Laparoscopic Management of Early Stage Endometrial Cancer

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C. Pomel, J.L Achard, J. Dauplat, G. Mage
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 ?

Surgical Route ?
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**
    - ASTEC Study Group. MRC ASTEC Trial. Lancet 2009

✓ **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 ?**
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?
## Laparoscopic Approach

### Retrospective Studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Patients n</th>
<th>Median follow-up. (month/year)</th>
<th>Recurrence</th>
<th>Survival DFS</th>
<th>Death n / %</th>
<th>Port-site metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holub and al. 2002</td>
<td>177/ 44</td>
<td>33.6</td>
<td>6.2 / 6.8 %</td>
<td>93.7 / 93.2</td>
<td>-</td>
<td>0</td>
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<tr>
<td>Magrina and al. 1999 2004</td>
<td>56/76</td>
<td>2.4 y</td>
<td>-</td>
<td>3y rate 2.5 % 94.7</td>
<td>10.8 %</td>
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<tr>
<td>Eltabbakh and al. 2002</td>
<td>100/86</td>
<td>27</td>
<td>7 / 10.5 %</td>
<td>90 / 92 %</td>
<td>-</td>
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<tr>
<td>Kuoppala and al.</td>
<td>40 / 40</td>
<td>34</td>
<td>2.5 / 2 %</td>
<td>100 / 95 %</td>
<td>-</td>
<td>0</td>
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<tr>
<td>Nezhat F. and al. 2008</td>
<td>67 / 127</td>
<td>36.3/29.6</td>
<td></td>
<td>88.5 / 85 %</td>
<td>-</td>
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### Laparoscopic Approach

#### Retrospective Studies

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<th>Median</th>
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<th>Laparotomie (USD)</th>
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<td>Spiritos 1996</td>
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<td>13809</td>
<td>17119</td>
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<td>Gemignani 1999</td>
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<td>11826</td>
<td>15189</td>
<td></td>
<td></td>
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<tr>
<td>Scribner 1999</td>
<td></td>
<td></td>
<td></td>
<td>5198</td>
<td>5331</td>
<td>10,8 %</td>
<td>0</td>
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<td>Eltabbakh 2000</td>
<td></td>
<td></td>
<td></td>
<td>13003</td>
<td>11878</td>
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Surgical Route – RCTs

Laparoscopy vs Laparotomy / Surgical Outcomes
« advantage: laparoscopy »

Fram and al. Int J Gynecol Cancer 2002
Tozzi and al. J Mini Invasive Gynecol 2005
Zorlu and al. JSLS 2005
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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<tr>
<th>Studies</th>
<th>Patients n</th>
<th>Median follow-up. (month/ year)</th>
<th>Survival DFS %</th>
<th>Overall Survival %</th>
</tr>
</thead>
<tbody>
<tr>
<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 / 38</td>
<td>79</td>
<td>82.5 / 84.2</td>
<td>80 / 81.6</td>
</tr>
</tbody>
</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

1990

2005

1990-2005
207 patients with a clinical stage I endometrial carcinoma treated by laparoscopy

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

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

Contractions:
- COELIO
- LAPARO

Laparoscopy and endometrial carcinoma
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**

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
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<tr>
<td>Age ≥ 70 y old</td>
<td>27 %</td>
</tr>
<tr>
<td>BMI &gt; 30</td>
<td>25 %</td>
</tr>
<tr>
<td>Conversion</td>
<td>4.3 %</td>
</tr>
<tr>
<td>Complications</td>
<td>5.5 %</td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>3</td>
</tr>
<tr>
<td>Operative Time</td>
<td>168 ’TLH+BSO+PL</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>5 days</td>
</tr>
<tr>
<td>Nodes</td>
<td>10</td>
</tr>
<tr>
<td>DFS / 5 y</td>
<td>90.4 %</td>
</tr>
<tr>
<td>OS / 5 y</td>
<td>90.7 %</td>
</tr>
<tr>
<td>Surgeons</td>
<td>11</td>
</tr>
</tbody>
</table>
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)

Underestimation of preop. stage = 11.6 %
Histological results

Grades of differentiation

<table>
<thead>
<tr>
<th>Grade</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>153</td>
</tr>
<tr>
<td>Grade 2</td>
<td>24</td>
</tr>
<tr>
<td>Grade 3</td>
<td>21</td>
</tr>
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</table>
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>5.2</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>Recurrences (%)</td>
<td>7.3</td>
<td>8.5</td>
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<td>Surgeons (n)</td>
<td>11</td>
<td>11</td>
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Future interest of robotic to perform lymphadenectomies in obese

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?
Thank you very much!