Fertility Sparing Surgery
(Oncofertility)
in
Gynecological Cancers

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Department of Obstetrics and Gynecology
Cancer Treatment

Objective Cure

Adverse Effects
- Psychological effects
- Cosmetic problems
- Loss of organ function
- Sexual and reproductive dysfunction

Fertility Sparing Surgery (FFS)?
✓ Oncologic out-come after fertility sparing surgery should not be effected negatively

✓ Evidence-based Data

Fertility Sparing Surgery
The patient with cancer should be informed for fertility preservation.
Fertility preservation in cancer

Non Gynecologic cancers
- Embryo freezing
- Oocyte freezing
- Ovarian tissue freezing
- Ovarian transplantation

Cervical cancer
- Less radical tumor excision (Large cone)
- Radical tracheectomy and Pelvic LND
- Vaginal tracheectomy
- Abdominal tracheectomy (Via laparotomy or laparoscopy)

Neoadjuvant chemotherapy followed by radical tracheectomy (for larger tumors)

Gynecologic Cancers
- Endometrial cancer
  - Hysterectomy without oopherectomy
  - Surrogacy
- Ovarian cancer
  - Fertility sparing surgery (EOC or BOT)
  - Cystectomy/unilateral salpingo-oophorectomy and surgical staging

High dose systemic progestins
Fertility-Sparing in Gynecologic Oncology

- Age + Ovarian reserve
- Desire to preserve fertility
- Tumor factors
  - Histologic type, grade
- Stage of disease
FSS in Cervical Cancer (CC)

- Mean age: 47.1
- Diagnosis at early stage: 20-25%
- According to SEER data, 42% of cervical cancer patients younger than 45 years of age
Fertility-sparing procedures in Early CC

- Oophoropexy (surrogacy)
- Fertility sparing surgeries
  - Standard procedures
    - Conization
    - Radical trachelectomy + LND
  - Individualized procedures
    - Cone or simple trachelectomy + LND
    - Cone or simple trachelectomy + LND after neoadjuvant CT
Principles of FSS in Early-Stage Cervical Cancer

- Tumor factors
  - Depth and width of invasion
  - Size of cervical lesion
  - LVSIs
  - Histologic type
FFS in Early-Stage Cervical Cancer

- ID < 3 mm
- LVSI (-)
- CONIZATION
- MARGIN (-)
- FOLLOW-UP
LVSI

Pelvic lymph node metastasis

Pelvic recurrence
Spread of Cervical Cancer

- Laterally (Dominant) → Parametrium
- Vertically (rare)
  - Stage Ib and Ila → 0%
  - Stage IIb → 20%
Radical Trachelectomy (Standard)

Jeng CJ, Gynecol Oncol, 2006
Radical Trachelectomy
Indications

- Fertility desire
- Tumor diameter and no upper endocervical canal involvement determined by MRI
- FIGO STAGE IA1 (LVSI +), IA2 – IB1 (Lesion <2 cm)
- Squamous, adenocarcinoma, adenosquamous (except e.g., neuro endocrine carcinoma)
- Lymph node negative (FROZEN/ULTRASTAGING)
- Tumor free endocervical surgical border >0.5 cm

Early Stage Cervical Cancer
Stage 1a LVSI(+) - 1b < 2cm

Fertility Desire

MIS, Conventional

Sentinel LN

(-) LN
LRT, LAVRT

(+/-) LN
Chemoradiotherapy

Renaud et al. Gynecol Oncol 2000
Sardi et al. Gynecol Oncol 1999
Childers et al. Gynecol Oncol 1992
Serviks Kanseri – SLN Saptama Oranları

- Literatür %55-100
- SENTICOL Study (Blue dye + Tec.99)
  En az 1 SLN saptama %98

Bilateral SLN saptama %77
PRINCIPLES OF EVALUATION AND SURGICAL STAGING WHEN SLN MAPPING IS USED

The key to a successful SLN mapping is adherence to the SLN algorithm, which requires the performance of a side-specific nodal dissection in cases of failed mapping and removal of any suspicious or grossly enlarged nodes regardless of mapping (Figure 3).

Figure 3: Surgical/SLN Mapping Algorithm for Early-Stage Cervical Cancer†

1. Excision of all mapped SLN†† (submit for ultrastaging if negative H&E)
2. Any suspicious nodes must be removed regardless of mapping
3. If there is no mapping on a hemi-pelvis, a side-specific LND is performed†††
4. Parametrectomy is performed en bloc with a resection of the primary tumor†††

H&E: Hematoxylin and eosin staining
LND: Lymphadenectomy
SLN: Sentinel lymph node

††Intracervical injection with dye, 99m technetium, or both.
†††Intracervical injection with dye, 99m technetium, or both.
## Expanding FSS with tumor > 2 cm

<table>
<thead>
<tr>
<th></th>
<th>Papers</th>
<th>range</th>
<th>pts</th>
<th>&gt;2 cm</th>
<th>recurrences</th>
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<td>11</td>
<td>2003-08</td>
<td>76</td>
<td>67</td>
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<tr>
<td>ART</td>
<td>9</td>
<td>2005-11</td>
<td>221</td>
<td>40</td>
<td>5 (12%)</td>
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</table>
Long-Term Outcomes After Fertility-Sparing Laparoscopic Radical Trachelectomy in Young Women With Early-Stage Cervical Cancer: An Asan Gynecologic Cancer Group (AGCG) Study

JEONG-YEOL PARK, MD, PhD,¹ WON DEOK JOO, MD, PhD,² SUK-JOON CHANG, MD, PhD,³ DAE-YEON KIM, MD, PhD,¹ JONG-HYEOK KIM, MD, PhD,¹ YONG-MAN KIM, MD, PhD,¹ YOUNG-TAK KIM, MD, PhD,¹ AND JOO-HYUN NAM, MD, PhD¹*

Tumor size
- < 2 cm (n=50)
- > 2 cm (n=29)

Cervical stromal invasion
- < 50% (n=57)
- > 50% (n=22)

Disease-free Survival

Follow-up Time (years)

P = 0.039

P = 0.016

Radical Trachelectomy
International Results

- Cases # >900
- **Recurrence rate 2.7-3%**
- Expected 5Y OS %98
- Mortality rate 2-3.2 %
- Increased risk of preterm birth
- Higher incidence of infertility due to cervical abnormalities

The prevalence of infertility and use of ART is higher in patients after ART than in patients after VTR

- Pregnancy 300
- Alive delivery 196

Tomao et al Curr Treat Options in Oncol (2016) 17:5
Oncologic outcomes

• In the past 2 decades, early CC can be managed with fertility preservation without compromising oncologic outcomes

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number</th>
<th>5-Year Survival</th>
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<tbody>
<tr>
<td>Hysterectomy</td>
<td>841</td>
<td>98 (96–99)</td>
</tr>
<tr>
<td>Fertility-conserving surgery</td>
<td>568</td>
<td>99 (97–99)</td>
</tr>
</tbody>
</table>

Data are % (95% confidence interval).

Wright et al. Obstet Gynecol 2010
Oncological outcomes after fertility-sparing surgery for cervical cancer: a systematic review

Enrica Bentivegna, Sebastien Gouy, Amandine Maulard, Cyrus Chargari, Alexandra Leary, Philippe Morice

<table>
<thead>
<tr>
<th>Serles and case reports</th>
<th>Dargent’s procedure</th>
<th>Abdominal radical trachelectomy</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Laparotomic</td>
</tr>
<tr>
<td>Number series or case reports*</td>
<td>21</td>
<td>28</td>
</tr>
<tr>
<td>Number of patients</td>
<td>1523</td>
<td>866</td>
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<tr>
<td>Patients excluded</td>
<td>159</td>
<td>206</td>
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</table>

**Fertility outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Dargent’s procedure</th>
<th>Abdominal radical trachelectomy</th>
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<tbody>
<tr>
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<td>Laparotomic</td>
</tr>
<tr>
<td>Pregnancies</td>
<td>487</td>
<td>175</td>
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<tr>
<td>Fetal loss (trimester 1 or 2)</td>
<td>103</td>
<td>37</td>
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<tr>
<td>Preterm delivery</td>
<td>104</td>
<td>21</td>
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<tr>
<td>Pregnancy rate†</td>
<td>21.6/343 (63%)</td>
<td>114/235 (49%)</td>
</tr>
</tbody>
</table>
Oncological outcomes after fertility-sparing surgery for cervical cancer: a systematic review

<table>
<thead>
<tr>
<th>Dargent's procedure</th>
<th>Abdominal radical tracheectomy</th>
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<td></td>
<td>Laparotomic</td>
</tr>
<tr>
<td><strong>Series and case reports</strong></td>
<td></td>
</tr>
<tr>
<td>Number of series or case reports</td>
<td>21</td>
</tr>
<tr>
<td>Number of patients</td>
<td>1523</td>
</tr>
<tr>
<td>Patients excluded</td>
<td>159</td>
</tr>
<tr>
<td><strong>Tumour characteristics</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td></td>
</tr>
<tr>
<td>IA</td>
<td>316</td>
</tr>
<tr>
<td>IB1</td>
<td>1065</td>
</tr>
<tr>
<td>All</td>
<td>At least 84</td>
</tr>
<tr>
<td>IB2</td>
<td>3</td>
</tr>
<tr>
<td>IIA</td>
<td>9</td>
</tr>
<tr>
<td><strong>Tumour type</strong></td>
<td></td>
</tr>
<tr>
<td>Squamous-cell carcinoma</td>
<td>892</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>432</td>
</tr>
<tr>
<td>Other, mixed, or unknown</td>
<td>199</td>
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<tr>
<td>LVSI positive</td>
<td>401</td>
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<tr>
<td><strong>Oncological outcomes</strong></td>
<td></td>
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<tr>
<td>Recurrent disease</td>
<td>58</td>
</tr>
<tr>
<td>Died from disease</td>
<td>3</td>
</tr>
</tbody>
</table>

159 studies
8098 patients

Lancet Oncol. 2016 Jun;17(6):e240-e253
Phase III Randomized Trial of Laparoscopic or Robotic Radical Hysterectomy vs. Abdominal Radical Hysterectomy in Patients with Early-Stage Cervical Cancer: LACC Trial

Pedro T. Ramirez, Michael Frumovitz, Rene Pareja, Aldo Lopez, Marcelo Vieira, Reitan Ribeiro, Alessandro Buda, Xiaojian Yan, Kristy P Robledo, Val Gebski, Robert L Coleman, Andreas Obermair
### Site of First Recurrence

<table>
<thead>
<tr>
<th>Site of Recurrence</th>
<th>TARH</th>
<th>TLRH/TRRH</th>
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</thead>
<tbody>
<tr>
<td>Total Recurrences</td>
<td>7</td>
<td>24</td>
</tr>
<tr>
<td>Vault</td>
<td>3 (43%)</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Pelvis</td>
<td>0 (0%)</td>
<td>7 (29%)</td>
</tr>
<tr>
<td>Abdomen</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Distant</td>
<td>1 (14%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Multiple</td>
<td>2 (29%)</td>
<td>7 (29%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (14%)</td>
<td>3 (13%)</td>
</tr>
</tbody>
</table>
What is new? Low Risk Early Stage Cervical Cancer

- Tumor diameter < 2 cm
- LVSI (-)
- Stromal invasion < 10 mm
- Negative lymph nodes

Parametrial involvement; 0.4-0.6%

Kinney et al., Covens et al., Wright et al., Frumovitz et al.
Simple Trachelectomy/ Conization with LND might be suitable

Low Risk Early Stage Cervical Cancer
Simple trachelectomy
# Oncological outcomes after fertility-sparing surgery for cervical cancer: a systematic review

*Enrica Bentivegna, Sebastien Gouy, Amandine Moulard, Cyrus Chargari, Alexandra Leary, Philippe Morice*

<table>
<thead>
<tr>
<th>Series and case reports</th>
<th>Simple tracheectomy or cone resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number series or case reports*</td>
<td>13</td>
</tr>
<tr>
<td>Number of patients</td>
<td>242</td>
</tr>
<tr>
<td>Patients excluded†</td>
<td>12</td>
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</table>

## Tumour characteristics

<table>
<thead>
<tr>
<th>Stage‡</th>
<th>Not Included</th>
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<tbody>
<tr>
<td>IA</td>
<td></td>
</tr>
<tr>
<td>IB1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>0</td>
</tr>
<tr>
<td>IB2</td>
<td>0</td>
</tr>
<tr>
<td>IIA</td>
<td>0</td>
</tr>
</tbody>
</table>

## Tumour type

- Squamous-cell carcinoma: 60
- Adenocarcinoma: 25
- Other, mixed, or unknown: 157
- LVSI positive: At least 71

## Oncological outcomes

- Recurrent disease: 4
- Died from disease: 0

## Fertility outcomes

- Pregnancies: 105
- Fetal loss (trimester 1 or 2): 15
- Preterm delivery: 13
- Pregnancy rate‡: 15/26 (57%)
Review

Management of low-risk early-stage cervical cancer: Should conization, simple trachelectomy, or simple hysterectomy replace radical surgery as the new standard of care?

Pedro T. Ramirez a,⁎, Rene Pareja b, Gabriel J. Rendón b, Carlos Millan c, Michael Frumovitz a, Kathleen M. Schmeler a

a Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA
b Department of Gynecologic Oncology, Instituto de Cancerología Las Américas, Medellín, Colombia
c Department of Gynecology, Hospital Quiron, Murcia, Spain
Individualized Conservative Approach in Low risk Early CC

Patient and tumor characteristics from published studies of conservative surgical treatment for early-stage cervical cancer.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>N</th>
<th>Median age (range), y</th>
<th>Histology</th>
<th>Stage</th>
<th>LVSI</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>SCC</td>
<td>AC</td>
<td>Other</td>
<td>IA1 + LVSI</td>
</tr>
<tr>
<td>Rob [13]</td>
<td>40</td>
<td>28.3°</td>
<td>32</td>
<td>7</td>
<td>1 adsq</td>
<td>3</td>
</tr>
<tr>
<td>Pluta [14]</td>
<td>60</td>
<td>44.6 (33–64)</td>
<td>50</td>
<td>10</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Maneo [15]</td>
<td>36</td>
<td>31 (24–40)</td>
<td>24</td>
<td>12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fagotti [16]</td>
<td>17</td>
<td>33 (30–43)</td>
<td>12</td>
<td>4</td>
<td>1 glassy</td>
<td>0</td>
</tr>
<tr>
<td>Palaia [17]</td>
<td>14</td>
<td>32 (28–37)</td>
<td>11</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Raju [18]</td>
<td>15</td>
<td>28 (20–40)</td>
<td>9</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Biliatis [19]</td>
<td>62</td>
<td>35 (27–67)</td>
<td>49</td>
<td>11</td>
<td>2 adsq</td>
<td>0</td>
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<tr>
<td>Plante [20]</td>
<td>16</td>
<td>30 (22–44)</td>
<td>10</td>
<td>6</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>260</td>
<td></td>
<td>197</td>
<td>59</td>
<td>4 (1.7%)</td>
<td>10 (3.8%)</td>
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Individualized Conservative Approach in Low Risk Early CC

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>No. of planned surgeries</th>
<th>Sentinel lymph node biopsy</th>
<th>Radical hysterectomy</th>
<th>Less radical procedures</th>
<th>Positive lymph nodes</th>
<th>Adjuvant radiotherapy</th>
<th>Adjuvant chemotherapy</th>
<th>Follow-up time median (range) months</th>
<th>Relapses</th>
<th>Deaths</th>
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<tbody>
<tr>
<td>Rob [13]</td>
<td>40</td>
<td>Yes</td>
<td>6</td>
<td>Cone biopsy + PLND = 10</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>47 (12–102)</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Pluta [14]</td>
<td>60</td>
<td>Yes</td>
<td>3</td>
<td>TH + PLND = 57</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>47 (12–92)</td>
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<td>0</td>
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<tr>
<td>Maneo [15]</td>
<td>37</td>
<td>No</td>
<td>N/A</td>
<td>Cone biopsy + PLND = 36</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>66 (18–168)</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Fagotti [16]</td>
<td>17</td>
<td>No</td>
<td>4</td>
<td>Cone biopsy + PLND = 13</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>16 (8–101)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Palaia [17]</td>
<td>14</td>
<td>No</td>
<td>0</td>
<td>Simple trach + PLND = 14</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>38 (18–96)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Raju [18]</td>
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<td>No</td>
<td>0</td>
<td>Simple trach + PLND = 15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>96 (12–120)</td>
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<tr>
<td>Biliatis [19]</td>
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<td>No</td>
<td>0</td>
<td>Cone biopsy + PLND = 35</td>
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<td>0</td>
<td>0</td>
<td>56 (13–132)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>TH + PLND = 27</td>
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<td></td>
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<td>27 (1–65)</td>
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<tr>
<td>Plante [20]</td>
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<td>Simple trach + PLND = 16</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>27 (1–65)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Total</td>
<td>261</td>
<td>13</td>
<td>247</td>
<td></td>
<td>13</td>
<td>5</td>
<td>2</td>
<td></td>
<td>2</td>
<td>1</td>
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</table>
# Pregnancy Results

Obstetrical outcomes in published studies of conservative surgical treatment for early-stage cervical cancer.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Planned surgeries</th>
<th>Less radical surgery</th>
<th>Attempting to conceive</th>
<th>Became pregnant</th>
<th>Number of pregnancies</th>
<th>Miscarriages</th>
<th>Deliveries</th>
<th>Patients pregnant at time of report</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rob [13]</td>
<td>40</td>
<td>34</td>
<td>24/32 (75%)</td>
<td>17</td>
<td>23</td>
<td>5</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Maneo [15]</td>
<td>37</td>
<td>36</td>
<td>NR</td>
<td>17</td>
<td>21</td>
<td>5</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Fagotti [16]</td>
<td>17</td>
<td>13</td>
<td>5/13 (38%)</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Palaia [17]</td>
<td>14</td>
<td>14</td>
<td>NR</td>
<td>8</td>
<td>8</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Raju [18]</td>
<td>15</td>
<td>15</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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<tr>
<td>Total</td>
<td>174</td>
<td>163</td>
<td>--</td>
<td>56</td>
<td>73</td>
<td>10</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

\(^a\) Numbers in bold represent the total number of surgeries and attempts.
Low Risk Early Stage Cervical Cancer

• 3 PRT IS GOING ON

✓ Schmeler et al. ConCerv trial

✓ Plante M. The SHAPE trial.

➢ Covens A. GOG Protocol 278.
Neoadjuvant CT

- Neoadjuvant CT can be used to decrease the tumor volume in patients with tumor greater than 2 cm
- But oncologic safety of neoadjuvant must be investigated further
Unresolved issues

➢ Staging LN dissection prior to NACT?
➢ Simple vs radical trachelectomy post NACT?
➢ What is best chemotherapy regimen?
Stage IB1 (2-4 cm) Cervical cancer treated with Neoadjuvant chemotherapy followed by fertility Sparing Surgery (CoNteSSa)

Marie Plante (CCTG)
Trachelectomy: The Future?

- Simple Trachelectomy / Cone
  - < 2 cm
  - > 2 cm

- NACT + Simple Trachelectomy / Cone

- Radical Trachelectomy

2-3 cm
Conclusion

Change FIGO classification?

Sub-divide stage IB1

- a: < 2 cm

- b: ≥ 2 cm
  < 4 cm
Ovarian Transposition
Kime Yapalım?

• Erişkinlerde
  – Anal
  – Rektal
  – Serviks

• Çocuklarda
  – Hodgkin – Non-Hodgkin lenfoma
  – Vajinal ve Uterin tm.
  – Ewing sarkom
  – Spinal tm.
# Ovarian Transposition

<table>
<thead>
<tr>
<th></th>
<th>Surgery Only</th>
<th>Surgery+BRT</th>
<th>Surgery+BRT+EBRT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ovarian Function</strong></td>
<td>94%</td>
<td>90%</td>
<td>65%</td>
</tr>
<tr>
<td><strong>Cyst formation</strong></td>
<td>13%</td>
<td>16%</td>
<td>5%</td>
</tr>
<tr>
<td><strong>Metastases</strong></td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
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Gubbala et al J Ovarian Research 2014, 7:69
Oncofertility in Endometrial Cancer

8% of endometrial cancer

≤ 45 years

Up to 25% PCOS
Oncofertility in EC

Partial preservation of fertility

Hysterectomy
At least one ovary preserved
Surrogacy

Total preservation of fertility

Uterus and ovaries preserved
High dose Progesterone

W.-L. Lee et al. / Taiwanese Journal of Obstetrics & Gynecology 51 (2012) 495e505
Ovarian preservation is safe?

N=495

Ovarian preservation: 176
10-y overall survival
94.5% ovarian preservation
91.3% BSO
Oncofertility in Endometrial Cancer

Inclusion Criteria

- Fertility desire
- Endometrioid Carcinoma (Type 1)
- G1
- Presence of PgR
- Normal serum levels of CA 125 (<35 u/mL) and CEA (< 5 ng/mL)
- Absence of synchronous Lynch II syndrome and ovarian cancer
- Absence of MI or extrauterine spread (by vaginal USG, MRI, PET-CT)
Progestogenic Agents

- MPA 200-600 /mg/d
- Megace 80-160 /mg/d
- IUD / Prog

**Response Rate**
- Hyperplasia with Atypia: 83-94%
- End. Ca: 57-75.6%

**Duration of Treatment**
- Range: 3-6 months
- Median: 9 months

**Recurrence**
- Hyperplasia with Atypia: 13%
- End. Ca: 11-50%
Oncofertility in Endometrial Cancer

- Repeated D&C; hysteroscopy (+tubal blockage?), transvaginal USG in every three months
- No residual disease
- Assisted reproduction
- Elective hysterectomy when the patient no longer desires to maintain fertility?
Oncofertility in Endometrial Cancer

- # 133 (1966-2007)
- Treatment
  - MPA 200-600 mg/d
  - Megestrol acetate 160 mg/d
  - LNG RIA
- Mean response time 12 week
- CR 76%
- Pregnancy rate: 28%

Chiva L, Gynecol Oncol, 2008
A Turkish Gynecologic Oncology Group study of fertility-sparing treatment for early-stage endometrial cancer

Polat Dursun a,*, Serkan Erkanli a, Ahmet Barış Güzel b, Murat Gultekin a, Nefise Cagla Tarhan a, Ozden Altundag a, Fuat Demirkiran c, Tugbo Beşe c, Yusuf Yildirim d, Gurkan Bozdag e, Hakan Yarali e, Tayyup Simsek f, Bulent Ozcelik g, Furat Ortaç h, Salih Taskin h, Tevfik Guvenal i, Nejat Ozgul j, Ali Haberal a, M. Ali Vardar b, Murat Dede i,k, Mufit Yenen i,k, Aytekin Altintas b, Macit Arvas c, Ali Ayhan a

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Oncofertility in Endometrial Cancer

Turkish Gyn.Oncology Group Experience

- 11 oncologic center (43 cases)
- Mean treatment time: 5 mo, mean follow-up: 49 mo.
- Response rate: 81.4%
- Pregnancy interval: 3-18 mo.
- Recurrence: 2 (4.6%)
- Pregnancy: 13 (41.9%)
Work-up for fertility preserving therapy

- Patients with **AH/EIN or grade 1 endometrioid endometrial cancer** requesting fertility preserving therapy must be referred to **specialised centres**
  - LoE: 5 - GoR: A - Consensus: 100% yes (37 voters)

- **D&C with or without hysteroscopy**
  - LoE: 4 - GoR: A - Consensus: 97.3% (36) yes, 2.7% (1) abstain (37 voters)

- **AH/EIN or grade 1 endometrioid endometrial cancer** must be confirmed/diagnosed by a **specialist gynecopathologist**
  - LoE: 4 - GoR: A - Consensus: 100% yes (37 voters)

- **Pelvic MRI** to exclude overt myometrial invasion and adnexal involvement. **Expert ultrasound** can be considered as an alternative
  - LoE: 3 - GoR: B - Consensus: 100% yes (37 voters)
Management schemes for fertility preserving therapy - 1

- MPA (400-600 mg/day) or MA (160-320 mg/day) is recommended.
  - However, treatment with LNG-IUD with or without GnRH-analogues can also be considered
  LoE: 4 - GoR: B - Consensus: 100% yes (37 voters)

- **Assessment response**: D&C, hysteroscopy and imaging at 6 months
  - No response after 6 months -> standard surgical treatment
  LoE: 4 - GoR: B - Consensus: 100% yes (37 voters)

- In case of complete response, conception must be encouraged and referral to a fertility clinic is recommended
Management schemes for fertility preserving therapy - 2

- Responders who wish to delay pregnancy: maintenance treatment
  LoE: 4 - GoR: B - Consensus: 100% yes (37 voters)

- Patients not undergoing hysterectomy should be re-evaluated clinically every 6 months
  LoE: 4 - GoR: B - Consensus: 97.3% (36) yes, 2.7% (1) abstain (37 voters)

- After completion of childbearing
  - HT & BSO
  - Preservation of the ovaries can be considered depending on age and genetic risk factors
  LoE: 4 - GoR: B - Consensus: 100% yes (37 voters)
Fertility Preservation in Ovarian Malignancies
Fertility Sparing Surgery in EOC

- 3-17% of EOC<40yo

- **Optimal Staging is essential** (Upstaged 30%)
  
  Wedge resection of the contralateral ovary is not recommended (if macroscopically normal)

- Endometrial biopsy is performed to exclude EC
Invasive Epithelial Ovarian Cancer

Desire for fertility

Endometrial biopsy

Optimal Staging

FROZEN

Stage Ia
G1
No further treatment

Stage Ia
G2(?)
G3
Clear cell
Stage Ic
Chemotherapy

Stage II-III
Selected cases
Requested by patients herself
Preliminary reports.
Patients with stages IA, IB, IC, and >II disease had 5-year DFS rates of 83%, 100%, 78%, and 33%, respectively (p=0.0396), and 5-year OS rates of 91%, 100%, 88%, and 33%, respectively (p=0.0014).
results suggest that laparoscopic comprehensive surgical staging of EOC is as safe and adequate as the standard surgical staging performed via laparotomy.

Abstract

Objective. To compare the results of laparoscopic staging of apparent early ovarian cancer (EOC) with those obtained with comprehensive surgical staging via laparotomy.

Methods. Consecutive patients undergoing comprehensive laparoscopic staging for presumed EOC (LPS group; N = 15) were compared with historical controls selected from consecutive women who have had conventional staging with open surgery (LPT group; N = 19).

Results. No difference was found in demographics and preoperative variables between the two groups. There were no significant differences between the two groups with regard to median number of lymph nodes and likelihood of identifying metastatic disease. No conversion to laparotomy and no intraoperative complication occurred in the LPS group. Operative time was significantly longer in the LPS group when compared with the LPT group (377 ± 47 vs. 272 ± 81 min, P = 0.002). One patient in the LPS group had a retroperitoneal haematoma recognized in the postoperative period, and this required laparotomy and ligature of the hypogastric arteries to achieve haemostasis. Minor postoperative complications occurred in 1 (6.7%) patient in the LPS group and in 8 (42.1%) patients in the LPT group (P = 0.047). Hospital stay was significantly shorter in the LPS group [3 (2–12) vs. 7 (4–14) days, P = 0.001]. Median (range) follow-up time was 16 (4–33) and 60 (32–108) months in the LPS and LPT group, respectively. Eleven (73.3%) patients in the LPS group and 13 (68.4%) in the LPT group received adjuvant treatment. There were no recurrences in the LPS group whereas 4 (7.1%) recurrences occurred in the LPT group. Overall survival was 100% in both groups.

Conclusion. Our results suggest that laparoscopic comprehensive surgical staging of EOC is as safe and adequate as the standard surgical staging performed via laparotomy.
Effect of Laparoscopy on survival

- Early stage EOC (n:289)
  - LS (n:131)
  - LT (n:139)
  - LS/LT (n:19)

Mean Survival
- LS 41.1 mo.
- LT 38.8 mo. (ns)

Abu-Rustum NR, Gynecol Oncol 2003

![Graph showing overall survival of patients with stage III-IV ovarian/peritoneal cancer from time of positive second-look operation.](image)
Fertility Sparing Surgery in Epithelial Ovarian Cancer

CONCLUSIONS

• Fertility sparing surgery in patients with Stage 1a,1c EOC

• For more advanced stages, additional investigation is needed

• After completion of fertility, residual ovary should be taken out because of

✓ High recurrence rate
✓ Screening method are unreliable.
Germ Cell Tumors (GCT)

- Mostly seen in children and young women
  - 5% of ovarian tumors in women <20 years old

- 50-70% are Stage I and unilateral

- Improvement of prognosis by modern combined chemotherapy in advanced stage (60-80% survival rates in advanced stages)

- Unilateral oophorectomy with optimal staging recommended (biopsy from the other ovary - controversial)

- 29/38 (79%) patients (stage I-III) achieved pregnancy
Conclusion

• Regardless of the stage, FSS is a safe and practicable procedure in the absence of involvement of CONTRALATERAL OVARY AND UTERUS
Borderline Epithelial Tumors

• Median age 39 (history of infertility [OR 1.9] or infertility treatment [OR 4.0])
• 5-year survival is 77-99%
• Cystectomy not recommended, affected ovary should be removed (high recurrence rate) except bilaterality
• Abdominal debulking is essential, lymphatic debulking?
• It is still unknown if later infertility treatment affects the natural progression of the disease.

Moric P, Eur J Cancer, 2005
As we discover what can be done, we need to learn what should be done.