Surgical Treatment Of PCOS

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The Goals Infertility Treatment

To minimize the risk of complications (OHSS, multiples, bleeding, infection ..)

To optimize pregnancy rates

To produce healthy, genetically normal, singleton full-term deliveries
A step-by-step approach to ovulation induction in PCOS

<table>
<thead>
<tr>
<th>Step</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Weight loss if BMI is elevated</td>
</tr>
<tr>
<td>2</td>
<td>Clomiphene citrate ± glucocorticoids</td>
</tr>
<tr>
<td>3</td>
<td>Insulin sensitizer as a single agent</td>
</tr>
<tr>
<td>4</td>
<td>Insulin sensitizer &amp; clomiphene citrate</td>
</tr>
<tr>
<td>5(3)</td>
<td>Gonadotropin treatment</td>
</tr>
<tr>
<td>6</td>
<td>Insulin sensitizer &amp; gonadotropin treat.</td>
</tr>
<tr>
<td>7(4)</td>
<td>Ovarian surgery</td>
</tr>
<tr>
<td>8</td>
<td>IVF/ICSI &amp; IVM</td>
</tr>
</tbody>
</table>

The potential problems of gonadotropin therapy

- Difficult to titrate the dose to achieve monofollicular ovulation.
- Multiple gestations (>30 percent)
- Risk of OHSS
- Need of careful monitoring
- High cost
- High spontaneous abortion rate

NICE Guidelines

Ovarian drilling

Women with PCOS who have not responded to CC should be offered laparoscopic ovarian drilling because it is as effective as gonadotrophin treatment and is not associated with an increased risk of multiple pregnancy.
**Technical options**

- Wedge resection
- Ovarian biopsy
- Capsule resection
- Electrodesiccation
- Laser vaporization
- Endocoagulation
Traditional Wedge resection

Side effects:
• POF rate 20-80%
• Pelvic adhesion rate 40-75%
• Lead to irreversible infertility

Laparoscopic ovarian drilling

Side effects:
- Pelvic adhesion rate: 19%–82%
- Ovulation dysfunction due to cicatricle on the surface of ovary
- Difficulty in control quality and depth of drillings

latrogenic exhaustion of ovarian reserve-POF?
Technique

- Two or three incision L/S approach
- 30-40 w per puncture for 3-5 seconds
- Avoid hilum avoid bleeding
- Continuous irrigation
- Various energy sources
- 5 to 6 punctures seems optimal
- One or both ovary, 2-3 mm çapında 3-4 mm derinliğinde

Tulandi T et al., 1998; Amer SA et al., 2003; Malkawi HY et al., 2005; Roy K et al., 2008
PCOS - OVARIAN DRILLING

Intraovarian mechanisms

Destruction of the androgen producing stroma

Drainage of follicles with high androgen and inhibin content

Alterations in the levels of various intraovarian growth factors
PCOS - OVARIAN DRILLING

Central mechanisms

Markedly reduced LH amplitudes with no change in pulse frequency

Markedly attenuated response to GnRH challenge test
Why does ovarian surgery in PCOS help?  
Endocrine implications

- Ovarian surgery
  - Rapid reduction in all ovarian hormones
    - With increased pituitary hormones
  - Initiation of folliculogenesis
    - Increase ovarian hormone production

Continuation of follicle growth in subsequent cycles after ovarian surgery occurs in an environment with less androgens and lower LH and FSH levels compared with pretreatment levels.

*Systematic review. Hendriks, ML et al. Hum Reprod 2007*
1. Is there still a role for surgical treatment?

2. How should surgery be performed?
# Ovulation and pregnancy rates

Table 1. Ovulation and pregnancy rates following laparoscopic ovarian drilling.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Ovulation (%)</th>
<th>Pregnancy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aakvaag and Gjonnaess(^a)</td>
<td>1985</td>
<td>58</td>
<td>72</td>
<td>NA</td>
</tr>
<tr>
<td>Daniell and Miller(^b)</td>
<td>1989</td>
<td>85</td>
<td>71</td>
<td>56</td>
</tr>
<tr>
<td>Utsunomiya et al.(^c)</td>
<td>1990</td>
<td>16</td>
<td>94</td>
<td>50</td>
</tr>
<tr>
<td>Campo et al.(^c)</td>
<td>1993</td>
<td>23</td>
<td>56</td>
<td>43</td>
</tr>
<tr>
<td>Gjonnaess(^a)</td>
<td>1994</td>
<td>252</td>
<td>92</td>
<td>84</td>
</tr>
<tr>
<td>Kriplani et al.(^a)</td>
<td>2001</td>
<td>66</td>
<td>82</td>
<td>55</td>
</tr>
<tr>
<td>Felemban et al.(^a)</td>
<td>2000</td>
<td>112</td>
<td>73</td>
<td>58</td>
</tr>
</tbody>
</table>

Performed with \(^a\)electrosurgery, \(^b\)laser, \(^c\)biopsy. NA = not reported.
Cumulative probability of conception among 112 clomiphene-resistant anovulatory women with polycystic ovaries (median, 10.2 months).
Table 1 Reproductive outcomes after electrocoagulation laparoscopic ovarian drilling

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean follow-up (months)</th>
<th>Starting time of other OI agents (months)</th>
<th>Number of patients</th>
<th>Regular cycles (%)</th>
<th>Ovulation rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>Aoi et al., 2005 [35]</td>
<td>~29.7</td>
<td>–</td>
<td>45</td>
<td>93</td>
<td>NR</td>
</tr>
<tr>
<td>Kucuk and Kilic-Okman, 2005 [36]</td>
<td>12</td>
<td>6</td>
<td>22</td>
<td>68</td>
<td>95</td>
</tr>
<tr>
<td>Malkawi and Oublan, 2005 [12&lt;sup&gt;”&lt;/sup&gt;]</td>
<td>12</td>
<td>3</td>
<td>63</td>
<td>68</td>
<td>57</td>
</tr>
<tr>
<td>Palomba &lt;i&gt;et al.&lt;/i&gt;, 2005 [33&lt;sup&gt;”&lt;/sup&gt;]</td>
<td>6</td>
<td>6</td>
<td>55</td>
<td>63.6</td>
<td>76.4</td>
</tr>
<tr>
<td>Bayram &lt;i&gt;et al.&lt;/i&gt;, 2004 [20]</td>
<td>12</td>
<td>2</td>
<td>83</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Cleemann &lt;i&gt;et al.&lt;/i&gt;, 2004 [37]</td>
<td>NR</td>
<td>3</td>
<td>57</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Amer &lt;i&gt;et al.&lt;/i&gt;, 2004 [16]</td>
<td>12</td>
<td>2</td>
<td>97</td>
<td>78.4</td>
<td>83.5</td>
</tr>
<tr>
<td>Malkawi &lt;i&gt;et al.&lt;/i&gt;, 2003 [31]</td>
<td>12</td>
<td>3</td>
<td>75</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Amer &lt;i&gt;et al.&lt;/i&gt;, 2002 [22]</td>
<td>12</td>
<td>2</td>
<td>29</td>
<td>75</td>
<td>NR</td>
</tr>
<tr>
<td>Farquhar &lt;i&gt;et al.&lt;/i&gt;, 2002 [38]</td>
<td>6</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Felemban and Tunland, 2000 [9]</td>
<td>12</td>
<td>NR</td>
<td>112</td>
<td>NR</td>
<td>80</td>
</tr>
<tr>
<td>Li &lt;i&gt;et al.&lt;/i&gt;, 1998 [39]</td>
<td>36</td>
<td>No comment on starting time</td>
<td>118</td>
<td>79</td>
<td>87</td>
</tr>
<tr>
<td>Tulandi &lt;i&gt;et al.&lt;/i&gt;, 1997 [40]</td>
<td>12</td>
<td>–</td>
<td>34</td>
<td>NR</td>
<td>88.2</td>
</tr>
<tr>
<td>Merchant, 1996 [41]</td>
<td>12</td>
<td>No comment on starting time</td>
<td>30</td>
<td>83.3</td>
<td>70</td>
</tr>
<tr>
<td>Pelosi and Pelosi, 1996 [42]</td>
<td>12</td>
<td>3</td>
<td>74</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Naether &lt;i&gt;et al.&lt;/i&gt;, 1994 [43]</td>
<td>72</td>
<td>No comment on starting time</td>
<td>145</td>
<td>92.2</td>
<td>86</td>
</tr>
<tr>
<td>Gjonnaes, 1984 [6]</td>
<td>12</td>
<td>No comment on starting time</td>
<td>62</td>
<td>86.4</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR, not reported; OI, ovulation induction; GnRHa, gonadotropin releasing hormone analogs.

<sup>a</sup>Spontaneous (in original table).
Lapar. ovarian drilling
Crude ovulation and preg. rates

Ovulation rates
- Electrocoagulation - 64-92%
- Laser - 55-70%

Pregnancy rates
- Electrocoagulation - 52-80%
- Laser - 0-56%

Late endocrine effects of ovarian electrocautery in women with PCOS

Ovarian electrocautery normalizes ovarian function, including androgen production and the results seem to be stable for 18-20 years

<table>
<thead>
<tr>
<th>Observation period</th>
<th>normal weight</th>
<th>overweight weight</th>
<th>all weight</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mo</td>
<td>78(21/27)</td>
<td>65(13/20)</td>
<td>72(34/47)</td>
<td>NS</td>
</tr>
<tr>
<td>1 y</td>
<td>89(24/27)</td>
<td>65(11/17)</td>
<td>80(35/44)</td>
<td>NS</td>
</tr>
<tr>
<td>3 y</td>
<td>79(19/24)</td>
<td>50(10/20)</td>
<td>66(29/44)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>10 y</td>
<td>68(12/15)</td>
<td>71(12/17)</td>
<td>69(29/42)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;10 y</td>
<td>80(12/15)</td>
<td>69(11/16)</td>
<td>74(23/31)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Long term observational study; 165 infertile PCOS women (Gjonnaess H. - F&S 1998 April 69;4: 697-701)
The Evidence

Is it better than gonadotrophins?
## LOD versus FSH

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>No of women</th>
<th>Pregnant (%)</th>
<th>Miscarry</th>
<th>Multiple</th>
<th>LB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOD strategy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOD</td>
<td>83 (100)</td>
<td>31 (37)</td>
<td>3</td>
<td>-</td>
<td>28 (34)</td>
</tr>
<tr>
<td>LOD + CC</td>
<td>45 (54)</td>
<td>14 (31)</td>
<td>1</td>
<td>-</td>
<td>13 (29)</td>
</tr>
<tr>
<td>LOD + CC + FSH</td>
<td>23 (28)</td>
<td>18 (78)</td>
<td>3</td>
<td>1</td>
<td>12 (52)</td>
</tr>
<tr>
<td>LOD strategy total</td>
<td>83</td>
<td>63 (76)</td>
<td>7</td>
<td>1</td>
<td>53 (64)</td>
</tr>
<tr>
<td>FSH</td>
<td>85</td>
<td>64 (75)</td>
<td>7</td>
<td>9</td>
<td>51 (60)</td>
</tr>
</tbody>
</table>

Bayram et al, 2004
Conclusions of study

- An electrocautery strategy and ovulation induction with recombinant follicle stimulating hormone are similarly effective in inducing ovulation
- No OHSS
- Multiple pregnancies can largely be avoided by electrocautery and clomifene citrate before rFSH
### Analysis 01.06. Comparison 01 Ovarian drilling +/- medical ovulation induction versus gonadotrophins only, Outcome 06 Ovulation rate

Review: Laparoscopic "drilling" by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome

Comparison: 01 Ovarian drilling +/- medical ovulation induction versus gonadotrophins only

Outcome: 06 Ovulation rate

<table>
<thead>
<tr>
<th>Study</th>
<th>Ovarian Drilling</th>
<th>Gonadotrophins</th>
<th>Odds Ratio (Fixed)</th>
<th>Weight (%)</th>
<th>Odds Ratio (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farquhar 2002</td>
<td>15/29</td>
<td>13/21</td>
<td>0.66 [0.21, 2.07]</td>
<td>100.0</td>
<td>0.66 [0.21, 2.07]</td>
</tr>
</tbody>
</table>

Total (95% CI) 29/21

Total events: 15 (Ovarian Drilling), 13 (Gonadotrophins)

Test for heterogeneity: not applicable

Test for overall effect $z=0.71$ $p=0.5$
<table>
<thead>
<tr>
<th></th>
<th>CCR, 6 months **</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metformin</strong></td>
<td>39 / 54 (72.2%)</td>
</tr>
<tr>
<td><strong>LOD</strong></td>
<td>31 / 55 (56.4%)</td>
</tr>
</tbody>
</table>

** p=0.1
Analysis 01.03. Comparison 01 Ovarian drilling +/- medical ovulation induction versus gonadotrophins only, Outcome 03 Miscarriage rate (per pregnancy)

Review: Laparoscopic “drilling” by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome

<table>
<thead>
<tr>
<th>Study</th>
<th>Ovarian drilling</th>
<th>Gonadotrophins</th>
<th>Odds Ratio (Fixed)</th>
<th>Weight (%)</th>
<th>Odds Ratio (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayram 2004</td>
<td>7/63</td>
<td>7/64</td>
<td></td>
<td>49.5</td>
<td>1.02 [0.34, 3.09 ]</td>
</tr>
<tr>
<td>Farquhar 2002</td>
<td>3/8</td>
<td>3/7</td>
<td></td>
<td>16.0</td>
<td>0.80 [0.10, 6.35 ]</td>
</tr>
<tr>
<td>Lazoviz 1998</td>
<td>0/14</td>
<td>3/9</td>
<td></td>
<td>32.5</td>
<td>0.06 [0.00, 1.43 ]</td>
</tr>
<tr>
<td>Vegetti 1998</td>
<td>2/3</td>
<td>1/5</td>
<td></td>
<td>2.0</td>
<td>8.00 [0.31, 206.37]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>88</td>
<td>85</td>
<td></td>
<td>100.0</td>
<td>0.81 [0.36, 1.86 ]</td>
</tr>
</tbody>
</table>

Total events: 12 (Ovarian drilling), 14 (Gonadotrophins)
Test for heterogeneity chi-square=4.63 df=3 p=0.20 I² =35.3%
Test for overall effect z=0.49 p=0.6
Pregnancy Rates and Outcomes - Abortion

Women with PCOS have a higher than average frequency of spontaneous abortions (SAB), 40 to 53%.

The SAB rates following LOD range from 8 to 21% (similar to normal population) (Felemban A et al., 2000; Colacurci N, et al., 1997)

LOD may therefore reduce the SAB rates in PCOS patients by normalizing high LH levels?

AND reduction in androgen levels and insulin resistance may also contribute to lower SAB rates by improving oocyte quality or endometrial receptivity
Multiple Pregnancy

- Meta-analysis of 5 RCTs
- Multiple pregnancy with LOD is significantly lower (OR = 0.13, CI 0.17-0.98) than godadotrophin therapy

Consensus on infertility treatment related to polycystic ovary syndrome. Human Reprod 2008, 23:462
Repeat LOD: Ovulation /Pregnancy


- Prev. responders (n=12): 75%
- Prev. non-responders (n=12): 29%
- Overall (n=20): 53%
Laparoscopic Ovarian Drilling and in Vitro Fertilization

- LOD improves the effectiveness of gonadotropin treatment
- PCOS patients have a higher rate of cycle cancellation due to an exaggerated response to gonadotropin therapy with an associated increased risk of OHSS.
- Ovaries pretreated with LOD tend to respond to stimulation with parenteral gonadotropins in a more controlled fashion, similar to non-PCOS ovaries
Ovarian Drilling & IVF

1. Improves effectiveness to gonadotropin treatment / Decreases the number of ampulles used
2. Decreases OHSS rate
3. Decreases cancellation rate
4. Decreases Abortion rate
5. Decreases multiple pregnancy rate
6. Increase pregnancy rate

Tozer AJ et al., 2011
Advantages

Avoids the need for intensive cycle monitoring

Produces a normal hormonal environment

Induces resumption of spontaneous ovulation

Enables more favourable response with subsequent gonadotropin stimulation

Avoids OHSS

Avoids multiple gestation
Social Factors

- Cost effectiveness
- Patient preference for treatment with LOD
- Minimally invasive procedure that eliminates the inconvenient daily injections and frequent office visits required for gonadotropin treatment
LOD vs GONADOTROPHIN
ECONOMIC CONSIDERATIONS

Cost per live birth
Farquhar et al, 2004

LOD
US $2109 5

gonadotrophins
US $28744

Cost per live birth + delivery
Wely et al, 2004

LOD
Euro 11301

gonadotrophins
Euro 14489

Cost of term pregnancy: LOD 22-33% lower
PCOS - OVARIAN DRILLING

Complications

- Related to lapsc. and energy use
- Avulsion of the uteroovarian ligament
- Bleeding from the drilled holes
- Ovarian atrophy
- Adhesion formation
- Premature ovarian failure ?
- Ovarian cancer ?
### Table 2. Postoperative adhesions following laparoscopic ovarian drilling.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Adhesions (% of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weise et al.</td>
<td>1991</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>Gurgan et al.</td>
<td>1992</td>
<td>20</td>
<td>68</td>
</tr>
<tr>
<td>Corson and Grochmal</td>
<td>1990</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>Portuondo et al.</td>
<td>1984</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Naether et al.</td>
<td>1994</td>
<td>62</td>
<td>19</td>
</tr>
<tr>
<td>Felemban et al.</td>
<td>2000</td>
<td>15</td>
<td>27</td>
</tr>
</tbody>
</table>

Performed with "electrosurgery," "laser," and "biopsy."
PATIENT SELECTION

Everything in medicine is patient selection – the chief determinant of results
LH and Pregnancy rates in LOD

Pregnancy rate

<table>
<thead>
<tr>
<th>LH (iu/l)</th>
<th>Pregnancy rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>20%</td>
</tr>
<tr>
<td>&gt;10</td>
<td>60%</td>
</tr>
</tbody>
</table>
Free Androgen Index and the outcome of LOD

%  

OVULATION  PREGNANCY

<4  4-14.9  >14.9

FAI

* P < 0.05  ** P < 0.01  *** P < 0.001
BMI and the outcome of LOD

BMI (kg/m^2)

<table>
<thead>
<tr>
<th>BMI Range</th>
<th>Ovulation</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>80%</td>
<td>60%</td>
</tr>
<tr>
<td>29-34</td>
<td>70%</td>
<td>50%</td>
</tr>
<tr>
<td>&gt;34</td>
<td>30%</td>
<td>10%</td>
</tr>
</tbody>
</table>

* P < 0.05
** P < 0.01
*** P < 0.001
With proper patient selection, the pregnancy rate after laparoscopic ovarian diathermy is up to 80%
The value of measuring AMH in women with anovulatory polycystic ovary syndrome undergoing laparoscopic ovarian diathermy

*Human Reproduction 2009*

Amer, Li, and Ledger

High AMH (>7.7ng/ml) predicts poor response
<table>
<thead>
<tr>
<th></th>
<th>AMH &lt; 7.7</th>
<th>AMH &gt; 7.7</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ovulation</strong></td>
<td>18/19 (95%)</td>
<td>6/10 (60%)</td>
<td>0.036</td>
</tr>
<tr>
<td><strong>pregnancy</strong></td>
<td>12/19 (63%)</td>
<td>3/10 (30%)</td>
<td>0.095</td>
</tr>
</tbody>
</table>
Indications

- Patients going diagnostic or operative laparoscopy
- who have completed six ovulatory cycles without pregnancy / Not eligible for gonadotropin therapy
- PCOS patients with dysfunctional uterine bleeding and /or endometrial hyperplasia
- LOD as first line treatment / same results

Cleemann L et al., 2004; Amer SA et al., 2009
Randomized controlled trial comparing laparoscopic ovarian diathermy with clomiphene citrate as a first-line method of ovulation induction in women with polycystic ovary syndrome

Amer, Li, Metwally, Emarh & Ledger
Human Reproduction 2009
<table>
<thead>
<tr>
<th></th>
<th>LOD group (n=33)</th>
<th>Clomiphene group (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovulation</td>
<td>64%</td>
<td>76%</td>
</tr>
<tr>
<td>Conception after first treatment</td>
<td>27%</td>
<td>44%</td>
</tr>
<tr>
<td>Conception after second treatment (at 12m)</td>
<td>53%</td>
<td>63%</td>
</tr>
<tr>
<td>miscarriage</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Live Birth</td>
<td>46%</td>
<td>56%</td>
</tr>
</tbody>
</table>
Disadvantages of LOD is the requisite of laparoscopy?

- Less invasive techniques?
- Transvaginal hydrolaparoscopy
  Gordts et al., 2009
- Transvaginal ultrasound guided interstitial Nd-YAG laser or unipolar needle
  Kaajik et al., 1997; Api et al., 2009
- Simple aspiration of follicles under ultrasound guidance
  Badaway et al., 2009
Ovarian interstitial YAG-laser: An effective new method

- Transvaginal ultrasound guided ovarian interstitial laser-coagulation treatment in anovulatory women with PCOS.
  - Spontaneous ovulation rate of 84.2%, during the 6-month postoperative period.
  - Decrease in serum LH and testosterone
- No significant operative complications were encountered.
- The ultrasound-guided transvaginal ovarian interstitial laser treatment may be an effective new method to manage anovulation in PCOS patients.

Ultrasound-guided immature follicle aspiration (IMFA) to treat severe PCOS

Schematic diagram for ultrasound microinvasive surgery

A Ovary before puncture
B Reinspection two weeks after puncture
Laparoscopic ovarian diathermy, a very simple form of surgery, has a high success rate and has a definite, useful role in the management of anovulatory infertility in women with PCOS.
Laparoscopic ovarian diathermy is an excellent example to illustrate that the key to success of endoscopic surgery depends very much on:

1. careful patient selection
2. the use of proper techniques
Approach to ovulation induction in women with PCOS

1. PCOS
   - Overweight or Obese
     - Ovulation
   - Lean
     - No Ovulation
       - Clomiphene Citrate
         - Ovulation
         - No Ovulation
           - Clomiphene Citrate & metformin
             OR
             Clomiphene Citrate & dexamethasone
             OR
             aromatase inhibitors
             OR
             ovarian drilling
               - Ovulation
               - No Ovulation
                 - gonadotropins
                   OR
                   in vitro fertilization

Guzick DS, Clin Obs Gyn 2007;1;255-267
LOD’un Avantajları

Tek tedavi ile, medikal tedavilerdeki gibi tekrarlayan kür gereksinimi olmaksızın, tekrarlayan fizyolojik ovulasyonların ve olası gebeliklerin oluşmasını sağlar.

Daha önemlisi, monoovulasyon sağlayarak eskisinden fazla olmayan çoğul gebeliklere neden olur.

Aksine CC tedavisi, %5-10 ikiz gebelikle birliktedir. Üçüz gebelik insidansında yüksek bildirilmiştir.

LOD, CC ile karşılaştırıldığında, Abortus oranı anlamlı şekilde düşüktür. (LH ve/veya Androjenlerin serum seviyelerinin normalizasyonu nedeniyle)

Abdel-Gadir et al. 1990.

Hipotetik olarak, CC’nin uzun süreli kullanımları, artmış over kanseri riski ile birliktedir. LOD, bu riski arttırmamıştır.

Rosssing et al.1994

Ayrıca LOD, pelvik anatomiyi, HSG’ye gerek duyulmak丝毫不, tubal geçirgenliği değerlendirmeye ve fertiliteti etkileyen (endometriosis, adezyon gibi) faktörleri tedavi etme imkanı vermektedir.

Amer et al.2009
LOD’un etki mekanizması:

- LOD, LH ve Androjenlerin (T, A, DHEAS) serum sevyesini anlamlı olarak azaltır.

- LOD sonrası, AMH, LH ve Androjenlerdeki azalma dolaşımndaki FSH’ya folliküllerin duyarlığını artıracak, follikül büyümesine ve ovulasyona neden olacaktır. Dolayısıyla Gebeliğe neden olacaktır.

Endikasyonlar

- CC-dirençli, nonobes, başka infertilite faktörü olmayan PCOS,
- Başka amaçla L/S planlanan veya OI sürecinde yakın monitorizasyonu mümkün olmayan anovulatuar PCOS.
- Diğer (rölatif)
  - Persistan LH hipersekresyonyu,
  - Menstrüel irregülarite,
  - Hyperandrogenism

ASRM/ESHRE Consensus Workshop, 2008
Ovulasyon


LOD’dan sonra, ovulasyon oranı(%64), CC’den sonraki orandan (%76) istatistiksel olarak farklı değildir.

İkinci bir tedavi ilave edilirse, her iki yöntem de sırasıyla artış göstermiştür. (%85, %84)
Figure 2 Cumulative proportion of women with a first live birth in the group allocated to electrocautery and the group allocated to immediate treatment with recombinant follicle-stimulating hormone (log rank: 0.24, \( P = 0.63 \)).

Figure 3 Cumulative proportion of women with a second live birth in the group allocated to electrocautery and the group allocated to immediate treatment with recombinant follicle-stimulating hormone (log rank: 4.77, \( P = 0.03 \)).
Results from the meta-analysis of the randomized, controlled trials of laparoscopic ovarian surgery versus gonadotropins for (a) live-birth rate and (b) multiple pregnancy rate. Notes: Test for heterogeneity: chi-square = 0.35, df = 1 (p=0.55), I² = 0%. Test for overall effect: Z = 0.14 (p=0.89). (Farquhar et al., Cochrane Database Syst Rev 2007;3:CD001122. Copyright Cochrane Collaboration, reproduced with permission.)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
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<th>OR (95% CI)</th>
<th>Weight %</th>
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<td>Farquhar 2005</td>
<td>0.68</td>
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<td>0.69 (0.38, 1.28)</td>
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5RCT ile LOD ve Gonadotropin etkinliği karşılaştırılmış:

Canlı doğum oranında fark gösterilmemiştir.

Çoğul gebelik, gonadotropin kolunda anlamlı şekilde yüksek.

Düşük oranı fark yok.

2 RCT’nin ekonomik analizinde LOD, direk ve indirekt costu azaltmaktadır.
**Eve Giden Mesaj**

- LOD, CC-Rezistans kadınlara yapılabilir.
- LOD, OHSS ve çoğul gebelik riski olmadan Monofolliküler ovulasyon sağlar.
- LOD sonrası follikül gelişimi için monitorizasyona gerek yoktur.
- LOD tekniğine uygun yapılmalıdır.
- LOD, hala gonadotropinlerle birlikte, ikinci seçenek tedavi olup, gonadotropinlere alternatif biridir.
- LOD, LH/FSH oranı: >2 olan ve non-obes hastalarda ve monitorizasyonun imkansız olduğu kişilerde daha etkilidir.
Eve Giden Mesaj

- Ünilateral/Bilateral LOD arasında, sonuçlar açısından fark yoktur.
- LOD, deneyimli bir cerrah tarafından sadece bir defa yapılmalıdır.
- Cerrahinin riskleri minimal olup, L/S 'nin riskleri yanında adezyon, over tahribatı da düşünülmelidir.
- Adezyonları azaltmak için tek overe özellikle sağ tarafa, mümkünse Laser, monopolar enerji ile LOD yapılmalıdır.
- Over volümü üzerine dayalı LOD tercih edilmelidir. 60j/cm³
- Adezyon oluşumunda delik sayısı önemli değildir.
Eve Giden Mesaj

- LOD, nonfertilite endikasyonlar için yapılmamalıdır.
- Gelecekte fertiloskop ile LOD daha popüler olabilir.