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>
<td>177/ 44</td>
<td>33.6</td>
<td>6.2 / 6.8 %</td>
<td>93.7 / 93.2</td>
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<tr>
<td>Magrina and al. 1999 2004</td>
<td>56</td>
<td>2.4 y</td>
<td>-</td>
<td>3y rate 2.5 % 94.7</td>
<td>10,8 %</td>
<td>0</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>
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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>
<td>-</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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<td>Magrina and al. 1999</td>
<td>Gemignani 1999</td>
<td>11826</td>
<td>12.5 / 13.5 %</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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<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><em>Tozzi 2005</em></td>
<td>63 / 59</td>
<td>44</td>
<td>87.3 / 91.5</td>
<td>82.5 / 86.4</td>
</tr>
<tr>
<td><em>Malzoni 2009</em></td>
<td>81 / 78</td>
<td>38.5</td>
<td>91.4 / 88.5</td>
<td>93.2 / 91.1</td>
</tr>
<tr>
<td><em>Zullo 2009</em></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

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:

Year
- 1990
- 1992
- 1994
- 1996
- 1998

COELIO
LAPARO

Stage I clinical

Laparoscopy

Intra peritoneal disease

Grade 1 - 2

Hysterectomy

Hysterectomy

No intra peritoneal disease

Grade 3

Pelvic lymphadenectomy + omentectomy

Frozen section

± paraaortic

Pelvic myometrial invasion

Frozen section

± paraaortic

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>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<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

- Grade 1: 153
- Grade 2: 24
- Grade 3: 21
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 perfomed (%)</td>
<td>14.6</td>
<td>9.2 NS</td>
</tr>
<tr>
<td>Recurrences (%)</td>
<td>7.3</td>
<td>8.5</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 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!