Ovarian reserve and salpingectomy: Systematic review.

Dott.ssa S. Borgato
**Ovarian reserve**: reproductive potential as a function of the **number and quality** of remaining oocytes.

Decline with age, fertility varies significantly among women of a similar age.

Biochemical measures and ovarian imaging, collectively known as **ovarian reserve tests**, have been proposed to help predict ovarian reserve and/or reproductive potential.
Ovarian reserve tests

- **biochemical tests**
  - AMH (antimullerian hormone);
  - FSH (follicle-stimulating hormone);
  - ESTRADIOL

- **ultrasound imaging of the ovaries**
  - AFC (antral follicle count)
Basal serum FSH concentrations increase on day 2, 3, or 4 of the menstrual cycle with advancing reproductive age. Consistently elevated FSH concentrations confer a poor prognosis.
The vast majority of studies have found that basal estradiol does not differ between women with and without DOR. Basal estradiol alone should not be used to screen for DOR. Only as an aid to correct interpretation of a “normal” basal serum FSH value.
AMH

Glycoprotein hormones primarily secreted by granulosa cells of primary, preantral, and antral follicles.

size of the pool of antral follicles, representing the quantity of the remaining primordial follicles.

After an initial increase until early adulthood, **AMH concentrations slowly decrease with increasing age** until becoming undetectable 5 years before menopause when the stock of primordial follicles is exhausted.
Most studies have defined antral follicles as those measuring 2–10 mm in mean diameter in the greatest two-dimensional (2D) plane;

- some have defined antral follicles as those measuring 3–8 mm in mean diameter.

**AFC**

Antral follicle count is the **sum of antral follicles in both ovaries**, as observed with transvaginal ultrasonography during the early follicular phase.

**good inter-cycle reliability** and Interobserver reliability in experienced centers.
1. Advanced age (>35)
2. Family history of early menopause
3. Past chemotherapy
4. Past radiotherapy
5. History of pelvic surgery
6. History of pelvic infection or tubal diseased
7. History of severe endometriosis
8. Smoking
How surgery reduced RO?

- Thermal damage: electrical devices used during surgery increased local temperature which produced injury to surrounding tissues by thermal diffusion

- Damage to blood vessels in the mesosalpinx: median ovarian artery is closed to medial tubal artery at their origins so injudicious surgery can jeopardize ovarian artery supply

Effect of laparoscopic excision of endometriomas on ovarian reserve: serial changes in the serum antimüllerian hormone levels

Inflammatory cytokine expression following the use of bipolar electrocoagulation, ultracision harmonic and cold knife biopsy.

Litta F, Saccardi C, Sizzo S, Conte L, Ambrosi G, Sisii C, Palumbo M.
In our experience several patients, also young, underwent unilateral or bilateral salpingectomy before IVF.

Does salpingectomy affect the ovarian reserve and the ovarian response to gonadotropin during in vitro fertilization – embryo transfer cycles?
Aim of the Review

Evaluate the influence of unilateral or bilateral salpingectomy to ovarian reserve and the subsequent in vitro fertilization

- Effect of salpingectomy on serum anti-Mullerian hormone level
- Effect of salpingectomy on Antral follicle count

Evaluate the effect of salpingectomy on ovarian response in controlled ovarian hyperstimulation
Data Sources

- Interval time from 1998 to 2015

- Key search terms:
  - Salpingectomy and OR
  - Salpingectomy and AMH
  - Salpingectomy and AFC
  - Salpingectomy and ART
  - Salpingectomy and IVF

- Outcomes:
  - AMH/AFC before and after unilateral or bilateral salpingectomy
  - AMH/AFC after salpingectomy vs infertile women
  - IVF outcome before and after salpingectomy in infertile women
Available Methods

Study group: unilateral or bilateral laparotomic or laparoscopic salpingectomy

Control group:
- same group before surgery
- non operated ovary
- non surgical group

Ectopic pregnancy

Hydrosalpinx

AFC antral follicle count

AMH serum antiMullerian hormone level
Results

**Effect of salpingectomy on ovarian reserve and subsequent IVF**

<table>
<thead>
<tr>
<th>Authors &amp; Years</th>
<th>Type of Study</th>
<th>Patients (Total)</th>
<th>Patients (Salpingectomy)</th>
<th>Patients Controls (Non-salpingectomy)</th>
<th>Age (mean ± SD)</th>
<th>BMI (± SD)</th>
<th>Indication for Surgery</th>
<th>Number of Patients</th>
<th>Reason for Sterilization</th>
<th>Duration of Sterilization (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al 2003</td>
<td>P</td>
<td>102</td>
<td>65 (72 no surgery)</td>
<td>37 (Age 21-34, BMI 19-24)</td>
<td>25.4 ± 4.5</td>
<td>22 ± 4.4</td>
<td>ECP</td>
<td>2</td>
<td>1.3-3</td>
<td>2 years after surgery</td>
</tr>
<tr>
<td>Tal et al 2004</td>
<td>P</td>
<td>79</td>
<td>60 (26 salpingectomy, 54 LUP, 12 HY)</td>
<td>19 (Age 22-35, BMI 18-25)</td>
<td>22.3 ± 3.4</td>
<td>20 ± 3.5</td>
<td>ECP</td>
<td>1</td>
<td>0</td>
<td>20 cases of infertility</td>
</tr>
<tr>
<td>Chan et al 2003</td>
<td>R</td>
<td>32</td>
<td>18 (14 unilateral LUP, 4 bilateral LUP)</td>
<td>14 (Age 24-35, BMI 15-21)</td>
<td>26.3 ± 5.4</td>
<td>21 ± 4.4</td>
<td>ECP</td>
<td>1</td>
<td>3</td>
<td>3 months of infertility</td>
</tr>
<tr>
<td>Olshan et al 2006</td>
<td>R</td>
<td>651</td>
<td>442 (Age 16-41, BMI 18-28)</td>
<td>209 (Age 16-41, BMI 18-28)</td>
<td>26 ± 4.4</td>
<td>21 ± 3.5</td>
<td>ECP</td>
<td>2</td>
<td>1</td>
<td>10 years after surgery</td>
</tr>
<tr>
<td>Olshan et al 2006</td>
<td>R</td>
<td>15</td>
<td>12 (15 unilateral LUP)</td>
<td>3 (Age 24-35, BMI 15-21)</td>
<td>26 ± 4.4</td>
<td>21 ± 3.5</td>
<td>ECP</td>
<td>1</td>
<td>1</td>
<td>10 years after surgery</td>
</tr>
<tr>
<td>Xi et al 2010</td>
<td>R</td>
<td>139</td>
<td>88 (Age 18-40, BMI 18-24)</td>
<td>51 (Age 18-40, BMI 18-24)</td>
<td>24 ± 4.4</td>
<td>21 ± 3.5</td>
<td>ECP</td>
<td>2</td>
<td>1</td>
<td>10 years after surgery</td>
</tr>
<tr>
<td>Castellanos et al 2015</td>
<td>R</td>
<td>71</td>
<td>46 (Age 25-40)</td>
<td>25 (Age 25-40)</td>
<td>24 ± 4.4</td>
<td>21 ± 3.5</td>
<td>ECP</td>
<td>2</td>
<td>1</td>
<td>10 years after surgery</td>
</tr>
<tr>
<td>Song et al 2013</td>
<td>R</td>
<td>142</td>
<td>97 (75 unilateral LUP, 3 bilateral LUP)</td>
<td>45 (Age 25-40)</td>
<td>24 ± 4.4</td>
<td>21 ± 3.5</td>
<td>ECP</td>
<td>2</td>
<td>1</td>
<td>10 years after surgery</td>
</tr>
</tbody>
</table>

- **2269 Patients (1248 salpingectomy, 1021 Controls)**
- **Age < 40 years**
- **BMI < 25**
- **Indication for surgery : ECP or HY**
## Results

### Effect of salpingectomy on AMH

<table>
<thead>
<tr>
<th>Authors &amp; Years</th>
<th>Type of Study</th>
<th>Patients (total)</th>
<th>Patients - Controls (No surgery)</th>
<th>Age (year ± SD)</th>
<th>BMI (± SD)</th>
<th>Indication for Surgery</th>
<th>Years from Surgery</th>
<th>Reason of Infertility</th>
<th>Duration of Infertility (year ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grynnerup et al 2013</td>
<td>F-CD</td>
<td>71</td>
<td>a) 16 (uni/bilateral LPS) b) 55 no surgery</td>
<td>a) 34 (25-37) b) 35 (20-37) c) 32 (27-36)</td>
<td>n.a</td>
<td>a) HY b) HY 1G c) Unexplained 13</td>
<td>n.a</td>
<td>4-5 years</td>
<td></td>
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<tr>
<td>Hii et al 2013</td>
<td>PC</td>
<td>184</td>
<td>a) 26 bilateral b) 34 unilateral c) 23 oviducts interruption by hysteroscopy LPS</td>
<td>a) 29.2+2.38 b) 30.1+2.37 c) 30.6+3.32 d) 29.1+3.36</td>
<td>n.a</td>
<td>a) ECP, HY b) HY c) HY</td>
<td>n.a</td>
<td>2.00 ± 1.67</td>
<td>2.14 ± 2.12, 4.62 ± 2.81, 3.98 ± 2.44</td>
</tr>
<tr>
<td>Ye et al 2015</td>
<td>R</td>
<td>195</td>
<td>a) 63 unilateral b) 41 bilateral not specified c) 74 no surgery</td>
<td>a) 33.0 ± 4.05 b) 33.5 ± 3.95 c) 33.8 ± 4.67</td>
<td>n.a</td>
<td>a) ECP 79 TOA 1 b) ECP 24 HY 16 TOA 1</td>
<td>n.a</td>
<td>2.31 ± 1.33</td>
<td>2.85 ± 2.81 secondary infertility b) 0.82 ± 1.96 primary infertility c) 3.25 ± 3.24 secondary infertility</td>
</tr>
<tr>
<td>Venturella et al 2015</td>
<td>RCT</td>
<td>185</td>
<td>a) 91 unilateral standard LPS b) 95 unilateral wide* LPS Controls: same patients before surgery</td>
<td>a) 41.16 ± 5.33 b) 41.56 ± 3.45</td>
<td>n.a</td>
<td>a) Myomectomy, tubal surgical sterilization</td>
<td>n.a</td>
<td>n.a</td>
<td>n.a</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Articles</th>
<th>Patients</th>
<th>Salpingectomy</th>
<th>Controls</th>
<th>n.a</th>
<th>n.a</th>
<th>n.a</th>
<th>n.a</th>
<th>n.a</th>
<th>n.a</th>
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<tbody>
<tr>
<td>4</td>
<td>589</td>
<td>386</td>
<td>389</td>
<td>n.a</td>
<td>n.a</td>
<td>n.a</td>
<td>n.a</td>
<td>n.a</td>
<td>n.a</td>
</tr>
</tbody>
</table>
Results

- AMH significantly higher in women without tubal surgery
- This data suggest that salpingectomy is associated with decreased ovarian reserve

**Ye et al 2015**

**Table 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unilateral salpingectomy (n = 53)</th>
<th>Bilateral salpingectomy (n = 41)</th>
<th>Without surgery (n = 74)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>33.02 ± 4.90</td>
<td>33.58 ± 3.99</td>
<td>33.6 ± 4.67</td>
<td>.353</td>
</tr>
<tr>
<td>AMH, fmol/mL</td>
<td>37.56 ± 127.03</td>
<td>127.11 ± 93.23</td>
<td>183.48 ± 104</td>
<td>.337</td>
</tr>
<tr>
<td>E2, pg/mL</td>
<td>38.3 ± 14.91</td>
<td>41.41 ± 16.59</td>
<td>36.43 ± 16.77</td>
<td>.291</td>
</tr>
<tr>
<td>Progesterone, nmol/L</td>
<td>0.52 ± 0.29</td>
<td>0.55 ± 0.33</td>
<td>0.54 ± 0.32</td>
<td>.484</td>
</tr>
<tr>
<td>LH, mIU/mL</td>
<td>4.06 ± 1.46</td>
<td>3.04 ± 1.71</td>
<td>4.26 ± 2.00</td>
<td>.63</td>
</tr>
<tr>
<td>FSH,</td>
<td>8.42 ± 2.3</td>
<td>9.13 ± 3.2</td>
<td>7.85 ± 2.69</td>
<td>.048</td>
</tr>
<tr>
<td>AFC,</td>
<td>10.7 ± 3.62</td>
<td>9.58 ± 3.73</td>
<td>11.22 ± 4.16</td>
<td>.097</td>
</tr>
</tbody>
</table>

**Grynnerup et al 2013**

- AMH levels were significantly lower in the salpingectomy infertility group compared with no salpingectomy tubal factor infertility group
- AMH predict poor response (5 o < oocytes) at 19 pmol/L cut off value
## Results

### Effect of salpingectomy on AFC

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<tr>
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<th>Patients (total)</th>
<th>Patients (Salpingectomy)</th>
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<th>Age (year ± SD)</th>
<th>BMI (± SD)</th>
<th>Indication for Surgery</th>
<th>Years from Surgery</th>
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<th>Duration of Infertility (year ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan et al 2003</td>
<td>R</td>
<td>32</td>
<td>a) 18 unilateral LPS b) 14 unilateral LPT</td>
<td>Controls: non-operated site a) 34 (21.38) b) 26 (23.44)</td>
<td>a) 20.96 b) 21.44</td>
<td>a) b) ECP</td>
<td>At least 3 months</td>
<td>n.s</td>
<td>n.s</td>
<td>n.s</td>
</tr>
<tr>
<td>Orveto et al 2011</td>
<td>R</td>
<td>15</td>
<td>a) 15 uni/bilateral not specified</td>
<td>Controls: same patients before surgery</td>
<td>32 ± 4.4</td>
<td>24 ± 5.5</td>
<td>a) HY</td>
<td>n.s</td>
<td>n.s</td>
<td>n.s</td>
</tr>
<tr>
<td>Luyar et al 2013</td>
<td>P</td>
<td>162</td>
<td>a) 33 patients LPS/LPT - 26 salpingectomy - 3 tubal sterilization b) 49 MTX c) 80 no surgery</td>
<td>a) 21.1±5.1 b) 29.7±5.0 c) 28.9±6.0</td>
<td>n.s</td>
<td>a) b) ECP</td>
<td>n.s</td>
<td>n.s</td>
<td>n.s</td>
<td>n.s</td>
</tr>
<tr>
<td>Ni et al 2015</td>
<td>PC</td>
<td>124</td>
<td>a) 25 bilateral b) 14 unilateral c) 23 oviducts interruption by hemoclip - LPS</td>
<td>51 no surgery</td>
<td>a) 26.3±2.93 b) 30.1±2.73 c) 30.6±3.22 d) 29.1±2.36</td>
<td>a) 21.2±2.05 b) 21.37±1.69 c) 20.78±2.04 d) 20.95±1.66</td>
<td>a) b) ECP, HY c) HY</td>
<td>n.s</td>
<td>n.s</td>
<td>a) 2.00±1.67 b) 3.14±2.12 c) 4.51±2.91 d) 3.98±2.44</td>
</tr>
<tr>
<td>Ye et al 2015</td>
<td>R</td>
<td>198</td>
<td>a) 83 unilateral b) 41 bilateral not specified</td>
<td>74 no surgery</td>
<td>a) 33.0±6.46 b) 33.58±3.95 c) 33.8±4.97</td>
<td>a) 21.63±2.46 b) 21.3±2.89 c) 21.45±2.32</td>
<td>a) ECP 79 b) TOA 1 c) ECP 24 TOA 1</td>
<td>n.s</td>
<td>n.s</td>
<td>a) MF 45 MF &amp; FF 25 b) MF 15 MF &amp; FF 15 c) WP 88 MF &amp; FF 25 d) MF 45 MF &amp; FF 25</td>
</tr>
<tr>
<td>Venturella et al 2015</td>
<td>RCT</td>
<td>186</td>
<td>a) 91 unilateral standard b) 95 unilateral wide LPS</td>
<td>Controls: same patients before surgery</td>
<td>a) 41.36±5.33 b) 41.58±5.48</td>
<td>n.s</td>
<td>a) b) Myomectomy, tubal surgical sterilization</td>
<td>n.a</td>
<td>n.a</td>
<td>n.a</td>
</tr>
</tbody>
</table>
Results

Orvieto et al 2011
Chan et al 2003

Reduced ovarian response of the ipsilateral ovary after unilateral salpingectomy

TABLE I. Ovarian function between the operated and the non-operated side in the laparotomy group (n = 14).

<table>
<thead>
<tr>
<th></th>
<th>Operated side</th>
<th>Non-operated side</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antral follicle count</td>
<td>6.5 (1.8–10.3)</td>
<td>4.0 (2.8–9.3)</td>
<td>0.185</td>
</tr>
<tr>
<td>Ovarian volume (mL)</td>
<td>7.25 (4.60–14.4)</td>
<td>6.29 (4.77–10.74)</td>
<td>0.085</td>
</tr>
<tr>
<td>VI (%)</td>
<td>0.84 (0.11–1.42)</td>
<td>0.73 (0.24–1.29)</td>
<td>0.683</td>
</tr>
<tr>
<td>FI (0–100)</td>
<td>26.58 (23.74–28.37)</td>
<td>24.37 (22.77–26.70)</td>
<td>0.397</td>
</tr>
<tr>
<td>VFI (0–100)</td>
<td>0.23 (0.03–0.39)</td>
<td>0.18 (0.06–0.32)</td>
<td>0.510</td>
</tr>
</tbody>
</table>

Values are median (interquartile range).
*Wilcoxon signed ranks test.
VI = vascular index; FI = flow index; VFI = vascularization flow index.

TABLE II. Ovarian function between the operated and the non-operated side in the laparoscopy group (n = 18).

<table>
<thead>
<tr>
<th></th>
<th>Operated side</th>
<th>Non-operated side</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antral follicle count</td>
<td>5.0 (3.0–7.3)</td>
<td>7.5 (4.8–8.3)</td>
<td>0.014</td>
</tr>
<tr>
<td>Ovarian volume (cm³)</td>
<td>6.35 (4.07–8.96)</td>
<td>5.95 (4.57–8.24)</td>
<td>0.349</td>
</tr>
<tr>
<td>VI (%)</td>
<td>0.55 (0.22–0.87)</td>
<td>1.03 (0.39–2.53)</td>
<td>0.020</td>
</tr>
<tr>
<td>FI (0–100)</td>
<td>24.97 (22.06–26.95)</td>
<td>27.70 (24.71–33.78)</td>
<td>0.020</td>
</tr>
<tr>
<td>VFI (0–100)</td>
<td>0.14 (0.05–0.23)</td>
<td>0.37 (0.10–0.84)</td>
<td>0.020</td>
</tr>
</tbody>
</table>

Values are median (interquartile range).
*Wilcoxon signed ranks test.
VI = vascular index; FI = flow index; VFI = vascularization flow index.
Results

Effect of salpingectomy on IVF

Eterogenity of the study:
- Different protocol of stimulation
- Salpingectomy LPS or LPT or not specified
- Different indication for surgery

16 manuscript focused on this topic

Patients who underwent salpingectomy retrieved significantly **fever oocytes**

Required **higher dose of gonadotropine** to attain the same number of mature oocytes

**Similar** implantation rate, clinical pregnancy rate and LBR

Similar number of follicles retrieved ipsilateral to the operated side

Salpingectomy **improving IVF** outcome
Results

Effect of salpingectomy on IVF

- Retrospective
- Good numerosity: 76 salpingectomy vs 80 control
- Indication: ECP
- LPS salpingectomy had no detrimental effect on ovarian response during IVF-ET

Propective cohort
- Unilateral, bilateral salpingectomy
- Indication: HY, ECP
- Salpingectomy improved IVF outcome especially for hydrosalpinx

Retrospective
- Good numerosity: 124 salpingectomy (unilateral–bilateral)
- Indication: ECP, HY
- Patients treated with salpingectomy retrieved fewer oocytes, poorer IVF outcomes
Salpingectomy seems to be associated with decreased AMH level (thermal damage), but few studies found no significant differences of AMH level before and after surgery.

Also AFC seems to be reduced after salpingectomy → need further study.

IVF outcome after salpingectomy is more controversial:
- No effect on IVF
- Improved IVF outcome especially for hydrosalpinx
- Undermines OR and reduced oocyte retrieved (interrupted ovarian blood supply)

Experienced surgeon
Define technique

Define the grade of hydrosalpinx that require surgery

Grazie per l’attenzione