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?

Surgical Route?

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)
  • Risk of para-aortic nodal metastasis without positive pelvic nodes or poor pronostic factors (Boronow and al. Obstet Gynecol 1984, Morrow and al. Gynecol Oncol 1991)
• 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 P AN+, 67 % of P AN+ above inferior mesenteric artery
  - NO: Abu-Rustum and al. Gynecol Oncol 2009
    - 1 % of P AN+

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
- Attractive for patients with comorbid medical conditions

Laparoscopy = Gold Standard in 2009?

Laparoscopic Approach

Retrospective Studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Patients</th>
<th>Median follow-up (y)</th>
<th>Recurrence</th>
<th>Survival 5Y</th>
<th>Death (%)</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>6.2/6.6%</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>2.4 y</td>
<td>76</td>
<td>3y rate 2.5%</td>
<td>94.7</td>
<td>10.8%</td>
</tr>
<tr>
<td>Eltabakh and al. 2002</td>
<td>100/36</td>
<td>27</td>
<td>7.10.5%</td>
<td>90/92%</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Nezhat F. and al. 2008</td>
<td>67 / 127</td>
<td>36.3/29.6</td>
<td>88.5/85%</td>
<td>-</td>
<td>0</td>
<td>0</td>
</tr>
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</table>
Laparoscopic Approach

Retrospective Studies

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<thead>
<tr>
<th>Studies</th>
<th>Patients</th>
<th>Median follow-up</th>
<th>Conversion CMC (%)</th>
<th>Conversion UMD (%)</th>
<th>DFS (%)</th>
<th>Overall Survival (%)</th>
</tr>
</thead>
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<tr>
<td>Holub and al. 2002</td>
<td></td>
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<tr>
<td>Gemignani and al. 1999</td>
<td></td>
<td>11826</td>
<td>15189</td>
<td>-</td>
<td>10.8%</td>
<td>0</td>
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<tr>
<td>Eltabakh and al. 2000</td>
<td></td>
<td>13003</td>
<td>11878</td>
<td>-</td>
<td>10.8%</td>
<td>0</td>
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<tr>
<td>Kuoppala and al.</td>
<td></td>
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<tr>
<td>Gemignani and al. 1999</td>
<td></td>
<td>13100</td>
<td>13113</td>
<td>-</td>
<td>0</td>
<td>10.8%</td>
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Median follow-up (month/year):
- Holub and al. 2002: 33.6/6.2%
- Magrina and al. 1999/2004: 2.4y/76%
- Zullo and al. 2005: 2.5/2%

Surgical Route – RCTs

Laparoscopy vs Laparotomy / Surgical Outcomes

« advantage: laparoscopy »

- Fram and al. Int J Gynecol Cancer 2002
- Tozzi and al. J Minim Invasive Gynecol 2003
- 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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<th>Overall Survival (%)</th>
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</thead>
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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>
</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 / 83.6</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 + CRUC Jean Perrin, Clermont-Fd

1990

- Beginning of experience
- 207 patients with a clinical stage I endometrial carcinoma treated by laparoscopy

Preoperative staging:
- clinical 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)

- 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></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, NS</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>
</tbody>
</table>

Future interest of robotic to perform lymphadenectomies in obese patients.
Gehrig and al. Gynecol Oncol 2008
Seamon and al. Obstet Gynecol 2008
AAGL 2005

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?