The management of ovarian masses prior to ART

Presentation Objectives
- Introduction
- Simple cysts – Corpus luteum cysts
- Follicular cysts
- Endometriomas and implants
- Fertility Sparing surgery
- IVF Vs FSS Vs combined medical & Surgical treatment
- Surgery techniques: Bipolar / Monopolar
- Dermoid cysts
- Low Malignant Tumours and FSS
- Ovarian cancer and FSS

How can surgery increase the success rate in ART?
- 6-7 May 2011
- ESHRE Campus
- SIG Reproductive Surgery
- Grado – Italy

Vasilios Tanos, MD, PhD.
Professor in Obstetrics and Gynaecology
Hadassah University Hospital

Ovarian masses and pelvic lesions
- corpus luteum cysts
- functional / simple cysts
- endometriomas and implants
- dermoid cysts
- Pelvic masses due to PID / Abscess
- Adhesion conglomerates

Functional ovarian cysts and Oral Contraceptives treatment
- common gynecological problem of reproductive age worldwide
- when large, persistent, or painful, may require operations
- treatment with oc common practice since 70s
- 7 RCTs from 4 countries - 500 women.
- with cysts that occurred spontaneously and/or after ovulation induction
- Results: most cysts resolved without treatment within a few cycles
- persistent cysts tended to be endometrioma or para-ovarian cyst
- Conclusion: Combined oc has no benefit in ovarian cyst resolution

Cochrane Database of Systematic Reviews 2006
DA Grimes et al. 2009
Benign ovarian cysts in US
Prospective Observational longitudinal study

- 323 women, 19-50 y old, with ovarian cysts
- 120 study group, 6-12 months follow up
- Endometriomas 3.3cm (SD 1.5)
- Simple cyst 4.1cm (SD 1.6)
- Dermoid cyst 3.2cm (SD 1.4)
- Haemorrhagic cyst 3.5cm (SD 1.2)
- Follow up median 42 months (18-94 months)
- 8.3% disappear during follow up
- Non developed to ovarian Ca
- Conclusion: Conservative management is recommended for Bg ovarian cysts
  J L Alcazar et al. 2005 Hum Reprod

Ovarian reserve is damaged after excision of ovarian masses

- gonadal damage is at least partly caused by the presence of an ovarian mass per se preceding surgery
- laparoscopic / laparotomy by stripping or excision or
- electro surgical coagulation /bipolar /monopolar causes
- local inflammation
- vascular compromise following
- lack of local fibrinolytic response and
- creation of adhesions and
- destruction of microvascularization

Reduced ovarian reserves after Surgery

- 20 w Bg ovarian cysts – lappic cystectomy
- AMH & ovarian volume by US
- AMH level recovered to 65% of the preop level 3 months pop
- AMH level was higher 1 week pop in endometriosis as compared to non endometriotic cysts
  H J Chang et al 2010 - Fertil Steril
The difference between Ovarian & peritoneal endometriosis: In Fertility perspective

- infertility cases main concern is the choice of treatment medical or surgical
  Take in consideration that:
  - a spontaneously regressive phenomenon
  - the risk of recurrence
  - the results of in-vitro fertilization Vs medical treatment Vs combined therapy

Conclusion: Whatever type of surgery is performed the IVF results / ET are not impaired, especially if ovarian cortex stays intact

M Nisolle - Current Opinion in Obstetrics and Gynecology, 2002

The role of endometriosis on ART

- Does endometriosis affect the outcome of ART?
- Does surgical treatment for endometriosis prior to or after ART affect the PR
- Is ART a risk factor for endometriosis recurrence after medical or surgical therapy?

A De Hondt, et al. 2006
Ovarian endometriomas derange the physiological mechanisms of ovulation

Advanced Endometriosis causes
- lower reproductive performance
- is due to the lower number of oocytes achieved
- not due to lower oocyte quality.
- mechanical and vascular effects due to adhesions may decrease the number of M2-oocytes retrieved

(M.Vilela et al Argentina P-473 Poster ESHRE 2010)

Endometriotic ovarian cysts
Reduce ovulation rate

Q: - ovarian reserve is damaged after excision of ovarian endometriomas?
Q: - gonadal damage caused by the existence of endometriosis per se?

- 70 women with unilateral endometriomas operated
  - serial US followed to determine the side of ovulation
  - Results
    - Ovulation occurred in the affected ovary in 22 cases (31%; 95% CI: 22–43%)
    - Assuming that the expected rate of ovulation in both ovaries in healthy women is similar, this difference was of statistical significance ($P = 0.002$).
    - Conclusion: The physiological mechanisms leading to ovulation are deranged in ovaries with endometriomas.

Laura Benaglia et al. 2010

Oocytes from endometriosis are altered?
Do they develop lower quality embryos?

Q: - whether endometriosis per se affects fertility?
Q: - whether surgical removal of implants should be performed at all?

Results
- in untreated control subjects followed for spontaneous PR
- 6RCTs with medical treatment and 2RCTs with surgical treatment
- overall pregnancy rate in the (untreated) controls of all RCTs together - 28% (24–33%)
- Taylor and Collins review 20 studies of 2026 couples with essentially unexplained infertility of 33% (31–35%) NO significant difference found
Endometriosis Surgery - Benefits Vs Risks

2 RCTs studied PR after surgical resection or ablation but,

- Results were mixed up since apart from ablation, also lysis of adhesions
- Surgery for minimal or mild endometriosis might modestly enhance fecundity in women with otherwise unexplained subfertility
- but it cannot be excluded that this improvement is due to removal of adhesions rather than implants

Johannes L. H. Evers - 2004

The Impact of Electrocoagulation on ovarian reserve (2)

- PRS 191 pts underwent laparoscopic ovarian cystectomy
- G1 laparoscopy coagulation or harmonic scalpel
- G2 laparotomy + suturing

Results:

- Electrocoagulation group had after 12 months follow up
  - FSH > 10 IU/L significant reduction by
  - the antral follicle number was significantly reduced

C-Z Li et al. Fertil Steril 2009

The Impact of Electrocoagulation On Ovarian reserve (2)

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Characteristic of patients:</th>
<th>Bipolar</th>
<th>Ultrasound coag.</th>
<th>S. Aire</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Characteristic</td>
<td>Unilateral</td>
<td>Bilateral</td>
<td>Unilateral</td>
</tr>
<tr>
<td>Number</td>
<td></td>
<td>18</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Pregnant</td>
<td></td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ovarian</td>
<td></td>
<td>34 ± 1.9</td>
<td>31 ± 2.3</td>
<td>34 ± 2.3</td>
</tr>
<tr>
<td>Cyst size</td>
<td></td>
<td>64 ± 7.1</td>
<td>60 ± 5.4</td>
<td>64 ± 7.1</td>
</tr>
<tr>
<td>Ovaries</td>
<td></td>
<td>54 ± 4.7</td>
<td>51 ± 4.7</td>
<td>54 ± 4.7</td>
</tr>
<tr>
<td>Oocytes</td>
<td></td>
<td>20 ± 4.7</td>
<td>17 ± 4.7</td>
<td>20 ± 4.7</td>
</tr>
</tbody>
</table>

- Results: Electrocoagulation group had after 12 months follow up
  - FSH > 10 IU/L significant reduction by
  - the antral follicle number was significantly reduced

C-Z Li et al. Fertil Steril 2009

| Note: Datas are presented as mean ± standard deviation or number. NS = not statistically significant |
|-------|---------------------------------------------------------------|
|       | *Values in group bipolar vs ultrasound coagulation group. |
|       | †Values in group bipolar vs S. Aire group. |

C-Z Li et al. Fertil Steril 2009
The effect of Endometrioma size and Number ovarian reserves

70 women mean age 35,
- 46 (66%) dysmenorrhea, 21 (30%) dispareunia and 21 (30%) chronic pelvic pain
- 35 (51%) patients were infertile
- One cyst was present in 54 (77%) cases
- More than one cyst in 10 (23%).
- The endometrioma(s) affected the right ovary in 33 (47%) and left ovary in 37 (53%) cases
- The mean±SD diameter of the cysts was 31±16 mm

Results:
- Ovulation occurred in the affected ovary in only 22/70 cases (32%)
- The rate of ovulation was affected according to the number of endometriomas present
  - 35% when one cyst and when 2 cysts 19%
- The impact of the dimension of the cysts, focused on women with only one endometrioma
  - when the diameter of the cyst was 30mm ovulation was 34%
  - when cyst >30mm was 30%

Edgardo Somigliana et al 2010

IVF–ICSI outcome after bilateral endometriomas surgery

Women selected for IVF–ICSI, previously underwent bilateral endometriomas cystectomy, were matched (1:3) for age and study period with patients who did not undergo prior ovarian surgery
- 68 cases and 136 controls

Results:
- had higher withdrawal rate for poor response (P < 0.001) and needed higher doses of HMGs
- Significantly lower number of
  - follicles (P = 0.006); oocytes retrieved (P = 0.024)
  - embryos obtained (P = 0.034)
  - clinical PR in cases 7% and controls 19 % (P = 0.037)
  - delivery rate in cases 4% and controls 17 % (P = 0.013)
- IVF outcome is significantly impaired in women operated on for bilateral ovarian endometriomas.

Edgardo Somigliana et al 2010
IVF poor results Space-occupying endometrioma lesion Vs endometriosis itself

85 - endometrioma 10–50 mm directly to IVF treatment compared
83 - simple ovarian cysts of 10–35 mm detected during stimulation

• endometrioma group
  HMGs more (3,013 vs. 2,451 IU; p = 0.001),
  OPU significantly less oocytes (13.9 vs. 16.4; p = 0.03)
  ET grade I embryos ratio better in the cyst group (79.7 vs. 70.7 % p = 0.03)
  Implantation rate significantly higher in cyst group (28 % vs. 19 % p = 0.02)
  Oocyte maturation rate – similar
  Pregnancy and ongoing pregnancy rates were similar

• endometriosis associated with a lower embryo quality and implantation rate

BKS KG Karlikaya, S Lacin, A Guney - Gynecol Obstet Invest, 2008

Ovarian reserve after endometrioma surgery
one step Vs 3 step surgery

• PRS – 30w with endometriomas
  laparoscopic cystectomy for endometrioma (group 1)
  “three-step procedure” (group 2)
  Before and 6 months after laparoscopy all patients were evaluated
  12 months postoperatively they underwent ultrasound scan examination
  - ovarian reserve damage was estimated alterations AMH, antral follicle
  count, FSH, LH, E2 and inhibin B

Results:
• Mean serum AMH
  Group 1 3.9 to 2.90 ng/mL significant reduction
  Group 2 4.5 to 3.59 ng/mL
• Ovarian reserve determined by AMH is less diminished after the three-step procedure compared with cystectomy of endometriomas.

Tsialidakis et al 2010
Role of Laparoscopic surgery in Endometriosis and Infertility - Review

- There is good enough evidence endometrioma >3cm should be excised
- There is no RCT that specifically address if laparoscopic surgery in moderate or severe endometriosis improve Pregnancy Rate

<table>
<thead>
<tr>
<th>Study</th>
<th>Cohort</th>
<th>Intervention</th>
<th>Duration</th>
<th>Follow-up</th>
<th>Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>39</td>
<td>Laparoscopic excision</td>
<td>4 weeks</td>
<td>1 month</td>
<td>38.7%</td>
</tr>
<tr>
<td>2007</td>
<td>47</td>
<td>Laparoscopic excision</td>
<td>12 months</td>
<td>64.4%</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>37</td>
<td>Laparoscopic excision</td>
<td>3 years</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>14</td>
<td>Laparoscopic excision</td>
<td>24 months</td>
<td>83.3%</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>108</td>
<td>Laparoscopic excision</td>
<td>17 months</td>
<td>95.9%</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>41</td>
<td>Laparoscopic excision</td>
<td>1 year</td>
<td>37%</td>
<td></td>
</tr>
</tbody>
</table>

G Premkumar J Laporoscopic Surgery 2008

Surgical management of endometriosis in infertility is an ongoing controversy

Efficacy of surgical treatment

- Complete resolution of endometriosis is not yet possible and current therapy has three main objectives:
  1. to reduce pain;
  2. to increase the possibility of pregnancy; and
  3. to delay recurrence for as long as possible.

- Probably a consensus will never be reached on the optimal treatment of minimal and mild endometriosis.

- In cases of moderate and severe endometriosis-associated infertility, the combined operative laparoscopy with GnRhAs may be the 'first line' treatment.

- The mean PR of 50% following surgery provides scientific proof that RS should first be the first choice in order to give patients the best chance of conceiving naturally.

- In cases of rectovaginal adenomyotic nodules, surgery is essential.

Dermoid section - Dermoid cysts

Patients’ Age & US findings

- dermoid cysts registered in 20 tertiary and secondary hospitals multicentric review 2000 and 2005 RS 306 cases
- Results: - patients’ mean age 32 and median age 30

- Average size 7cm (2-30cm)
- Mostly Cystic (solid in 1/3)
- Bilateral 8.5%

M Arab et al J Gyn Surgery 2010
Dermoid spill facts

- Spillage in laparoscopy 15–100% and Spillage in laparotomy 4–13%
- 26 laparoscopic dermoid cysts excision 1999 - 2005
- 31 cysts with mean diameter 7.5cm,
- 28 dermoid cysts – treated with conservative cystectomy
- Encountered 14 spillages. The chemical peritonitis risk was (1/14) 0.2%

Review of 14 studies
- 470 laparoscopic dermoid cystectomies and Spillage in 310 cases (66%)
- The incidence of chemical peritonitis was 0.2%
- Only 1 case post op 9 mo developed granulomatous peritonitis

O Shawki et al 2007

Mg transformation in ovarian dermoid cyst

- 10 centers in Australia, Canada, Germany, and Austria.
- 33 patients mean age 49, followed between 1979 – 2007
- Frequency of Mg transformation was 1% to 2%

Results:
- 15 pts at S I and most of S II and S III were optimally debulked.
- Platinum-based regimens most commonly used
- Chemotherapy after surgery was not effective
- 4 S I had fertility-sparing surgery (FSS) with good outcomes
- 2 pts had a sustained remission after second surgery for relapsed disease
- 5 pts had a good outcome 2 alive and well at 12 months of follow-up

Conclusions:
- FSS may be an option in Stage I young patients willing to have a child
- Patients with advanced disease do poorly, regardless of treatment


Pregnancy outcome with dermoid and other benign ovarian cysts (1)

- 93 occurred in patients with benign ovarian cysts
- Benign cystadenoma 41.9%, adenofibroma 1.8%, dermoid cyst 36.7%
- 12.9% were diagnosed during pregnancy by US
- 10.8% were diagnosed before pregnancy
- The mean diameter at diagnosis was 9.05 ± 7.6 cm for cystadenoma
- 6.09 ± 3.0 cm for dermoid cyst
- 4.55 ± 4.1 cm for adenofibroma.

L Katz et al Archives of Gynecology, 2010
Pregnancy outcome with dermoid and other benign ovarian cysts (2)

Results:

- Only 3 cases of ovarian torsion were noted (3.2%), and 15 cases hospitalized due to abdominal pain (16.2%).
- Pregnancy and perinatal outcome with dermoid and other benign ovarian cysts is favorable.
- The cysts should be managed conservatively with routine US follow up during the pregnancy since complications are extremely rare.

L. Katz et al. Archives of Gynecology, 2010

Borderline Ovarian Tumors

Management of BOT (borderline ovarian tumors)
The role of FSS (fertility-sparing surgery) (1)

- 360 BOT pts treated FSS, retrospective review, 1989 – 2008,
- recurrence, survival and pregnancy outcomes evaluated and
- compared between groups that underwent radical operation
- FSS = preservation of uterus and ovarian tissue in one or both adnexa
- 344 - S I, 1 – S II, and 15 - S III disease
- 176 - radical surgery (23 lap/py and 153 lap/my),
- 184 - FSS (48 lap/py and 136 lap/my),
- 45 - adjuvant chemotherapy, post–op

Jeong-Yeol Park et al. 2009
**Management of BOT (borderline ovarian tumors)

The role of FSS (fertility-sparing surgery) (2)**

**Results:**
- After a median follow-up of 70 months (range, 3–216 months)
- 18 patients had recurrent disease and 5 died of disease.
- RR - radical 4.9% and FSS 5.1% - similar
- FSR (free survival rate) – similar ($p = 0.651$).
- In FSS the most common recurrence site was the remaining ovarian tissue
- 34 full-term deliveries by women with FSS
- FSS is safe for young patients wishing to preserve fertility

Jeong-Yeol Park et al. 2009

**Management of BOT (borderline ovarian tumors)

The role of FSS (fertility-sparing surgery)**

- 62 BOTs, USO 40pts and 22 only cystectomy
- 63 - Follow up 88 months
- Recurrence rate USO 22.7% and Cystectomy 27.5% (NS)
- Disease free interval USO 41 mo and Cystectomy 23.6 mo (NS)
- 25/62 (40.3%) pregnant
- Conclusion: Conservative management in BOT is acceptable

Yimun Y et al 2007 Fertil Steril

**RCT comparing 2 FSS approaches for bilateral BOT**

- Standard care is USO plus contralateral cystectomy or BSO
- 32 women with bilateral early-stage BOTs who desired to conceive were randomized
  - bilateral cystectomy (experimental group, $n = 15$)
  - oophorectomy plus contralateral cystectomy (control group, $n = 17$).

**Results:** follow-up period of 81 months
- the cumulative pregnancy rate (CPR) 14/15 versus 9/17; $p = 0.003$
- cumulative first pregnancy signif. higher in bil. cystectomy ($p = 0.011$)
- No significant ($p = 0.358$) difference between groups was detected in cumulative probability of first recurrence

**Conclusion:**
- The laparoscopic bilateral cystectomy is an effective surgical strategy for patients with bilateral early-stage BOTs who desire to conceive as soon as possible.
- TAH BSO must follow at the first recurrence or after childbearing completion

S. Palomba
Epithelial Ovarian cancer (EOC)

Expression of HPV in ovarian cancer after ISH (sample 76) radioactive method, bright field

FSS for epithelial ovarian cancer Safety and Reproductive outcomes (1)

- EOC young patients frequently want to preserve their fertility
- 62 patients underwent FSS, (preservation of ovarian tissue in one or both adnexa and the uterus)
- 1990 – 2006, retrospective review
- 36 - S IA, 2 - S IB, 21 S - IC, and 1 - S IIB, 1 - S IIIA, 1 - S IIIC;
- 48 - G I, 5 - G II, and 9 - G III
- 48 - platinum-based chemo (mean 4.6 cycles, range 1–9 cycles)

JY Park, et al. 2008

Results:

- median follow-up of 56 months (range, 6–205 months),
- 11 –with tumor recurrence, 6 died of disease, 2 were alive with disease
- 54 alive without disease
- Patients with stage > IC (p = 0.0014) or grade III (p = 0.0002) tumors had significantly poorer survival.
- 19 attempted to conceive, 22 - term pregnancies, with no congenital anomalies in any of the offspring.

Conclusion:
Fertility-sparing surgery in young patients with EOCs at S IA–C and G I–II who desire to preserve their fertility seems to be acceptable

JY Park, et al. 2008
Conclusion

Surgery for endometriosis provides good chances for spontaneous pregnancy and increases ART pregnancy rate.

FSS is accepted in LMP and EOCs at early stage I and low grade I tumors, in young patients willing to be pregnant.

😊 Thank U!!!