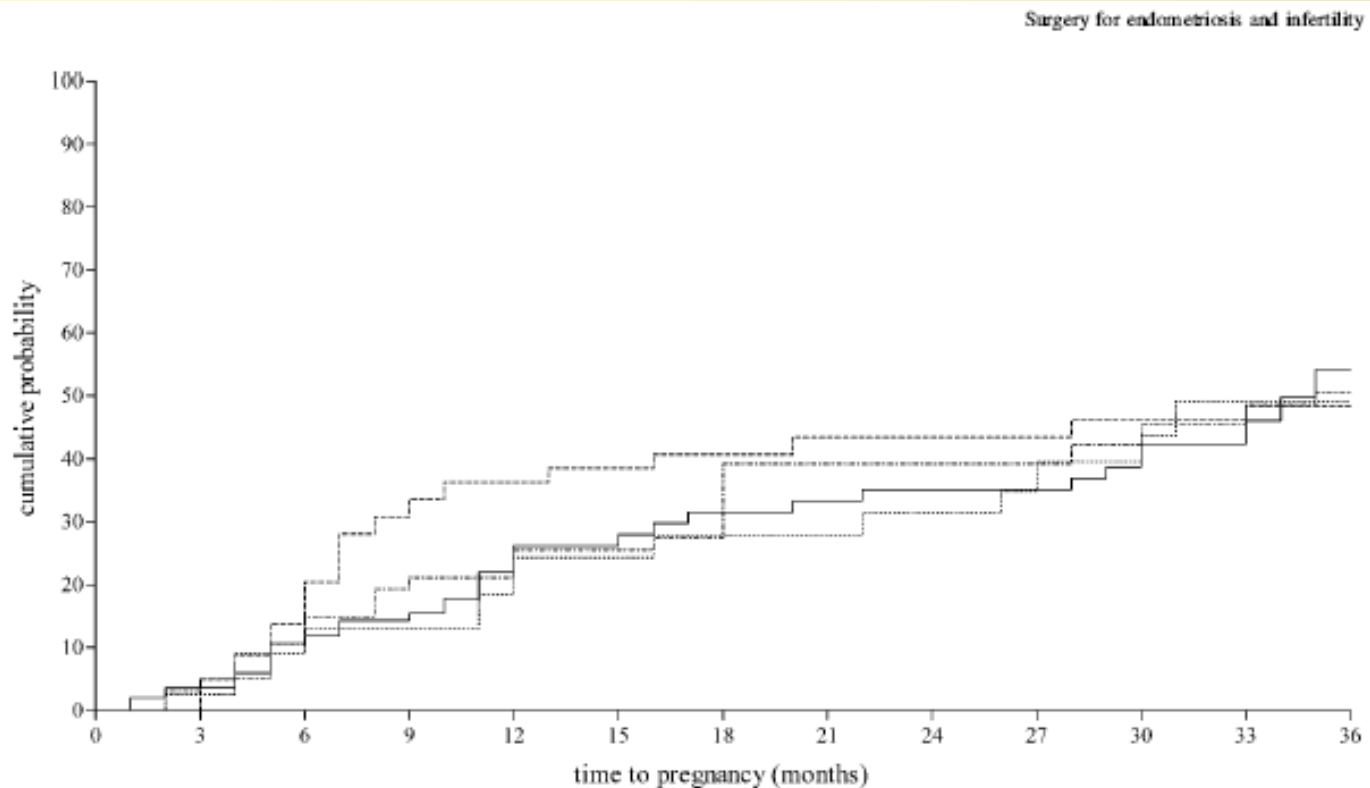


Figure 1: Cumulative 36-month probability of becoming pregnant by disease stage in 222 infertile women who underwent conservative surgery for endometriosis and had no other infertility factor (continuous line, stage I; dotted line, stage II; dashed line, stage III; dash-dotted line, stage IV). From Vercellini *et al.* (2006a), with permission.

L/S Ablation vs No surgery - Stage I-II Endometriosis

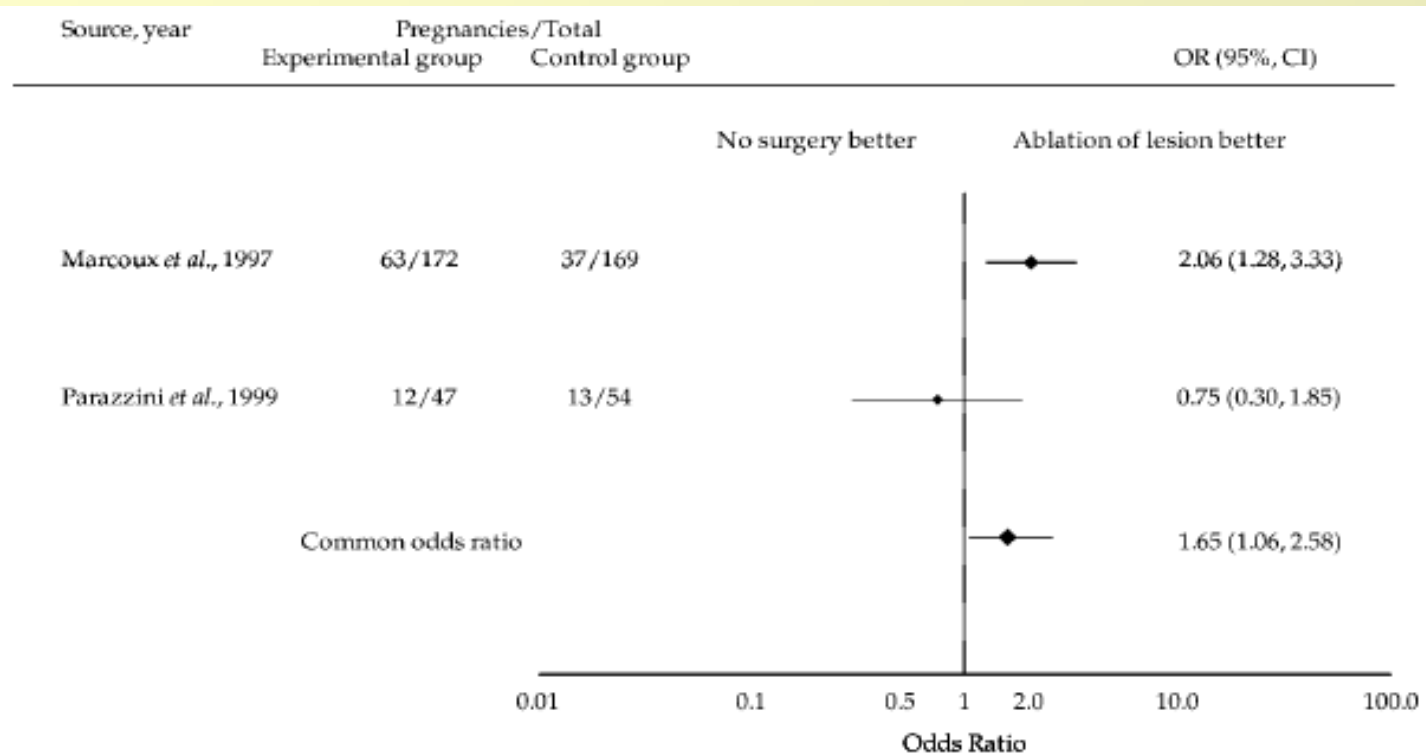


Figure 2: Overview of RCTs comparing laparoscopic ablation of lesions with no surgery in infertile women with minimal or mild endometriosis. Diamonds represent odds ratio of conception and horizontal lines 95% CIs. Breslow-Day test for heterogeneity: $\chi^2 = 13.24$, $P = 0.42$. Data from Al-Inany *et al.* (2000).

Meta-analiz

- Geç gebelik: % 8 cerrahi lehine (%26 vs %18)
- NNT = 12
- Endometriozis sıklığı %30-%50
 - $NNT = 12 \times 2 - 12 \times 3 = 24 - 36 (30)$

Al Inany et al. Hum Reprod 2000, 15: 2447-8.

PR's after L/S excision of endometrioma

Vercellini *et al.*

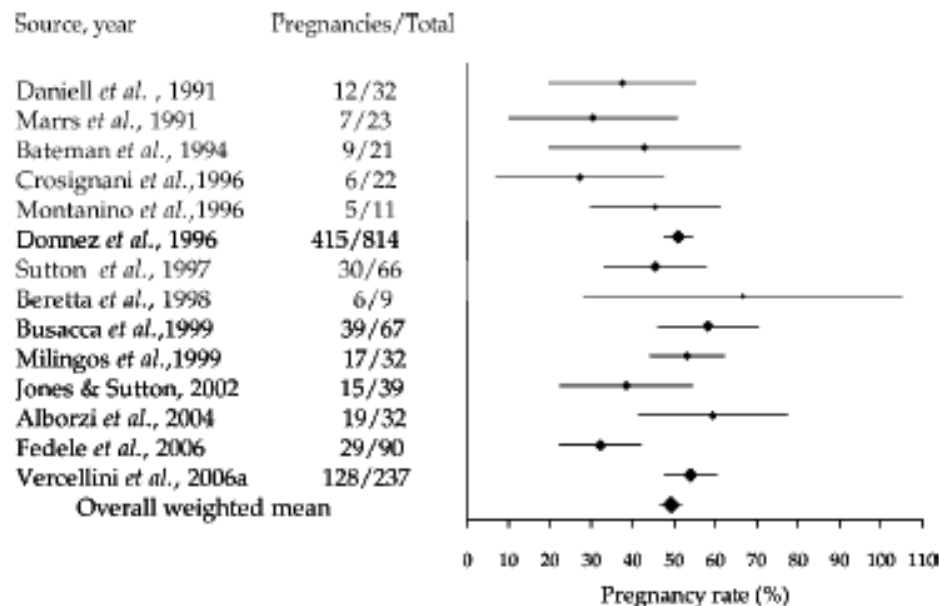


Figure 3: Pregnancy rates observed after laparoscopic excision of endometriomas. Diamonds represent percentage point estimates and horizontal lines represent 95% CIs. Modified from Jones and Sutton (2002), with permission.

PR's after L/S excision of endometrioma

Overestimation

- **Inclusion of women who did not try to conceive pre-operatively (Selection bias)**
- **Publication bias**
- **Exclusion of drop-outs**
- **Rarely specification of uni- and bi-lateral cysts**
- **Few specification of conceivment with IVF**
- **Lack of adequate control group**

PR's after L/S excision of endometrioma

Overestimation

- **Absolute benefit increase over background pregnancy rate 12 months after surgery in women with patent tubes could be 25% rather than 50%.**

Endometrioma - Cerrahi Tedavi

Ne zaman ?

Surgery for Endometriosis

- **Should be offered early when infertility is at the work-up stage**
- **Surgery just before ART offers little benefit**

Surgery for Endometriosis

Considerations

- **Ovarian reserve**
- **Availability of time**
 - Female age
 - Duration of infertility
- **Capacity to conceive naturally**
 - Tubal status
 - Male status

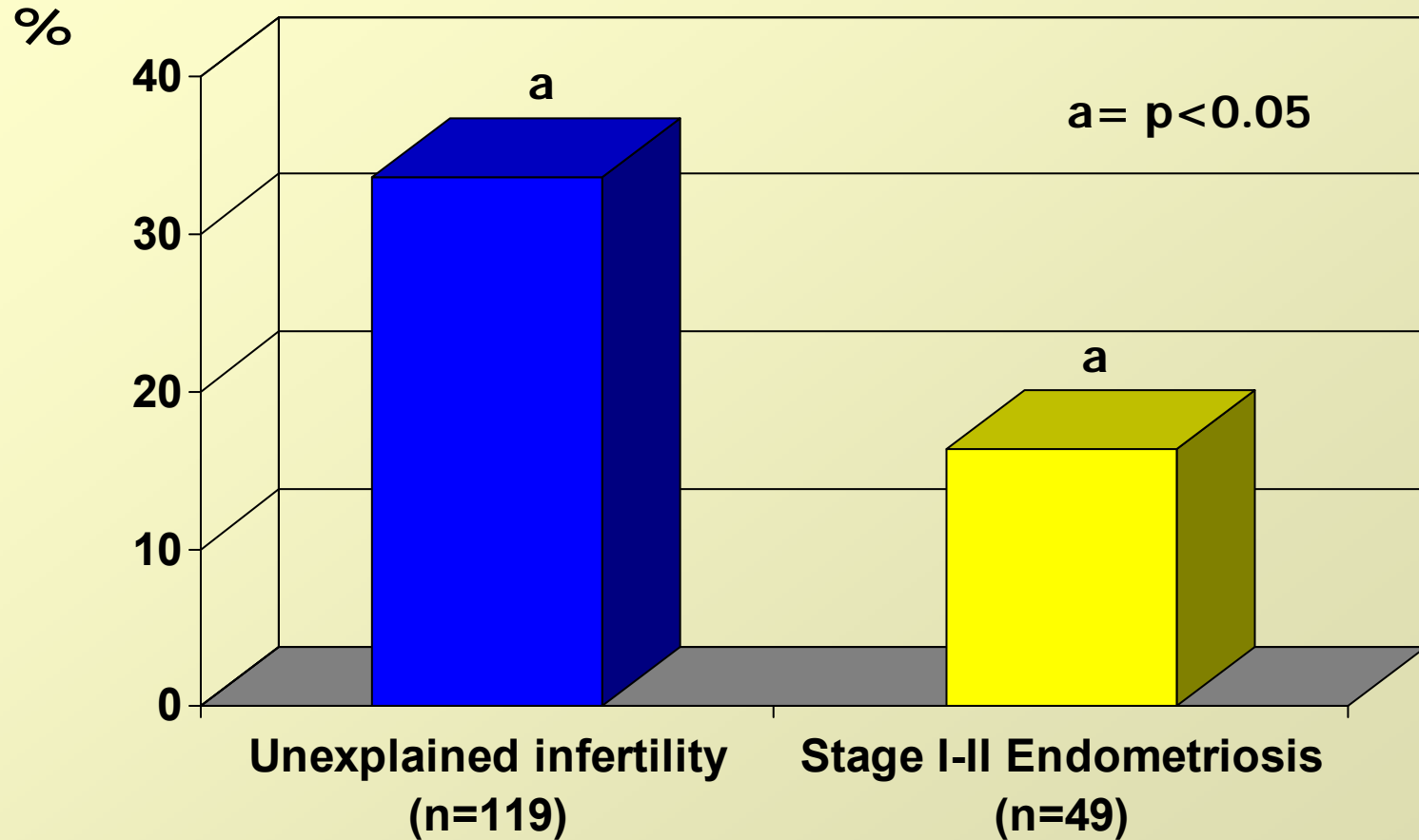
International Guidelines

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
Post-operative adjuvant 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

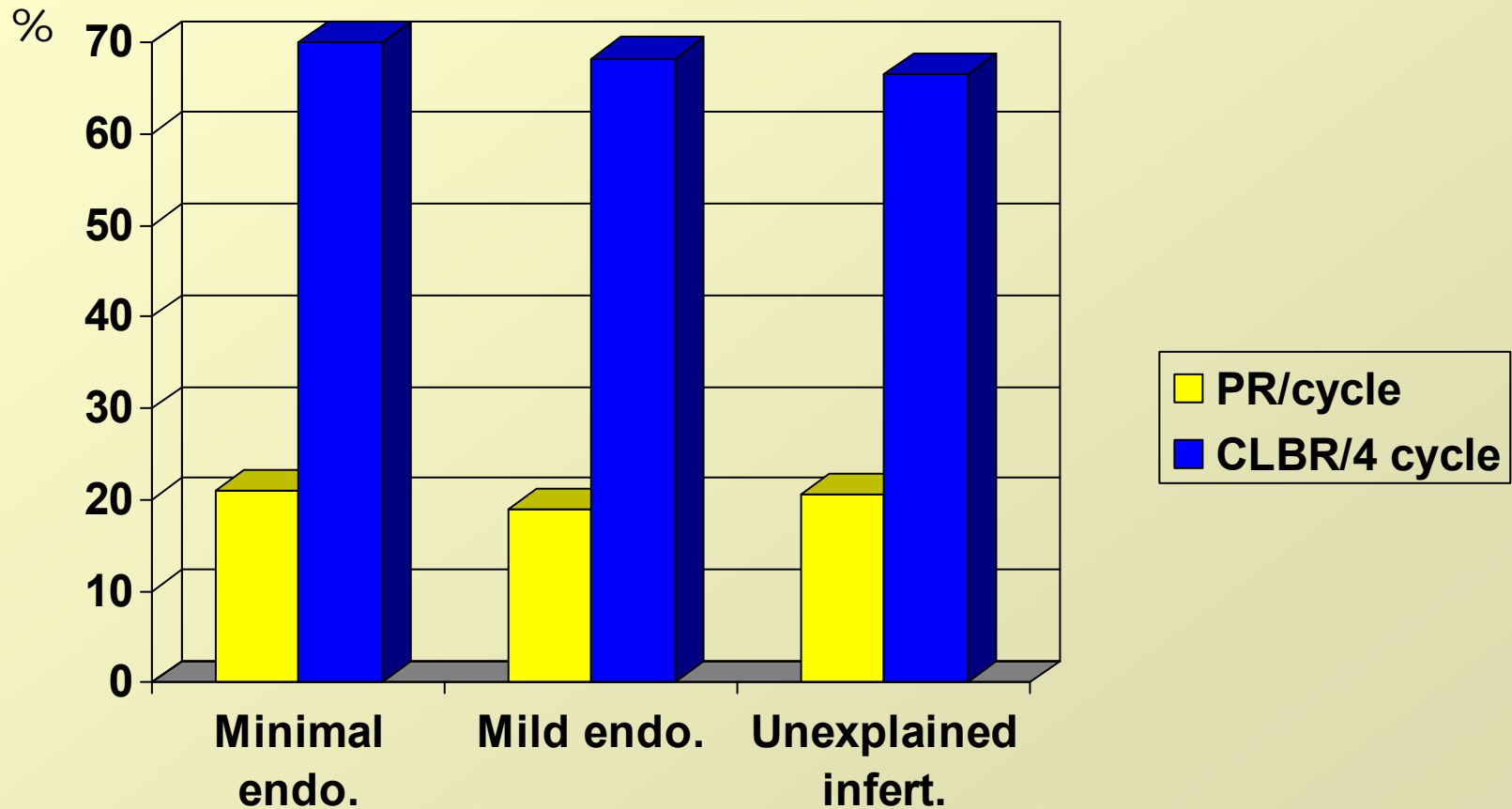
***Endometriosis-Infertility &
ART***

COH&IUI-PR's



Omland et al. Human Reprod 13: 2602-5, 1998

PR's following surgically treated minimal and mild endometriosis

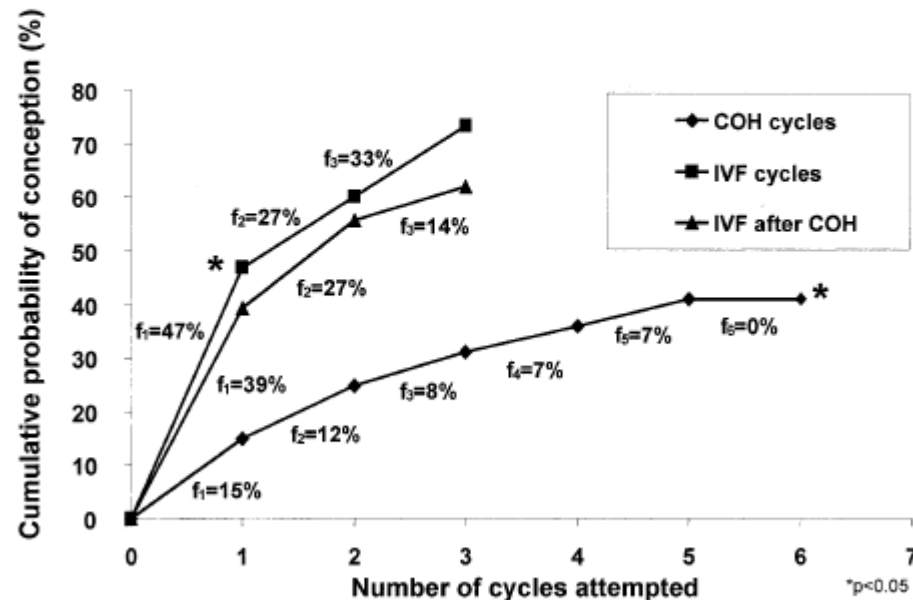


Werbrouck et al. Fertil Steril 86: 566-71, 2006

COH&IUI and IVF – Cycle specific and cumulative PR's

FIGURE 1

Cycle and cumulative fecundity in women with endometriosis undergoing COH-IUI, IVF-ET, or IVF-ET after failed COH-IUI.



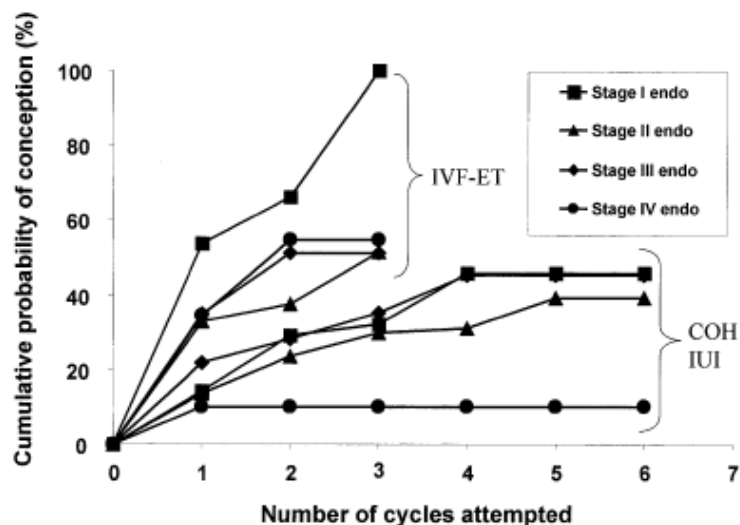
Dmowski. Fecundity with COH or IVF in endometriosis. Fertil Steril 2002.

Dmowski et al. Fertil Steril 78: 750-6, 2002

COH&IUI and IVF – Cycle specific and cumulative PR's

FIGURE 2

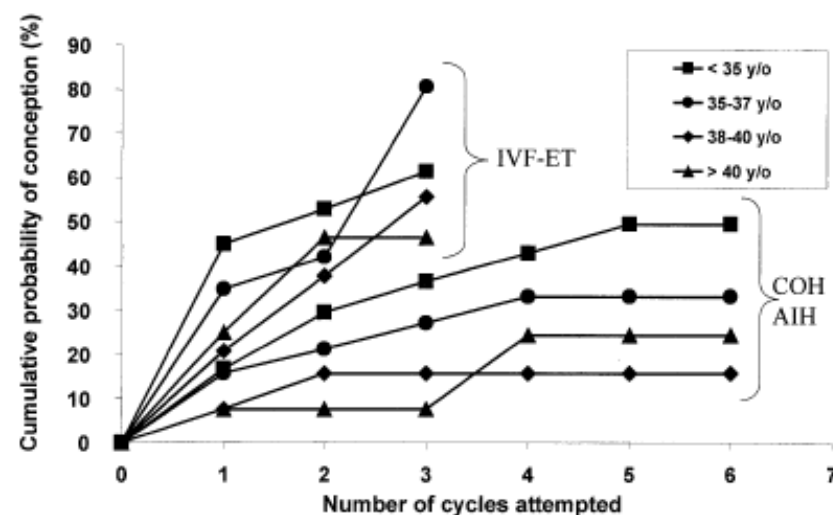
Effect of COH-IUI or IVF-ET on fecundity according to the stage of endometriosis.



Dmowski. Fecundity with COH or IVF in endometriosis. Fertil Steril 2002.

FIGURE 3

Effect of COH-IUI or IVF-ET on fecundity according to the age of the women with endometriosis.

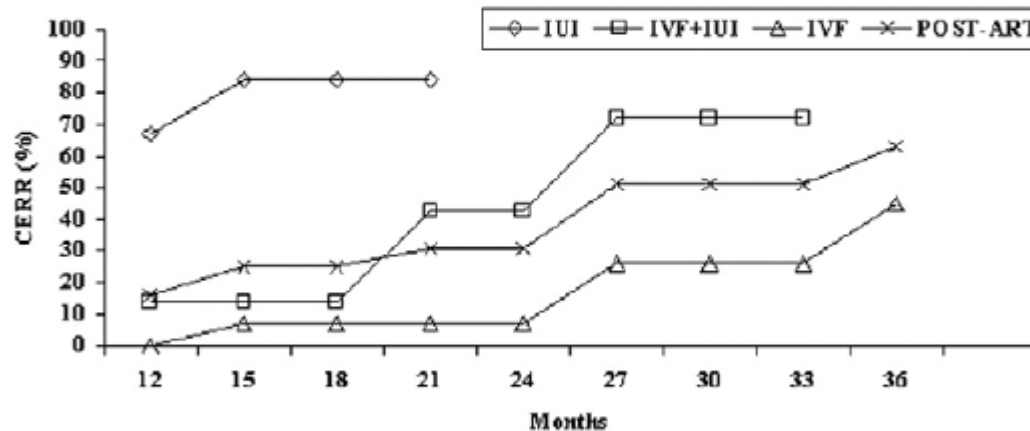


Dmowski. Fecundity with COH or IVF in endometriosis. Fertil Steril 2002.

Endometriosis recurrence following COH&IUI and IVF

FIGURE 1

Post-ART recurrence study: CERR after treatment with IUI, IVF, or a combination of IUI and IVF.



D'Hooghe. Endometriosis recurrence after ovarian hyperstimulation. Fertil Steril 2006.

D'Hooghe et al. Fertil Steril 86: 283-90, 2006

***Endometriosis-Infertility &
IVF – Ne zaman?***

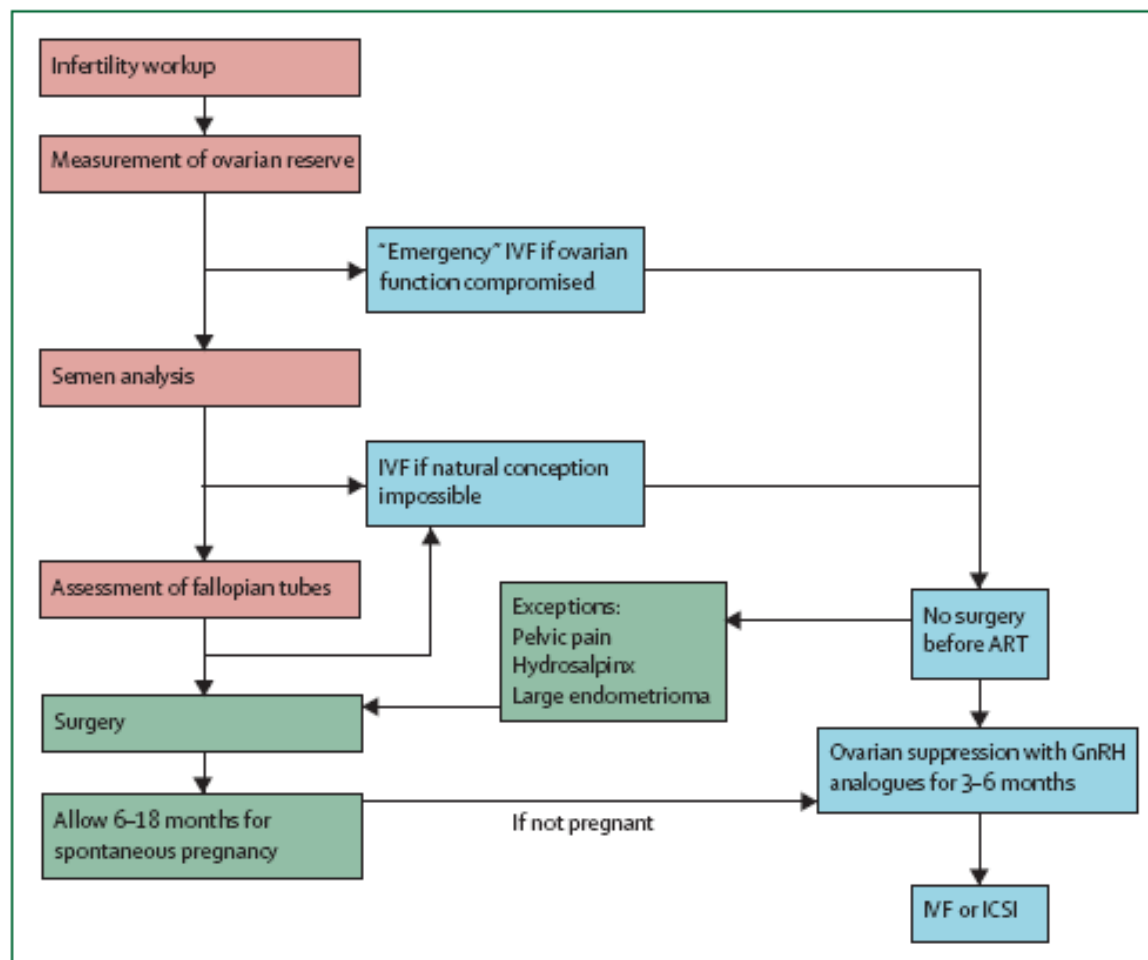


Figure 2: Algorithm for management of infertility associated with endometriosis
 IVF=in-vitro fertilisation. ART=assisted reproductive technologies. GnRH=gonadotropin-releasing hormone.
 ICSI=intracytoplasmic sperm injection.

Endometriosis-IVF Outcome

TAKE-HOME BABY

OVARY



ENDOMETRIUM



The presence and extent of endometriosis do not effect clinical pregnancy and implantation rates in patients undergoing intracytoplasmic sperm injection

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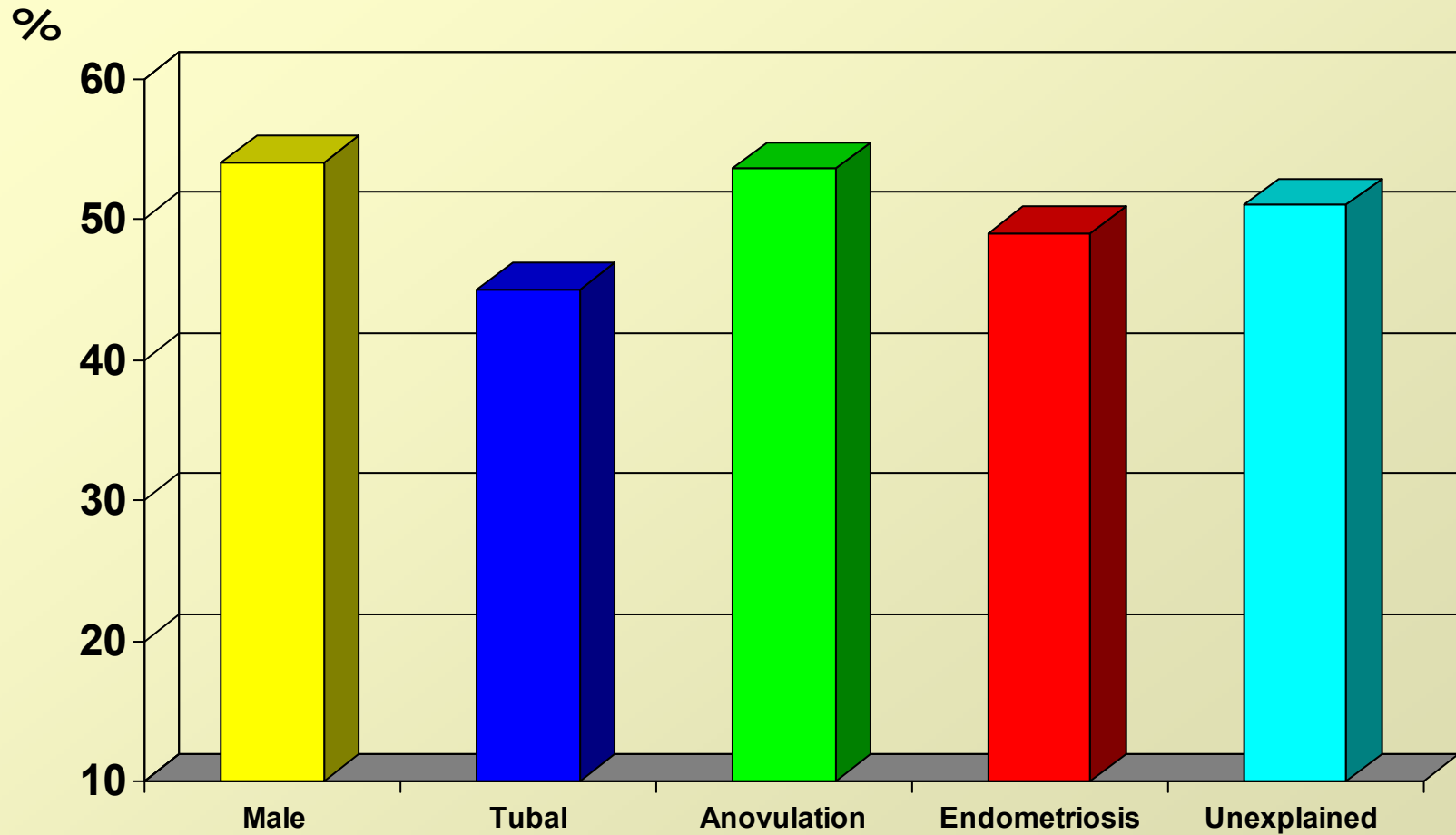
Table 4

Implantation rates and clinical pregnancies after ICSI and embryo transfer in control and endometriosis groups^a

	Controls	Minimal-mild endometriosis	Moderate-severe endometriosis
Implantation rate (%)	419/3241 (12.9)	20/186 (10.7)	12/107 (11.2)
Individual implantation rate (%)	24.9±22.0	34.0±29.7	23.0±18.0
Clinical pregnancy rate per transfer (%)	250/895 (27.9)	10/49 (20.4)	7/29 (24.1)
Take-home baby rate per transfer (%)	205/895 (22.9)	9/49 (18.3)	6/29 (20.6)

^a All comparisons are not significant.

Anatolia IVF Center-PR ($n=7,224$)



Endometriosis – IVF: Meta-analysis

Outcome	Endometriosis	Control	Adjusted OR
Preg. rate	25.4	29.5	0.63 (0.51-0.77)
Fertil.rate	56.7	65.9	0.87 (0.85-0.88)
Implan.rate	12.7	18.1	0.86 (0.85-0.88)
No.of oocytes	7.8	7.3	0.92 (0.85-0.99)

n= 2,909; Adjusted for stimulation regimen, publication data and age

Barnhart et al. Fertil Steril 77: 1148-55, 2002

Endometriosis – IVF: Meta-analysis

Outcome	Stage III-IV	Stage I-II	Adjusted OR
Preg. rate	13.8	21.1	0.64 (0.35-1.17)
Fertil.rate	74.5	58.4	Not interpretable
Implan.rate	10.2	11.3	0.21 (0.15-0.32)
No.of oocytes	6.7	8.2	0.31 (0.24-0.39)

Adjusted for publication data and age

Barnhart et al. Fertil Steril 77: 1148-55, 2002

Endometriosis & IVF

Endometrial receptivity

Impact of Stage III-IV endometriosis on recipients of sibling oocytes

	Study group		
	Endometriosis (Stage III-IV)	Control	p
No. of patients	25	33	
Age	35.0 ± 3.4	38.5 ± 4.9	0.004
No. of oocytes donated	7.8 ± 1.6	7.7 ± 1.9	NS
No. of embryos transferred	4.0 ± 0.7	4.1 ± 1.2	NS
Implantation rate (%)	14.8	16.0	NS
No. of pregnancies	10 (40%)	15 (46%)	NS
Miscarriage (%)	30%	26%	NS
Live birth (%)	28%	27%	NS

Diaz et al. Fertil Steril 74: 31-4, 2000

Endometriosis – Endometrial receptivity

Conclusion

- Endometrial receptivity is not affected

Endometrioma cystectomy – Ovarian reserve Conclusions

- Endometrioma cystectomy does reduce the ovarian reserve
- Such damage, however, may at least in part, be due to endometrioma per se

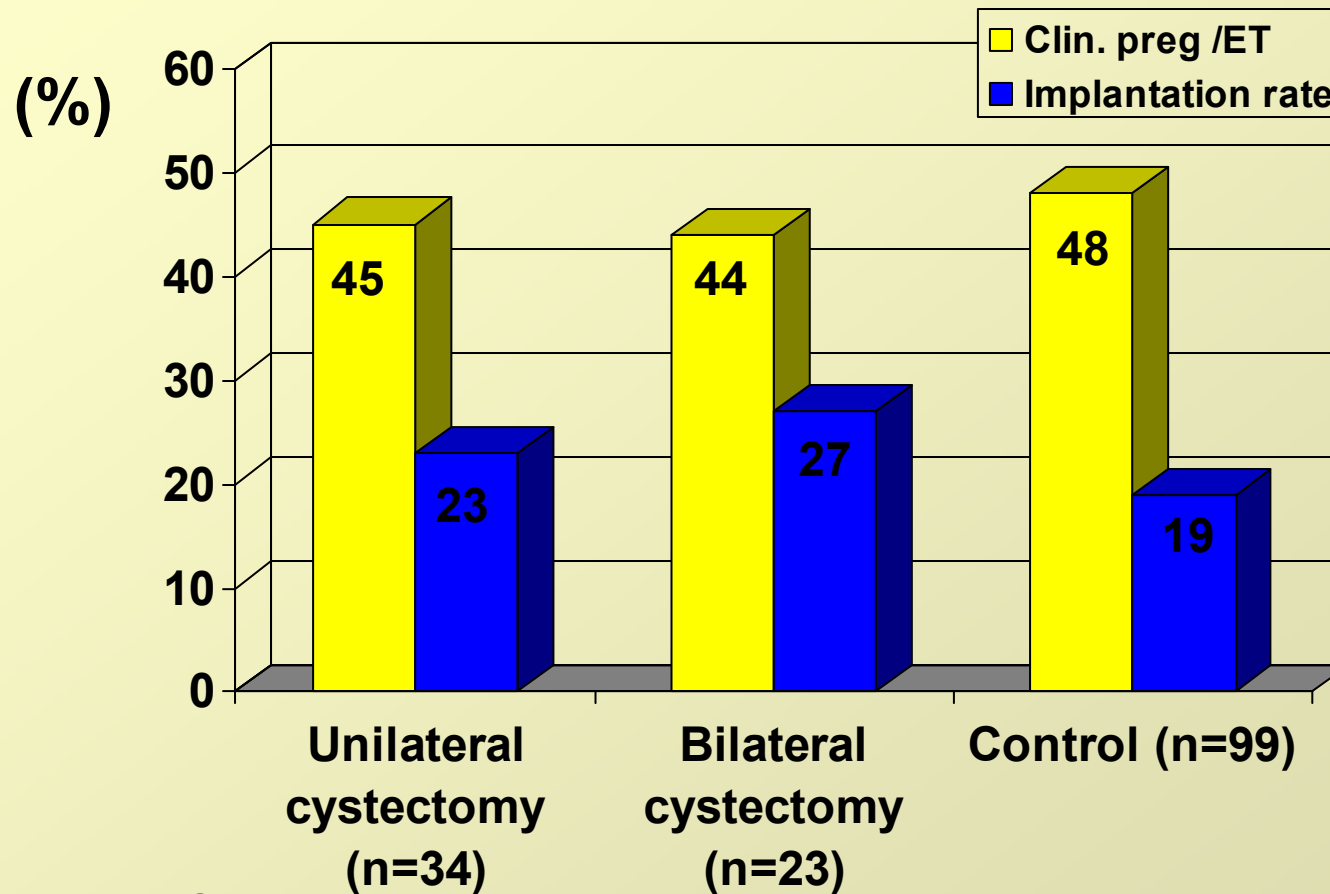
Endometrioma & IVF
Clinical studies

Should endometriomas be excised before IVF?

Variables that may affect outcome

- **Different patient types undergoing IVF**
 - Endometrioma with no previous surgery
 - Surgically resected endometrioma and disease free at the time of ART
 - Surgical resected endometrioma with recurrence at the time of ART
- **Diameter of the endometrioma**
- **Bilaterality**
- **Surgical technique**
- **Length of follow-up (surgery – IVF)**

ICSI outcome following laparoscopic endometrioma cystectomy



Literature review - ART outcome – Previous surgery vs controls

Author	Cases	PR (cases)	Controls	PR (controls)	p
Canis (2001) ^a	39	35.9%	187	31.0%	NS
Donnez (2001) ^a	85	37.4%	289	34.6%	NS
Marconi (2002) ^a	39	38.4%	39	33.3%	NS
Pabuçcu (2004) ^a	44	25.0%	46	30.0%	NS
Garcia-Velasco (2004) ^b	147	25.4%	63	22.7%	NS
Loo (2005) ^a	127	31.8%	95	29.6%	NS
Yazbeck (2006) ^c	63	15.0%	50	25.7%	NS
Demiröl (2006) ^b	49	34.0%	50	38.0%	NS
Esinler (2006) ^a	57	45.0%	99	44.0%	NS
Matalliotakis (2007) ^a	133	35.0%	208	39.0%	NS

^a Control group comprised women with tubal factor infertility

^b Control group comprised women with intact endometriomas

^c Control group comprised women with minimal to mild endometriosis

Treatment of endometrioma before IVF

RISKS OF SURGERY

- Major (1.4%) /minor (7.5%) L/S complic. **a**
- Cost
- Increased time to conception

a= Chapron et al-2002

RISKS OF EXPECTANT MANAGEMENT

- Risk of pelvic abscess / rupture
- Risk of occult malignancy (0.8% **b**)
- Retrieval difficulties
- Contamination with endometrioma content
- Endometriosis progression

b= Mostoufizadeh and Scully-1980
Stern et al-2001

Table 1 Clinical variables to be considered when deciding whether to perform surgery or not in women with endometriomas selected for IVF

Characteristics	Favours surgery	Favours expectant management
Previous interventions for endometriosis	None	≥ 1
Ovarian reserve ^a	Intact	Damaged
Pain symptoms	Present	Absent
Bilaterality	Monolateral disease	Bilateral disease
Sonographic feature of malignancy ^b	Present	Absent
Growth	Rapid growth	Stable

^aOvarian reserve is estimated based on serum markers or previous hyperstimulation cycles; ^bsonographic feature of malignancy refers to solid components, locularity, echogeniety, regularity of shape, wall, septa, location and presence of peritoneal fluid.

Garcia-Velasco and Somigliana. Human Reprod 24: 496-501, 2009

Conclusions

Does endometrioma per se decrease ovarian reserve?

YES

Does surgery for endometrioma decrease ovarian reserve?

YES

Is implantation affected by Stage III-IV endometriosis?

NO

Does surgery for endometrioma improve pregnancy rate with IVF?

NO

Surgery after failed IVF

- **Littman et al.** *Fertil Steril 2005; 84: 1574-8.*
 - 22/29 (76%) conceived post-operatively with surgery vs 13/35 (37%) without surgery
- **Drawbacks**
 - Fertility factors not controlled
 - Inappropriate matching of controls in terms of pain symptoms, presence of endometriomas and disease stage
 - Within surgery group: 12 spontaneous; 2 with CC&IUI; 8 with IVF
 - Unusual 100% prevalence of endometriosis in the surgery group

Conclusions

- **Surgery may be offered early in the course of endometriosis when there is available time, ovarian reserve and capacity to conceive naturally (tubal and sperm status)**
- **Role of COH&IUI is questionable**
- **Surgery before IVF offers little benefit with exceptions of pelvic pain, hydrosalpinx and large endometriomas**