Laparoscopic Management of Early Stage Endometrial Cancer

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Early Stage of Endometrial Cancer
Most of cases diagnosed (clinical stage I)

Surgery is the primary treatment

Objectives:
• Removal of the uterine tumor
• Pronostic factors determination (Surgical staging-FIGO 1988)
• With a minimal morbidity profile

Surgical Procedure

Early Stage, standard surgery

- Peritoneal inspection and peritoneal washings
- Total hysterectomy + bilateral salpingo-oophorectomy
- +/- Pelvic and Para-aortic lymphadenectomies

- Recommended by FIGO, SGO, ACOG
- But usual practice observed is a compromise between:
  - Risk of nodal metastasis according to myometrial invasion and grade (Creasman and al. Cancer 1987)
  - Patients characteristics and medical comorbidity
Surgical Procedure / lymphadenectomy remains highly controversial in 2009 for early stage

**Therapeutic role and necessity?**
- Yes in high risk tumor: retrospectives studies
- **NO:** 2 recent RCTs:

**Systematic para-aortic extension?**
- Related to isolated para-aortic nodal metastasis without positive pelvic nodes
- Yes in high risk lesions: Mariani and al. Gynecol Oncol 2008
  - 16% isolated PAN+, 67% of PAN+ above inferior mesenteric artery
- **NO:** Abu-Rustum and al. Gynecol Oncol 2009
  - 1% of PAN+

**The Future: sentinel lymph node technique?**

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Surgical Route in early stage EC

Laparoscopy: a major change in the management

**Laparotomy:** « historical » approach
- ...could compromise morbidity.

**Vaginal surgery**
- ...doesn’t allow a complete surgical staging

**Laparoscopy**
- Initially proposed in early 1990s:
  - Childers JM. Gynecol Oncol 1993
  - Mage G. J Gynecol Obstet Biol Reprod 1995
- All steps required for surgical staging became feasible
- Sentinel lymph node technique
- Attractive for patients with comorbid medical conditions

Laparoscopy = Gold Standard in 2009?

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Laparoscopic Approach

**Retrospective Studies**

<table>
<thead>
<tr>
<th>Studies</th>
<th>Patients</th>
<th>Minimum Follow-up (yr)</th>
<th>Recurrence</th>
<th>Survival DFS %</th>
<th>Death %</th>
<th>Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holshue and al. 2002</td>
<td>177/44</td>
<td>33.6</td>
<td>6.2 / 6.8%</td>
<td>93.7 / 95.2</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Magrina and al. 1999 2004</td>
<td>56</td>
<td>24y</td>
<td>76</td>
<td>-</td>
<td>3y Rate 2.5% 94.7</td>
<td>10.8%</td>
</tr>
<tr>
<td>Eltabakh and al. 2002</td>
<td>100/86</td>
<td>27</td>
<td>7 / 10.5 %</td>
<td>90 / 92%</td>
<td>-</td>
<td>0</td>
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<tr>
<td>Kocoppola and al.</td>
<td>40 / 40</td>
<td>24</td>
<td>2.5 / 2.2 %</td>
<td>100 / 95 %</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Nezhat F. and al. 2006</td>
<td>67 / 127</td>
<td>36.3 / 29.6</td>
<td>-</td>
<td>88.5 / 85%</td>
<td>-</td>
<td>0</td>
</tr>
</tbody>
</table>
### Laparoscopic Approach

#### Retrospective Studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Patients</th>
<th>Median Follow-up</th>
<th>Conversion (%)</th>
<th>Node Metastasis (%)</th>
<th>Overall Survival (%)</th>
<th>Overall Rank</th>
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<td>- / -</td>
<td>- / -</td>
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<td>Magrina and al. 1999</td>
<td>11826</td>
<td>11286</td>
<td>11826</td>
<td>93.7 / 93.2</td>
<td>- / -</td>
<td>- / -</td>
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<td>7 / 10.5</td>
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<td>- / 0</td>
<td>- / 0</td>
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<tr>
<td>Kuoppala and al. 2004</td>
<td>40 / 40</td>
<td>34</td>
<td>2.5 / 2</td>
<td>100 / 95</td>
<td>- / 0</td>
<td>- / 0</td>
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</table>

### Surgical Route – RCTs

#### Laparoscopy vs Laparotomy / Surgical Outcomes

- **« Advantage: laparoscopy »**
  - Fram and al. Int J Gynecol Cancer 2002
  - Tozzi and al. J Min Invasive Gynecol 2005
  - Zorlu and al. JSLS 2003
  - Malzoni and al. Gynecol Oncol 2009
  - Walker and al. GOG LAP 2, JCO 2009 (multicenter)

- Feasible, low rate of conversion (except LAP 2!)
- Similar radicality
- Longer operative time
- Fewer complications
- Shorter hospital stay
- Improvement of quality of life (Zullo 2005, SF-36)

### Surgical Route – RCTs

#### Laparoscopy vs Laparotomy / Survival

- **« No Difference »**

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<td>Tozzi 2005</td>
<td>63 / 59</td>
<td>44</td>
<td>87.3 / 91.5</td>
<td>82.5 / 86.4</td>
</tr>
<tr>
<td>Malzoni 2009</td>
<td>81 / 78</td>
<td>38.5</td>
<td>91.4 / 88.5</td>
<td>93.2 / 91.1</td>
</tr>
<tr>
<td>Zullo 2009</td>
<td>40 / 35</td>
<td>79</td>
<td>82.5 / 84.2</td>
<td>80 / 81.6</td>
</tr>
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</table>

*Long term results of large studies (LAP2, LACE) are still requested*
Meta-Analysis

Laparoscopy vs Laparotomy

- Lin and al. Int J Gynecol Cancer 2008
- Palomba and al. Gynecol Oncol 2008
- Ju and al. Int J Gynecol Cancer 2009

« Advantage of laparoscopy in terms of complication and hospital stay »
« No difference in terms of survival and recurrence rate with actual follow-up »

Our Retrospective Experience
Polyclinique + CRLC Jean Perrin, Clermont-Fd

Année

Preoperative staging:
iclinal examination, chest X-ray, MRI in most of cases

Contraindications to laparoscopic procedure:
- anesthetic risk factors
- large uterus, poor vaginal access
- evidence of lymphadenopathy on MRI

Patients (n=207)
Clinical Characteristics

- Mean age 62.9 years old (36-88)
- Age ≥ 70 y : 27 %
- Mean BMI 26.2 (16-56)
- BMI > 30 in 52 patients (25%)
- 183 post-menopausal patients (88%)
- 36 nulliparous (17.3%)
Laparoscopic Procedure

1. Inspection
2. Peritoneal washings
3. Total hysterectomy + BSO
4. Frozen section

Laparoscopic Pelvic Lymphadenectomy
right side

Results
1990-2005, n= 207 patients

- Age ≥ 70 y old 27%
- BMI > 30 25%
- Conversion 4.3%
- Complications 5.5%
- Blood Transfusion 3
- Operative Time 168’ TLH-BSO-PL
- Hospital Stay 5 days
- Nodes 10
- DFS / 5 y 90.4%
- OS / 5 y 90.7%
- Surgeons 11
Conversions to laparotomy, \( n = 9/207 \)
4.3 %

- 4 evidence of extra-uterine spread
- 2 obliterated pelvic access due to severe adhesions
- 1 failure in pneumoperitoneum creation (previous bowel resection, BMI=32)
- 1 morbid obesity (BMI = 56) and difficult exposure
- 1 severe subcutaneous emphysema

Complications, 5.5 %

- Gas embolism: 1
- Pulmonary embolus: 1
- Phlebitis: 2
- Reoperation / haemorrhage: 1 on day 2
- Blood transfusion: 3
- Bladder injury: 1 treated by laparoscopy
- Vesicovaginal fistula: 1 after 3 months
- Vaginal disunion: 1 after 6 years
- Port site hernia with repair: 1
- Obturator nerve neuralgia: 3
- Lymphocyst: 2
- Urinary tract infection: 5.5 %

Histological results

**FIGO stage (198 patients)**

<table>
<thead>
<tr>
<th>FIGO Stage</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>36</td>
</tr>
<tr>
<td>IB</td>
<td>13</td>
</tr>
<tr>
<td>IIA</td>
<td>2</td>
</tr>
<tr>
<td>IIB</td>
<td>0</td>
</tr>
<tr>
<td>IIIA</td>
<td>2</td>
</tr>
<tr>
<td>IIIB</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>1</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
</tr>
</tbody>
</table>

**Underestimation of preop. stage = 11.6 %**
Histological results

Grades of differentiation

Results, long term follow-up

1990-2005, n= 198 patients (conversions excluded)

- Median follow-up: 67 months
  - Last follow-up: October 2008 (Study still in progress)
  - 11 patients with a follow-up < 36 months

- Recurrence: 10.6 % (n=21)
  - Mean interval: 35 months (6 - 143)
  - 9 FIGO stages I
  - 8 grades 3
  - 13 deaths

- Five year disease free survival (1): 90.4 %
- Five year overall survival (2): 90.7 %
- No port-site recurrence

Limitations

- Anaesthetic contraindications
- Tumoral dissemination?
- Large uterus +/- poor vaginal access
- Surgical training
- Morbid obesity (BMI > ?)
Surgical Education and Training

- The key to prevent bad results
- A perfect knowledge of laparoscopic surgery and oncological principles is mandatory

Conversion rate from RCTs
- in single institutions with expertise in laparoscopy: < 10 %
- in a large multicentric trial (Walker and al. JCO 2009): 25.8 %

Limitations

Obesity, Laparoscopy and Endometrial Cancer

- Obesity is common among endometrial cancer
- Obese patients can benefit the most from this approach
- Considered to be a relative contraindication to laparoscopy

- Technical limits for laparoscopic surgery:
  - Entry in the peritoneal cavity
  - Tolerance to the pneumoperitoneum and Trendelenburg position
  - Exposure of pelvic and abdominal vessels
- Could compromise the feasibility of lymphadenectomies

Results, Clermont-Ferrand 1990-2001

161 patients with endometrial cancer treated by laparoscopy

<table>
<thead>
<tr>
<th>AAGL 2005</th>
<th>Obese, n=42</th>
<th>Non obese, n=119</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conversion (%)</td>
<td>2.3</td>
<td>4.2</td>
</tr>
<tr>
<td>Major complications (%)</td>
<td>2.4</td>
<td>6.5</td>
</tr>
<tr>
<td>Blood transfusion (n)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Op. Time</td>
<td>159'</td>
<td>155'</td>
</tr>
<tr>
<td>Hosp. Stay (days)</td>
<td>5.5</td>
<td>5</td>
</tr>
<tr>
<td>Nodes (n)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Lymphadenectomies not performed (%)</td>
<td>14.6</td>
<td>9.2</td>
</tr>
<tr>
<td>Recurrence (%)</td>
<td>7.3</td>
<td>8.5</td>
</tr>
<tr>
<td>Surgeons (n)</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

NS

Future interest of robotic to perform lymphadenectomies in obese patients by Gehrig and al., Gynecol Oncol 2008
Seamon and al. Obstet Gynecol 2008
Approach actually limited by a prohibitory cost
Conclusions

- Laparoscopy offers major advantages in terms of morbidity with probably similar survival rates to 'historical' approach.
- If the gold standard status requires 'officially' long term oncological results of trials in progress.
- On the other hand:
  After an adequate laparoscopic learning would you perform a laparotomy in early stage endometrial cancer patient?