

# **OVARIAN ENDOMETRIOMA**

## **Is surgery necessary ?**

**Kutay Biberoglu**

# Endometriosis

- Annual incidence - 0.1% for visual & 0.06% for histologic disease
- Age-specific: 30-34, 35-39 & 40-44 yrs at 13/10,000 person-yrs each
- ✓ Age at Dx - mean 35 yrs (17-68), histologically verified mean age 38 yrs
- ✓ in central pelvis - 82.9% minimal/mild
- ✓ ovarian lesions - 76.7% moderate/severe
- youngest woman with predominantly ovarian disease - age 17 yrs
- ✓ 19.1% < age 30 yrs,
- ✓ 27.4% > age 40 yrs

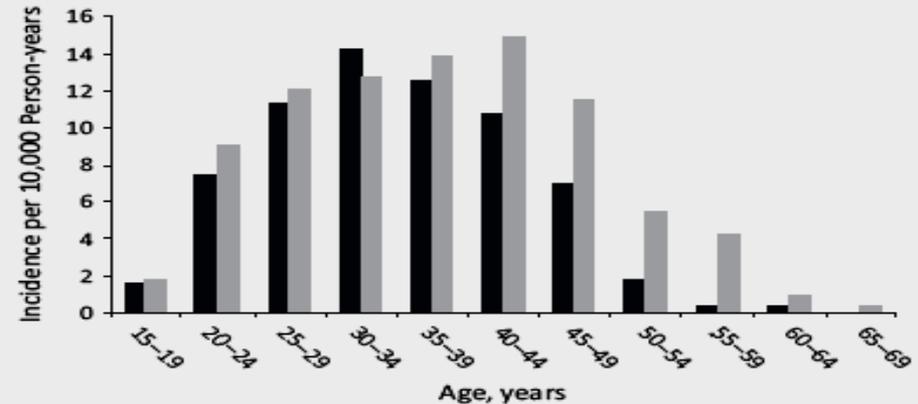


Figure 2. Age-specific incidence per 10,000 person-years of women with visually confirmed endometriosis in the Icelandic population during the first part of the study period, 1981–1990 (dark bars), and the later part of the study period, 1991–2000 (light bars).

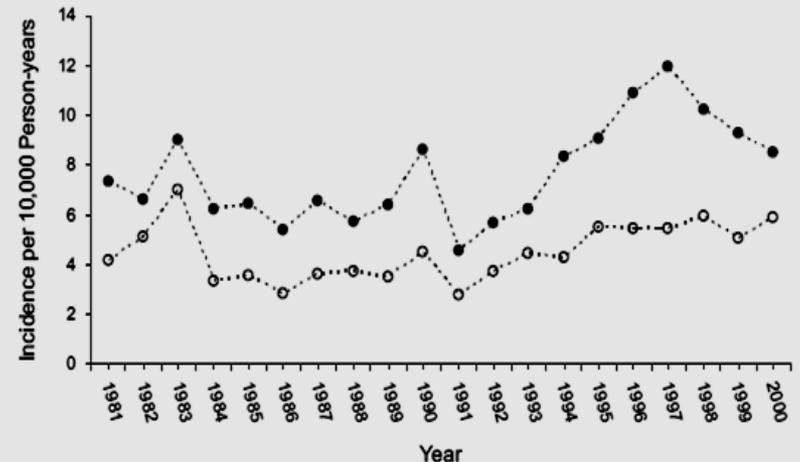


Figure 3. Age-standardized annual incidence per 10,000 person-years of visually confirmed endometriosis (dark circles) and histologically verified endometriosis (white circles) in Icelandic women aged 15–49 years during the whole study period (1981–2000).

# Endometriosis

- **Women with infertility : 50%**

Goldstein DP et al. J Repr Med 1980;24:251

Eskenazi B, Warner ML. Obs Gyn Clin North Am 1997;24:235

- **..rose from 42% in 1982 to 72% in 1992, due to greater awareness of subtle lesions**

Martin DC et al. Fertil Steril. 1989;51:63

- **Focal pain/tenderness on PE :**

- ✓ **pelvic disease in 97%**

- **If titers for chlamydia were negative – endometriosis in 83%**

Ripps BA, Martin DC. J Repr Med 1991;36: 470

- ✓ **%1 of surgery for all gynecologic indications**

- **Reproductive age : 6-10%**

- **Women with chronic pelvic pain : 16–33% ; adhesions 24–40%**

Neis KJ, Neis F. Gyn Endoc 2009;25:757

- ✓ **outpatient visits for chronic pelvic pain : 10%**

- ✓ **in adolescents with pain 25–38.3%; not responding to conventional Rx; up to 69–73 % have endometriosis at LS**

Laufer MR et al. J Pediatr Adolesc Gyn 1997;10:199

# Endometrioma

- **...in 17-55% of patients with endometriosis**  
Jenkins S, Olive DL, Haney AF. Obs Gyn 1986;67:335
- **10-25% of IVF cases are diagnosed with endometriosis, 17-44% of whom have endometriomas**  
Jenkins S et al. Obs Gyn 1986;67:335  
Redwine DB. Fertil Steril 1999;72:310
- **..35% of all benign ovarian cysts**
- **R/o dermoid cyst, hemorrhagic cyst, neoplasm, ovarian abscess, and ectopic pregnancy**
- **..it took a minimum of 4 yrs from menarche to first surgery**  
Liu X et al. Gyn Obs Invest 2008;66:76
- **Surgery is recommended if >4 cm in diameter to confirm the diagnosis, to reduce the risk of infection, and to prevent progression**  
RCOG Green Top guideline (24) 2006
- **..frustrating aspect of surgery is high recurrence of pain & endometriomas (reoperation rate 58-62% within 5 yrs)**  
Shakiba K et al. Obs Gyn 2008;111:1285  
Porpora MG et al. Fertil Steril 2010;93:716

# Endometrioma

- **origin – unknown, ...a deposit of endometrium through the fallopian tube causing adherence of ovary to pelvic peritoneum, progressive invagination of the ovary**
- **..a pseudocyst, wall of which is inverted ovarian cortex, removal of which involves removal of ovarian tissue**  
Vercellini P et al. Am J Obs Gyn 2003;188:606
- **endometrioma wall contains endometriotic tissue covering the inner wall for 60% of the surface, does not penetrate > 1.5 mm**  
Muzii L et al. Fertil Steril 2007;87:362
- **The effect on fertility is unclear as it is rare to have a solitary endometrioma without pelvic endometriosis**  
Pritts EA, Taylor RN. Endocr Metab Clin North Amer 2003;32:653
- **small risk of (0.7%) malignant transformation & rupture**  
Del Carmen MG et al. Cancer 2003;98:1658  
Nishida M et al. Gyn Obs Invest 2000;50:18
- **The effect on fertility is controversial**

# Why operate ?

- **Why operate on symptomless women for academic interest only?**
- **..conditions to make the lesion more active, progressive and incline to recurrence probably include**
  - ✓ **genetic predisposition**
  - ✓ **patient's background variables**
  - ✓ **hormonal imbalance**
  - ✓ **altered immune-surveillance, inflammatory response**
  - ✓ **aberrant regulation of the endometrial cells**
- **Surgery can treat only the acute disease, not the underlying predisposing factors to disease recurrence**
- **the risk for reoperation, coupled with uncertainty and pain, makes endometriosis a truly dreadful disease**
- **Pelvic pain cannot be used as the only criterion, since half of women with pelvic pain have either IBS or genitourinary symptoms, or both**

# Why operate ?

- **..costly and not free from complications**
- **..major (1.4 %) & minor (7.5%) LS complications**  
Chapron C et al. Hum Reprod 2002;17:1334
- **..likelihood of hospital readmission within 4 yrs for additional surgery is 27%, reoperation occurs in > 50%, 27% of them require  $\geq$  3 surgeries**  
Weir E et al. J Minim Invasive Gyn 2005;12:486  
Cheong Y et al. J Obs Gyn 2008;28:82
- **..risks associated with expectant management are mostly anecdotal or of doubtful clinical relevance**
- **Overall, LS surgery does not offer any additional benefit in terms of fertility outcomes. .. proceeding directly to IVF to reduce time to pregnancy, to avoid surgical complications and to limit patient costs**
- **..should be limited to treat pain refractory to medical treatments, or when malignancy cannot be reliably ruled out, or in the presence of large cysts**
- **Given the somewhat vague scientific scenario, gynaecologists with personal interest in ART might be more prone to suggest IVF, whereas surgeons might push for laparoscopy**

# Why operate ?

- **Since a complete cure is not possible, the current therapy has three main goals:**
  - ✓ **to reduce pain**
  - ✓ **to increase pregnancy rate**
  - ✓ **to delay recurrence for as long as possible**
- **patients must be informed that the effect of endometrioma excision on reproductive prognosis is poorly defined and that the chances of conception without surgery are currently unclear**
- **..eliminate or even delay the recurrence - an unmet medical need**

# Potential risks of Expectant Strategy

- **Missing an occult early stage malignancy – a frequency of 0.7 %, rare but possible**

Del Carmen MG et al. Cancer 2003;98:1658

Nishida M et al. Gyn Obs Invest 2000;50:18

- ✓ **strict sonographic monitoring nearly annual ..**

Eskenazi B et al. Fertil Steril 2001;76:929

- **Pelvic abscess with puncture - 0.0% (0.0–1.7)**

Benaglia L et al. Fertil Steril 2008;89:1263

- **Progression - controversial**

- **Rupture, follicular fluid contamination, difficulties during oocyte retrieval, increased obstetric complications such as preterm birth or intrauterine growth restriction**

- ✓ **no evidence that surgery may significantly overcome the reported complications**

# Diagnosis

- **LS is gold standard, but an invasive procedure under general anaesthesia, associated with complication rate of between 5-11% (major 0.1-2.3%)**

Kontoravdis A et al. Int J Gyn Obs 1996;52:243

- **Only 54-67% of visually suspected lesions are confirmed histologically, 18% of clinically suspected have no evidence of endometriosis on pathology (inflammatory changes, hemangiomas, foreign body reaction, mesothelial hyperplasia, and hemosiderin deposits)**

Walter AJ et al. Am J Obs Gyn. 2001;184:1407

- ✓ **..a positive finding on LS will be incorrect in half, increasing likelihood of histologic confirmation to 31% (21- 46%) and negative result decreases likelihood to 0.7% (0.1-5.0%)**

Wykes CB et al. BJOG 2004;111:1204

# Diagnosis

- **biopsy of normal peritoneum has revealed lesion endometriosis in 6% with no visible lesions, in up to 25% of asymptomatic infertile women**  
Balasch J et al Hum Reprod. 1997; 12:1794
- **There is only a small chance that asymptomatic lesions found incidentally will become symptomatic later**  
Moen MH, Stokstad T. Fertil Steril. 2002;78(4):773
- **..lesions most likely to be histologically confirmed - large, mixed color lesions in the culde- sac or on the uterosacral ligaments**  
Stegmann BJ et al. Fertil Steril. 2008;89:1632
- **TVS : 84–100% sensitivity & 90–100% specificity**  
Garcia-Velasco JA, Somigliana E. Hum Reprod 2009; 24:496  
Savelli L. Ultrasound Obs Gyn 2009;33:497
- **MRI is superior in rectosigmoid & bladder lesions**  
Ballyguier C et al. J Am Assoc Gyn Laparosc. 2002;9:15

# Diagnosis

- **83% with endometriosis reporting  $\geq 1$  of pain symptoms compared with just 29% of women without**  
Ballard K et al. Br J Obs Gyn 2008;115:1382
- **Severity of pelvic pain correlated with extent of pelvic & adnexal adhesions, deep & cystic endometriosis**  
Popora M et al. J Am Assoc Gyn Laparosc 1999;6:429  
Jacobson TZ et al. Cochrane Database of Systematic Reviews 2009, Issue 4. Art.No.: CD001300
- **..more likely to report pain as throbbing, more likely to have dyschezia when compared with normal pelvis**  
Ballard K et al. Fertil Steril 2010;94:20
- **21% with chronic pelvic pain have no pathology at LS**  
Kang SB et al. Surg Endosc 2007;21:916
- **..experienced clinicians can predict endometriosis based on Hx & PE in 80% of cases**  
Engemise S et al. BMJ 2010 ;340:1414

# Pelvic pain due to endometriosis

- **chronic (lasting  $\geq 6$  mths)**
  - ✓ **dysmenorrhea (in 50-90% of cases), dyspareunia, deep pelvic pain, lower abdominal pain  $\pm$  back & loin pain**  
Giudice LC. NEJM. 2010;362:2389
- **onset of pain to surgical diagnosis : 8-10.4 years**  
Hadfield R et al. Hum Reprod 1996;11: 878  
Ballard K et al. Fertil Steril 2006;86:1296
- ✓ **..with Stage I may have incapacitating pain while some with Stage IV may have no pain at all**  
Vercellini P et al. Fertil Steril 1996; 65:299
- ✓ **..with stage I were less likely to have relief in pain after surgery, compared to those with stage II-IV disease**  
Sutton CJ et al. Fertil Steril 1994; 62:696
- **Up to 20% with endometriosis have concurrent pain conditions, IBS, interstitial cystitis, fibromyalgia, and migraines... should be ruled out**  
Berkley KJ, Stratton P. In: Giamberardino MA, ed. Oxford: Oxford University Press; 2009:39

# **Pelvic pain due to endometriosis**

- **10-15% with CPP have asymptomatic endometriosis**
- **.. explain the frequently stated paradox of “patients with mild endometriosis often have the worst pain.”**
- **patients may have a component of pain not only from endometriosis but also from other pain generators**
- **upregulation occurs, inflammatory changes in one organ often induce inflammatory changes in another**
- **the “sham intervention” for patients with mild to moderate endometriosis demonstrated that 48% of the patients had pain relief 3 months after surgery**

**Sutton CJG et al. Fertil Steril. 1997;68:680**

**Abbott J et al. Fertil Steril. 2004;82:878**

- **.. time for requirement of additional Rx after “sham intervention” - 11.9 mths & after 2 yrs, 57% required pain medications - a resolution of placebo effect**

**Horstein M et al. Fertil Steril. 1997;68:860**

# Endometriosis – Natural History

- **sequential LS's have shown ... to be progressive**  
Mahmood TA, Templeton A. Hum Reprod 1990;5:965  
Telimaa S et al. Gynecol Endocrinol 1987; 1:13  
Thomas EJ, Cooke ID. BMJ 1987; 294:1117
- ✓ **rarity in adolescence (underdiagnosis) & relapse after surgical removal (incomplete treatment)**
- ✓ **..widespread belief that it is a progressive disease**
- **..almost 50% of adolescents had severe disease at time of LS**  
Reese KA, Reddy S, Rock JA. J Pediatr Adolesc Gyn 1996; 9:125
- **natural course is entirely unpredictable**
- **In the subset with persistent CPP after LS laser ablation, over 12-month period, of lesions..**
- ✓ **17-29% resolve spontaneously**
- ✓ **24-64% progress**
- ✓ **9-59% are stable**  
Sutton CJ et al. Fertil Steril 1997;68:1070

# Endometriosis – Natural History

- **deposits resolved spontaneously in up to a third, deteriorated in nearly half, and unchanged in the rest**

Abbott J et al. Fertil Steril 2004;82:878

- **deep rectovaginal nodules are progressive in <10%**

Fedele L et al. Am J Obs Gyn 2004; 191:1539

# Endometriosis – Natural History

- **menstrual reflux is a common occurrence**
- ✓ **...small implants occur frequently in asymptomatic women of reproductive age**
- ✓ **...some of what has been labelled pathologic may represent temporary phase of ongoing process of cytolysis of recently implanted fragments**

Vercellini P et al. Hum Reprod 1992;7:627

Thomas EJ. Hum Reprod 1996;11:103

Holt VL, Weiss NS. Epidemiology 2000;11:654

# Recurrence of Endometriosis

- **..quite variable**
- ✓ **due to differences in duration of follow-up**
- ✓ **criteria for definition of recurrence**
- ✓ **prognostic profile of subjects**
  
- **..risk appears to be higher in**
- ✓ **young age women with advanced disease**
- ✓ **women undergone medical treatment alone**
- **previously treated with post-op. medical therapy (just delay the endometrioma recurrence)**

Koga K et al. Hum Reprod 2006;21:2171

Chapron C et al. Hum Reprod Update 2002;8:591

Busacca M et al. Hum Reprod 2001;16:2399

Muzii L et al. Am J Obs Gyn 2000;183:588

# Recurrence of Endometriosis

- **Post-op GnRH-a for 6 months vs expectant management - less recurrence**

Jee BC et al. Fertil Steril 2009;91:40

- **COC's prevent recurrences effectively**

Vercellini P et al. Am J Obs Gyn 2008;198:504.e1

Takamura M et al. Human Reproduction, Vol.24, No.12 pp. 3042–3048, 2009

- **Post-op hormonal suppression (COC & GnRH<sub>a</sub>)  
– no advantage in preventing ovarian recurrence**

Busacca M et al. Hum Reprod 2001;16:2399

Muzii L et al. Am J Obs Gyn 2000;183:588

Sesti F et al. Eur J of Obs Gyn Reprod Biol 2009;147:72

- **'..insufficient evidence to conclude that post-op hormonal R/o is associated with a significant benefit'**

Yap C, Furness S, Farquhar C. Cochrane Database Syst Rev 2003;3:CD003678

# Recurrence of Endometriosis

- **Long-term treatment involves repeated courses of medical therapy ± surgical therapy**
- **Endometrioma recurrence affects between 8-32% of women**  
Busacca M et al. Am J Obs Gyn 1999;180:519  
Koga K et al. Hum Reprod 2006;21:2171  
Vercellini P et al. , Hum Reprod 2007;22:266  
Kikuchi I et al. Acta Obs Gyn Scan 2006;85:1120  
Busacca M et al. Am J Obs Gyn 2006;195:426  
Xishi L et al. Obs Gyn 2007;109:1411
- **Symptom recurrence (up to 3 yrs after Rx) varies from 37% for mild, to 74% in severe disease**  
Winkel CA. Obs Gyn 2003;102:397  
Abbott J et al. Fertil Steril 2004;82:878  
Redwine DB. Fertil Steril 1991;56:628  
Wheeler JM, Malinak LR. Am J Obs Gyn 1983;146:247
- **..with surgery alone, pain symptoms will persist or recur in over 40% within 1 year**  
Shaw RW. Lancet 1992; 340:1267
- ✓ **..a significant asymptomatic recurrence rate by TVS & 2° LS done within 48 months of Rx**
- ✓ **..it is possible that those with decreased severity of symptoms who did not require 2° LS potentially had regression of endometriosis as a result of treatment..**  
Doyle JO et al. J Pediatr Adolesc Gynecol (2009) 22:257

# Recurrence of Endometriosis

- **#39, 17 (44%) had one, 8 (20%) had two, and 4 (10%) had three previous LS's**
- **38% had new lesion at 2°LS, lesion at previously uninvolved region was present in 11% at 2° LS**
- **..was more likely to recur in the treated pelvic region than in an adjacent or distant pelvic region [RR 2.54 (1.63-3.97)] - incomplete excision or ablation?**
- **...not all persistent/recurrent pelvic pain is due to endometriosis in women who had surgery ; not all reoperated patients had endometriosis**
- **94% with persistent/recurrent CPP after surgery had less or no endometriosis at 2° LS - consequence of up-regulation of pain signals and not recurrent disease?**

# Recurrence of Endometrioma

- **Excisional surgery provides a more favourable outcome than drainage & ablation with regard to the recurrence of the endometrioma (OR 0.41, 95% CI 0.18-0.93) , recurrence of pain symptoms [dysmenorrhoea (OR 0.15, 0.06-0.38), dyspareunia (OR 0.08, 0.01-0.51) and non-menstrual pelvic pain (OR 0.10, 0.02-0.56)], and spontaneous pregnancy (OR 5.21, 2.04-13.29) in previously subfertile women**

Hart RJ et al. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD004992

# Effect of Combined Surgical-Medical Intervention on Progression of Endometriosis

- # 90, median age, stage at 1-2° LS, interval between surgeries–mths; 19 (12-24), I (max. III), 29 (6-112)
- continuous COC (91%), leuprolide acetate - P / EP add-back (78%), P only (including NETA & depot MPA) (12%)
- regardless of initial stage, no SS trend toward disease progression, stage II/ III most likely to exhibit improvement

**Table 2.** Change in Stage of Endometriosis between Surgeries

	Between 1st and 2nd Surgery	
	n	%
Improved by Two Stages	1	1%
Improved by One Stage	17	19%
Stage Unchanged	63	70%
Worsened by One Stage	9	10%
Total	90	100%
Likelihood of increase (worsening) in disease stage		<i>P</i> = 0.29
Likelihood of decrease (improvement) in disease stage		<i>P</i> < 0.0001
	Between 2nd and 3rd Surgery	
	n	%
Improved by Two Stages	1	3%
Improved by One Stage	6	18%
Stage Unchanged	23	70%
Worsened by One Stage	3	9%
Total	33	100%
Likelihood of increase (worsening) in disease stage		<i>P</i> > 0.99
Likelihood of decrease (improvement) in disease stage		<i>P</i> = 0.77

# Factors for Symptomatic Recurrence

- No significant association between postoperative pain and patient's age, number and size of ovarian endometriomas, presence of deep endometriosis, and disease stage
- **Unfavorable factors:**
  - ovulation induction drugs –
    - ✓ dysmenorrhea (RR 4)
    - ✓ CPP (RR 9.9)
  - Adnexal adhesions score at LS –
    - ✓ CPP (RR 2.6)
    - ✓ dyspareunia (RR 3.7)
    - ✓ dysmenorrhoea (RR 2.7)

Porpora MG et al. Fertil Steril 2010;93:716

# Recurrences of Ovarian Endometriomas

- 9.6- 30.4% ; 40% on the same, 20% on the opposite, and 40% on both ovaries
- 62.5% underwent a reoperation
  
- No effect** : Age, infertility, adenomyosis, rASRM score, number, site, bilaterality, type, extent of peritoneal lesions, postop Rx
  
- Unfavorable factors** :
  - ✓ prior surgery for endometriosis (RR 6.25)
  - ✓ presence & adnexal, cul-de-sac adhesions score at LS (RR 3.02)
  - ✓ ovulation induction drugs (RR 4.9)
  - ✓ previous medical treatment (RR 2.15)
  - ✓ the largest cyst size (RR 1.197)
  
- Favorable factors** : pregnancy (RR 0.27) ; no recurrence

Koga KK et al. Eur J Obs Gyn Reprod Biol 123 (2005) S1

Porpora MG et al. Fertil Steril 2010;93:716

# Endometriosis – Natural History

- **It is uncertain whether leaving endometriosis untreated accelerates the age related decline in fertility**
- **it is not known whether early surgical intervention will limit the progression and minimize the impact of endometriosis on future reproductive potential**

Marcoux S, Rodolphe M, Berube S. NEJM 1997; 337:217

- **Pelvic pain associated with endometriosis may recur, so offering surgery early in the course of treatment may predispose to multiple surgeries in the future**

Stavroulis AI et al. Eur J Obs Gyn Reprod Biol 2006;125:248

# Would Surgery Improve Fertility?

- **Ablation of endometriotic lesions/adhesiolysis in minimal/mild endometriosis, is effective (vs. diag. L/S)**  
Practice Committee of ASRM. Fertil Steril. 2006;86(5):S18  
Marcoux S et al. NEJM 1997;337 (4):217  
Jacobson TZ et al. Cochrane Database Syst Rev.2010;20(1):CD001398
- **No RCT's or meta-analyses in moderate/severe disease**
  - ✓ **...that normalizes pelvic anatomic distortion can enhance fertility**  
Parazzini F. Hum Reprod. 1999;14 (5):1332  
Adamson GD, Baker VL. Best Pract Res Clin Obs Gyn. 2003;17(2):169
  - ✓ **negative correlation between stage vs. pregnancy rate**  
Guzick DS et al. Fertil Steril. 1997;67 (5):822  
Osuga Y et al. Gynecol Obstet Invest. 2002;53 Suppl 1:33

# Would Surgery Improve Fertility?

- **L/S cystectomy vs. drainage & coagulation > 4 cm improves fertility**

Beretta P et al. Fertil Steril. 1998;70(6):1176

Chapron C et al. Hum Reprod Update. 2002;8(6):591

- **...excision compared with drainage or ablation resulted in less frequent recurrence of symptoms, as well as reduced rates of further surgery**

Hart RJ et al. Cochrane Database Syst Rev 2008;2:CD004992

- **Cogulation/laser vaporization - increased recurrence**

Vercellini P et al. Am J Obs Gyn. 2003;188(3):606

# Endometriosis-associated Infertility

- **Surgery [pregnancy (37.4%)], if not, IVF-ET [56.1%]**

Coccia ME et al. Eur J Obstet Gynecol Reprod Biol. 2008;138(1):54

- **Combined medical Rx & surgery – no benefit, may delay further therapy**

Practice Committee of ASRM. Fertil Steril. 2006;14:S156

- **IVF-ET without prior surgery as first-line treatment**

Aboulghar MA et al. Am J Obstet Gynecol. 2003;188(2):371

# Endometriosis & IVF

...if severe, tends to reduce success rates

✓ due to

- inflammatory effects, adhesions & ovarian involvement
- decreased ovarian reserve
- difficulty of oocytes retrieval
- quality of oocytes
- Implantation

Practice Committee of the ASRM. Fertil Steril 2004;82(Suppl 1):S40

Navarro J et al. Obs Gyn Clin North Am 2003;30:181

Aboulghar MA et al. Am J Obst Gyn 2003;188:371

Al-Fadhli R et al. J Obst Gyn Can 2006;28:888

fertilization ; pregnancy ; implantation rates

**0.81 (0.79–0.83) ; 0.56 (0.44–0.56) ; 0.86 (0.85–0.88)**

Barnhart K et al. Fertil Steril 2002;77:1148

cycle cancellation rate %50

Kuivasaari P et al. Hum Reprod 2005;20:3130

...but cumulative pregnancy rates remain favourable

Dechaud H et al. Gyn End 2009; 25(11): 717

**3 RCTs (#165) women with endometriosis should receive GnRHa for 3 consecutive months before ART - clinical pregnancy OR 4**

Sallam HN et al. Cochrane Database Syst Rev 2006;25, CD004635

# Endometrioma & IVF

- **Prior to IVF**

- ✓ **..always surgery**

Wong BC et al. , Am J Obs Gyn 2004;19:597

- ✓ **...never surgery**

Garcia-Velasco JA et al. Fertil Steril 2004;8:1194

Garcia-Velasco JA, Somigliana E. Hum Reprod 2009;24(3):496

- **..may hamper follicular development versus surgery can cause diminished ovarian reserve**

Gupta S et al. Reprod Biomed Online 2006;13:349

Kumbak B et al. Gyn Obs Invest 2008;65:212

- **postsurgical ovarian failure - 2.4%**

Busacca M et al. Am J Obs Gyn 2006;195:421

- **..puncturing endometrioma - abscess %2.3 vs 0.2**

Benaglia L et al. Fertil Steril 2008;89:1263

- **bilateral cystectomy - RR of prem. menopause x 2.4 (0.5–6.8)**

Busacca M et al. Am J Obs Gyn 2006;195:421

# Ultrasound-guided aspiration of Ovarian Endometriomas

- **no evidence in favour of drainage ...**
- **aspiration vs aspiration & in situ irrigation or injection with a sclerosing agent (tetracycline, MTX, rec. interleukin-2 ± ethanol) - evidence not convincing**
- **for whom decline surgery / contraindicated, ..may facilitate oocyte retrieval in IVF ; high recurrence rate**

Aboulghar M et al. Hum Reprod 1991;6:1408

Aboulghar M et al. J Assist Reprod Gen 1993;10:531

Acien P et al. Gyn Obs Invest 2003;55:96

Mesogitis S et al. Lancet 2000;356:429

Noma J, Yoshida N. Int J Gyn Obs 2001;72:35

# Conservative laparoscopic surgery of ovarian cysts

- **..in nonendometrial vs endometriotic cysts, ovarian tissue is removed in 6 vs 54% of cases respectively (pseudocyst with inverted ovarian cortex)**  
Muzzi L et al. Fertil Steril 2002;77:609  
Muzzi L et al. Hum Reprod 2005;20:1981  
Muzzi L et al. Hum Reprod 2005;20:1987
- **..damage may also be due to surgery-related local inflammation or vascular compromise following electrosurgical coagulation**
- **..ovarian tissue inadvertently removed with cyst wall in 48% by laparoscopy and 59% by laparotomy**
- ✓ **..no morphology of normal ovarian tissue**

Alborzi S et al. Fertil Steril 2009;92:2004

# Cystectomy before ART

- To improve access to follicles/improve response?
- in endometrioma  $\geq 3-4$  cm?
- ✓ ...arbitrary, no evidence to support which size..
  
- If follicles be reached, no surgery in cysts over even 5 cm; if hides, smaller cysts require surgery
  
- To confirm the diagnosis histologically
  
- Risks of reduced ovarian function/loss of ovary
  
- There is convincing evidence that responsiveness to gonadotrophins after ovarian cystectomy is reduced and the number and quality of oocytes retrieved are at least not improved

Demirol A et al. Reprod Biomed Online 2006;12:639

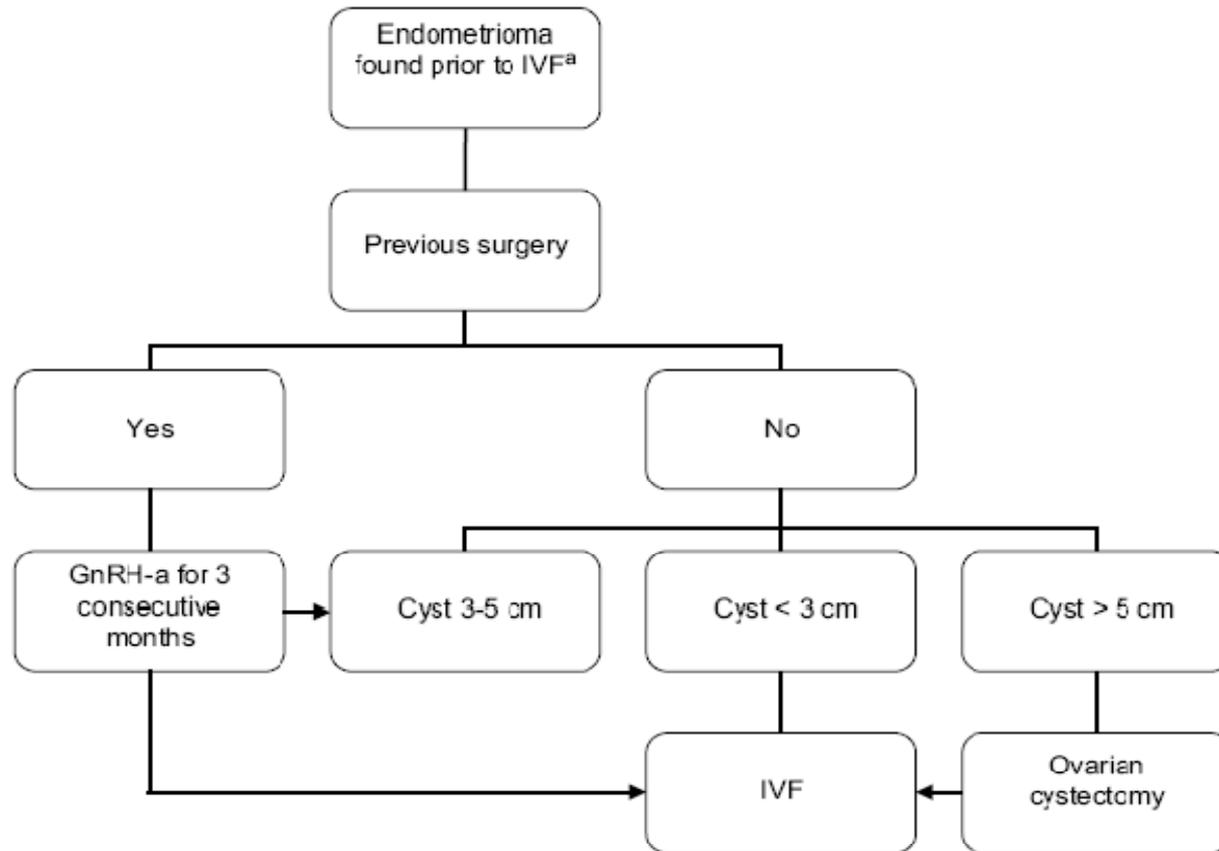
Garcia-Velasco JA et al. Fertil Steril 2004;81:1194

Garcia-Velasco JA, Somigliana E. Hum Reprod 2009;24(3):496

Tsompou I et al. Fertil Steril 2009;92:75

# Cystectomy before ART

Flow chart for management of endometrioma.



<sup>a</sup>: in vitro fertilization

*Tsompou. Surgery for endometrioma and IVF outcome. Fertil Steril 2009.*

# Variables in favouring surgery

- **no previous surgery**
- **intact reserve (serum markers/previous COH cycles)**
- **presence of pain**
- **monolaterality**
- **growth**
- **size  $\geq 4$  cm**
- **features of malignancy (solid components, septa, peritoneal fluid, multilocularity, hyperechogenicity, irregularity).**

# **Variables in favoring expectant management**

- **previous surgery**
- **poor reserve**
- **absence of pain**
- **bilaterality**
- **size < 4 cm**
- **no features of malignancy**
- **no growth**

# **to operate or not before IVF**

- **treatment should be individualized, decision must be made on a case-by-case basis**
- **Various factors influence clinical decisions;**
  - ✓ **size of the cyst**
  - ✓ **previous ovarian surgery**
  - ✓ **previous ovarian response to stimulation/IVF outcome**
  - ✓ **the patient's choice**
- **Patients should not be treated in boxes**

# **Effective management of Endometriosis**

- **Medical treatments should be reserved for patients with endometriosis-related pain**
- **With respect to endometriosis-related infertility, surgical removal of superficial & deep lesions and adhesiolysis may result in spontaneous pregnancy**
- **Various ART's are complementary approaches to spontaneous pregnancy or surgical intervention**
- **IUI may be offered for stage I/II endometriosis**
- **For more severe cases or in the presence of pelvic adhesions, IVF is proposed**

# Laparoscopic Treatment of Endometriomas

- **Despite lack of RCTs, general consensus is that LS surgery increases the chances of pregnancy (30-67%)**
- ✓ **Pregnancy OR 5.11 (2.03–12.85), NNT 2.7**

Chapron C et al. Hum Reprod Update 2002;8:591

Jones KD, Sutton CJ. Hum Reprod 2002;17:782

Beretta P et al. Fertil Steril 1998;70:1176

Alborzi S et al. Fertil Steril 2004;82:1633

- **Stripping vs opening & vaporizing / coagulating inner surface – endometrioma wall contains endometriotic tissue covering the inner wall for 60% of the surface and it does not penetrate > 1.5 mm**

Muzii L et al. Fertil Steril 2007;87:362

# Endometriosis & Ovarian Malignancies

- **...associated especially with endometrioid & clear-cell carcinoma**  
Vlahos NF et al. Best Pract Res Clin Obs Gyn 2010; 24: 39
- **..effect of uninterrupted ovulatory cycles on development & persistence..**  
Olive DL, Schwartz LB. NEJM 1993;328:1759  
Olive DL, Pritts EA. NEJM 2001;345:266
- **An environment rich in E & poor in P & additional genetic alterations seem to help its evolution to a malignant state – evidence has not been shown yet**  
Oxholm D et al. Acta Obs Gyn Scand.2007;4:1  
Soliman NF, Hillard TC Climacteric 2006;9:325
- **Exact molecular mechanisms leading to malignant transformation are not completely understood**
- ✓ **..in 20 686 patients, in 11.4 years, ovarian cancer incidence ratio 1.9 (1.3–2.8)**  
Brinton LA et al. Am J Obs Gyn 1997; 176: 572
- ✓ **..in 37434 women, RR 0.8 (0.2–2.4)**  
Olson JE et al. Cancer 2002; 94: 1612
- **..diameter of  $\geq 9$  cm (HR, 5.51;2.09–9.22) & postmenopausal status (HR, 3.21; 1.79–4.69) - independent predictive factors for cancer**  
Kobayashi H et al. Eur J Obs Gyn Reprod Biol 2008;138:187

# Endometriosis & Ovarian Malignancies

- ..should be carefully followed up, even after menopause
- although there is no evidence that progestin reduces the risk .. adding P to E is recommended
- even after surgery, patients have elevated risk..

