Laparoscopic Management of Early Stage Endometrial Cancer

B. Rabischong, M. Canis, G. Le Bouedec, 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>
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<td>Holub and al. 2002</td>
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<td>Magrina and al. 1999 2004</td>
<td>56</td>
<td>2.4 y</td>
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<td>3y rate</td>
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<td>Kuoppala and al.</td>
<td>40 / 40</td>
<td>34</td>
<td>2.5 / 2 %</td>
<td>100 / 95 %</td>
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<tr>
<td>Nezhat F. and al. 2008</td>
<td>67 / 127</td>
<td>36.3/29.6</td>
<td>88.5 / 85 %</td>
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# Laparoscopic Approach

## Retrospective Studies

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<td>Gemignani 1999</td>
<td></td>
<td></td>
<td>11826</td>
<td>15189</td>
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<td>Scribner 1999</td>
<td></td>
<td></td>
<td>5198</td>
<td>5331</td>
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<td>Eltabbakh 2000</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>
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<th>Overall Survival %</th>
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<tr>
<td>Tozzi 2005</td>
<td>63 / 59</td>
<td>44</td>
<td>87.3 / 91.5</td>
<td>82.5 / 86.4</td>
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<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>
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**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 - Beginning of experience

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

Graph:
- Stage I clinical
  - Laparoscopy
    - Intra peritoneal disease:
      - Laparotomy
      - Superficial myometrial invasion
      - Myometrial invasion:
        - Pelvic lymphadenectomy
        - Frozen section
        - ± paraaortic
    - No intra peritoneal disease:
      - Grade 1 - 2:
        - Hysterectomy
      - Grade 3:
        - Hysterectomy
        - Pelvic lymphadenectomy + omentectomy
        - Frozen section
        - ± paraaortic

Graph legend:
- COELIO
- LAPARO

Graph timeline:
- 1990
- 1992
- 1994
- 1996
- 1998
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)**

Underestimation of preop. stage = 11.6 %
Histological results

Grades of differentiation

<table>
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<th>n</th>
</tr>
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<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>
</tbody>
</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>
</tr>
<tr>
<td>Surgeons (n)</td>
<td>11</td>
<td>11</td>
</tr>
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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 term 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!