Surgery in early stage cervical cancer

Ali Ayhan, MD
Baskent University School of Medicine
Department of Obstetrics and Gynecology
Division of Gynecologic Oncology
<table>
<thead>
<tr>
<th></th>
<th>Incidence (N/100,000)</th>
<th>Death (N/100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Worldwide</strong></td>
<td>527.624 (7)</td>
<td>265.653 (7,5)</td>
</tr>
<tr>
<td><strong>Developed countries</strong></td>
<td>83.078 (2,9)</td>
<td>35.495 (2,7)</td>
</tr>
<tr>
<td><strong>Developing countries</strong></td>
<td>444.546 (11,6)</td>
<td>230,158 (10,2)</td>
</tr>
<tr>
<td><strong>Turkey</strong></td>
<td>1686 (2,7)</td>
<td>663 (2)</td>
</tr>
</tbody>
</table>
GYN CANCERS within years

Data of Ministry of Health
GYN CANCERS within years

Data of Ministry of Health
The First 10 Women Cancers within years (MoH)

- Meme: 40.6
- Tiroid: 18.6
- Kolorektal: 13.4
- Uterus Korpusu: 9.3
- Trakea, Bronş, Akciğer: 8.1
- Mide: 8.1
- Over: 6.9
- Non-Hodgkin lenfoma: 5.3
- Beyin, sinir sistemi: 5.0
- Uterus Serviksi: 4.5
New Cases vs Mortality in Turkey

Cervix

- Globocan 2002: 1,363
- Globocan 2008: 1,443
- Globocan 2012: 1,686

Ovary

- Globocan 2002: 1,628
- Globocan 2008: 1,804
- Globocan 2012: 2,400

Corpus

- Globocan 2002: 1,391
- Globocan 2008: 1,937
- Globocan 2012: 3,787

Legend:
- Green: New cases
- Red: Mortality
Therapy depends on

• Age, performance
• Accurate diagnosis
• Dept of invasion, LVSI
• Fertility desire
• Stage
• Lenf Node status
Staging (2009)

Early stage:
- Ia1, Ia2, Ib1
- and IIa1

Advanced stage:
- Ib2, IIb2
- And others

Pecorelli S., Int J Gynecol Obstet, 2009
Stage 0
Pre-invasive Lesions
Treatment of Cervical Cancer

Primary Lesion

Potential Metastatic Fields
Standard treatment of early stage cervical cancer (Stage 1a-1b1-2a1)

Rad His
(Pivertype III, Querlue C2)

Lymphadenectomy
(sentinel or systemic)

Radical Rad thrp
Brachy, Tele

BSO ±
Ovary Transposition

Same survival
Different Complications

Conventional(abd/vaj)
endoscopic(robotic,L/S)
# Radical hysterectomy classifications

- **Type A**
- **Type B (B1-B2)**
- **Type C (C1-C2)**
- **Type D (D1-D2)**

<table>
<thead>
<tr>
<th>Type A</th>
<th>Type I (Extrafascial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type B (B1-B2)</td>
<td>Type II (Mod RH)</td>
</tr>
<tr>
<td>Type C (C1-C2)</td>
<td>Type III (RH)</td>
</tr>
<tr>
<td>Type D (D1-D2)</td>
<td>Type IV (RH)</td>
</tr>
<tr>
<td></td>
<td>Type V (RH)</td>
</tr>
</tbody>
</table>

- Piver et al (1974)
- Querleu-Morrow (2008)
- Cibula (2011)
Radical hyst/trachelectomy

Complete primary tumor control

But

Parametrial resection related

İnf. Hipogastric plx
(Symphatic and Parasymphatic)

• More complication
• Vasculary
• Urologic
• GIS
• Sexual
• Loss of fertility
New Approaches

- Minimally invasive surgery
- Sentinel node not standartized
- Nerve sparing surgery – less postoperative, vesical, rectal and sexual dysfunc
- Limitation of parametrial resection??
- Fertility sparing
Minimally invasive surgery

- Laparoscopic
- Robotic
- LESS

(Long term oncologic outcomes?)
<table>
<thead>
<tr>
<th></th>
<th>Robotic</th>
<th>L/S</th>
<th>Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recc. (%)</td>
<td>3.79</td>
<td>5.58</td>
<td>6.72</td>
</tr>
<tr>
<td>Follow up ( month )</td>
<td>21</td>
<td>34</td>
<td>58</td>
</tr>
<tr>
<td>LN number</td>
<td>26</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Post-op inf/ non-inf morbidity (%)</td>
<td>3,8/7,8</td>
<td>6.5/18,3</td>
<td>18.2/19,4</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>3</td>
<td>5,5</td>
<td>8,4</td>
</tr>
<tr>
<td>Blood need (%)</td>
<td>2</td>
<td>5</td>
<td>25</td>
</tr>
</tbody>
</table>
Recurrance rates are the same

<table>
<thead>
<tr>
<th>RH MLIID</th>
<th>No.</th>
<th>Minimum (%)</th>
<th>Median (%)</th>
<th>Maximum (%)</th>
<th>Mean (%)</th>
<th>Std. Deviation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open RH</td>
<td>9</td>
<td>0</td>
<td>17.85</td>
<td>6.72</td>
<td>5.43</td>
<td></td>
</tr>
<tr>
<td>Laparoscopic RH</td>
<td>17</td>
<td>0</td>
<td>2.8</td>
<td>17.39</td>
<td>5.58</td>
<td>6.85</td>
</tr>
<tr>
<td>Robotic RH</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>14.28</td>
<td>3.79</td>
<td>5.59</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>0</td>
<td>3.125</td>
<td>17.85</td>
<td>5.33</td>
<td>6.11</td>
</tr>
</tbody>
</table>

Descriptive statistics for follow-up in months

<table>
<thead>
<tr>
<th>Type of RH</th>
<th>No.</th>
<th>Minimum</th>
<th>Median</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open RH</td>
<td>13</td>
<td>15.2</td>
<td>41</td>
<td>300</td>
<td>58.0</td>
<td>74.9</td>
</tr>
<tr>
<td>Laparoscopic RH</td>
<td>18</td>
<td>7.2</td>
<td>30</td>
<td>78</td>
<td>34.1</td>
<td>18.7</td>
</tr>
<tr>
<td>Robotic RH</td>
<td>10</td>
<td>9.0</td>
<td>19</td>
<td>36</td>
<td>21.1</td>
<td>11.2</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>7.2</td>
<td>29</td>
<td>300</td>
<td>38.5</td>
<td>45.5</td>
</tr>
</tbody>
</table>
Endoscopic vs. conventional

- Less intraop Bleeding
- Less hospital stay
- Early discharge
- Quality of life
- Low morbidity (Magnification and technique advantage of endoscopic instruments)
- Same dissected lymph node number
- Same recurrance and survival

Salicru S, J Minim Invasive Gynecol, 2011
Lymphadenectomy

- Extend of tumor
- Prognosis
- Treatment (KT/RT/Komb)
- Adjuvant RT margines
- Direct threapautic effect (Bulky LN)

Early and Late term Morbidity

Lymphedema
Lymphocytct
Infection
Lymphadenectomy

• Number of dissected nodes are similar (open-endoscopic)  
  Salicru S et al, Invasive Gynecol, 2011

• Related to overall survival (SEER 5522 women)  
  Suprasert et al, Int J Gynecol Ostet, 2012

• Dissection of bulky lymph nodes have therapeutic benefits  
  Shah et al, Cancer, 2011
Sentinel Node
(lymphatic mapping)

- Dual technique
  (Techn- 99, Isosulfan blue)
- Sensitivity 98.2%
- Negative Predictive Value 99.6%

Not Yet standardised

Low risk Group (1a2-1b1)

- Tumor size
  - ≤2cm
- Dept of invasion
  - ≤ 10 mm
  - ≤ %50 stromal invasion
- LVSI negative
- LN negative
### Parametrial involvement in Low risk Group

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Parametrium %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kinney</td>
<td>95</td>
<td>0.0</td>
</tr>
<tr>
<td>Covens</td>
<td>02</td>
<td>0.6</td>
</tr>
<tr>
<td>Stegeman 07</td>
<td>103</td>
<td>0.0</td>
</tr>
<tr>
<td>Wright 08</td>
<td>270</td>
<td>0.4</td>
</tr>
<tr>
<td>Frumovitz 09</td>
<td>125</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Retrospective review of early stage adeno carcinoma

<table>
<thead>
<tr>
<th>Stg</th>
<th>N</th>
<th>R.surg</th>
<th>Paramth</th>
<th>Lymph node</th>
<th>Rec</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a1</td>
<td>337</td>
<td>194/337</td>
<td>0/190</td>
<td>2/209</td>
<td>3/306</td>
</tr>
<tr>
<td>1a2</td>
<td>118</td>
<td>85/118</td>
<td>0/72</td>
<td>0/90</td>
<td>1/117</td>
</tr>
<tr>
<td>1b1</td>
<td>105</td>
<td>91/105</td>
<td>1/91</td>
<td>1/99</td>
<td>6/105</td>
</tr>
</tbody>
</table>

Clare J et all Gynecol oncol 2013 in press
Surgical approaches in low risk group

CONE
Simple Hyst.
TRACHELECTOMY

LND,SND
<table>
<thead>
<tr>
<th></th>
<th>Squamous cell</th>
<th>Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>5 yS %</td>
</tr>
<tr>
<td><strong>Stage 1A1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyst</td>
<td>1143</td>
<td>95.6</td>
</tr>
<tr>
<td>Kon</td>
<td>467</td>
<td>95.1</td>
</tr>
<tr>
<td><strong>Stage 1A2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyst</td>
<td>1072</td>
<td>96.3</td>
</tr>
<tr>
<td>Kon</td>
<td>317</td>
<td>90.2</td>
</tr>
</tbody>
</table>

SEER DATA 1a1-1a2
Five year survival by histology, stage and treatment
Spoozak et al AJOG2012(206-
Simple vs. Rad. hysterectomy

1B1-2A ≤ 4 cm

n:125

Type 1
N:62

Type 3
N:63

• No differences between
• Pattern of recurrence
• Survival

In patients stage 1B-2A ≤ 3 cm

Landoni et all EJSO 38 2012 203-209
<table>
<thead>
<tr>
<th>Author</th>
<th>Number</th>
<th>Sentinel LN</th>
<th>Less Radical</th>
<th>Radical</th>
<th>Poz LN</th>
<th>M. Foll. up</th>
<th>Rec</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rob</td>
<td>40</td>
<td>yes</td>
<td>Cone+PLND:10 Simple trach+PLND:24</td>
<td>6</td>
<td>6</td>
<td>47</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pluta</td>
<td>60</td>
<td>yes</td>
<td>TH+PLND:57</td>
<td>3</td>
<td>5</td>
<td>47</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maneo</td>
<td>36</td>
<td>no</td>
<td>Cone+PLND:36</td>
<td>0</td>
<td>0</td>
<td>66</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fagotti</td>
<td>17</td>
<td>no</td>
<td>Cone+PLND:13</td>
<td>4</td>
<td>1</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Palaia</td>
<td>14</td>
<td>no</td>
<td>Simple Trach+PLND:14</td>
<td>0</td>
<td>0</td>
<td>38</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Raju</td>
<td>15</td>
<td>no</td>
<td>Simple Trach+PLND:15</td>
<td>0</td>
<td>0</td>
<td>96</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Biliatis</td>
<td>62</td>
<td>no</td>
<td>Cone+PLND:35 TH+PLND:27</td>
<td>0</td>
<td>0</td>
<td>56</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Plante</td>
<td>16</td>
<td>yes</td>
<td>Simple Trach+PLND:16</td>
<td>0</td>
<td>0</td>
<td>27</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>261</td>
<td>247</td>
<td>13</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FSS in ECC

- 40.1% of CC are <45yo (SEER data)
- 20.78% are <39yo (Cochrane-US and Europe)

Radical Trachelectomy
Open
Vaginal
Endoscopic
Indications of Trachelectomy

- Desire preserving fertility
- No fertility problems
- Ia1, Ia2
- Ib1
  - (<2cm, stromal invasion <50%,)
- Additional several variations (NACT..)
- Except neuroendocrine histology

Oncologic Outcome
Trachelectomy vs. RH

No difference between groups
– Recurrence rate
– PFS, OS
– Morbidity

Meta analysis (587 participants)

Diameter more than >2cm has a higher risk for oncologic outcome
A study with 618 pts
Rob L, Lancet Oncol, 2011
Obstetric Outcomes

- 10-13% are infertile
- VRT is more fertility saving than ART
- Misscarriage rate
  - 1st trimester 20%
  - 2nd trimester 3%
- 73% of pregnancies reached 3rd trimester
- Of which 75% delivered at term

Kim et al. Gynecol Oncol 2012
**IA**
(Micro-invasive cancer)

<table>
<thead>
<tr>
<th>IAI</th>
<th>MEASUREMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth 0-3mm</td>
<td></td>
</tr>
<tr>
<td>Horiz &lt;7mm</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth 3-5 mm</td>
</tr>
<tr>
<td>Horiz &lt;7mm</td>
</tr>
</tbody>
</table>

LVSI, does not alter FIGO stage!
IA1 LVSI (-)

CONE

- Tumor free border and negative ECC after cone
- Positive margin or positive ECC

RE-CONE
IA
(Micro-invasive cancer)

IAI LVSII (-)
Conization or Hysterectomy

IAI, LVSII (+)
Type II Hysterectomy + Pelvic LND
BSO optional*

ENDOSCOPE/VAGINAL/ABDOMINALE

0.5 % ovary met in SCC. (GOG)
AIS-IA1 Adeno Ca

Simple Hysterec-tomy

Cone * ECC Cone Apex

*Fertility Desire
Stage IB1 – IIA (Sq and AdenoCa)

Type III(C2) Hysterectomy

PPALND

BSO*

1B1 adeno ca(0-7 %) sq (0.05) ovary met. (GOG)
These studies about conservative surgery are retrospective,
There are new ongoing prospective randomised studies;
MD Anderson
Gyn Cancer Intergroup Study (SHAPE)
GOG 278 study
(there are some diff in including criterias)

Main Criterias; 1a1 + LVSI, 1a2, 1b1(size <2cm, depth<1cm, stromal inv<50%)
Shape Trial

Patient Population
- Stage IA2-IB1
- Squamous and Adenocarcinoma
- < 2 cm and < 50% SI or < 10 mm DOI
- Grade 1, 2 & 3

Randomization

Control Arm
Radical Hysterectomy & PLND +/- SLN Mapping*
- Positive Nodes
- Extrauterine Disease

Yes
- Treatment According to Local Protocol
  - Abandon Hysterectomy vs. Completion Hysterectomy
    - +/- Para-aortic LND

No
- Treatment According to Randomization

Experimental Arm
Simple Hysterectomy with PLND +/- SLN Mapping*
- Positive Nodes
- Extrauterine Disease

No
- Treatment According to Randomization

Yes

LVSI allowed

*Sentinel lymph node mapping optional, laparoscopic approach preferred
*SI: Stromal Invasion; DOI: Depth Of Invasion
<table>
<thead>
<tr>
<th>RH Related Complications</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss and transfusion</td>
<td>23</td>
</tr>
<tr>
<td>Voiding dysfunction</td>
<td>40-42</td>
</tr>
<tr>
<td>Bowel disfunction</td>
<td>9-18</td>
</tr>
<tr>
<td>Fecal or flatal incontiniance</td>
<td>33</td>
</tr>
<tr>
<td>Risk of fistula formation</td>
<td>1-6</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>3-19</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>19-36</td>
</tr>
<tr>
<td>Loss of fertility</td>
<td></td>
</tr>
</tbody>
</table>
Adjuvant RCT in ECC

- **Low Risk**
  (GOG score <40mm)

- **Intermediate**
  (GOG score 40-120mm)
  (LVSI+, DSI, diameter >4cm)

- **High Risk**
  (GOG score >120)
  (LN +, surgical margin<0,5mm, parametrial involvement)

GOG 49 Delgado et al., 1990
Outcomes (Bilek and GOG 92-2006)

Two studies Stage IB
N: 397
RH + PLND ± RT

No difference in OAS
Radical Surgery With Individualized Postoperative Radiation for Stage IB Cervical Cancer
Oncologic Outcomes and Severe Complications

Samith Sandadi, MD, M.Sc.,* Edward J. Tanner, MD,* Fady Khoury-Collado, MD,* Alessandra Kostolias, MD,* Vicky Makker, MD,†§ Dennis S. Chi, MD,*§ Yukio Sonoda, MD,*§ Kaled M. Alektiar, MD,‡ Richard R. Barakat, MD,*§ and Nadeem R. Abu-Rustum, MD*§

n: 222 (IB1/IB2)  RH(158) , RTr(64)

69 RT other NT

Toxicity  12% vs 32%
5y PFS  93% vs 90%
5y OAS  96% vs 91%

International Journal of GYN Cancer 2013, 23, 553-558
n: 2,268 patients
RH + PLND ± RT or CT

OS: 86.5%
DFS: 84.5%

1010 CT
OS: 82.8%
DFS: 81.4%

1258 RT

Recurrence
| 14.3% | 22.4% |
| Local Rc | 9.7% | 14% |
| Distance Rc | 7.7% | 11% |

stage IB the 5-year OS and DFS rates were significantly higher in the CT group.
### Stage vs Survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>At initial diagnosis</th>
<th>5 year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized Stage</td>
<td>49 %</td>
<td>91,2 %</td>
</tr>
<tr>
<td>Regional LN or beyond primary</td>
<td>35 %</td>
<td>57,8 %</td>
</tr>
<tr>
<td>Distant Met.</td>
<td>11 %</td>
<td>17,0 %</td>
</tr>
<tr>
<td>Unknown (Unstaged)</td>
<td>5 %</td>
<td>58,1 %</td>
</tr>
</tbody>
</table>

#### TURKEY DATA

Survival 42,5 mts

- **Lokalize**: 52,1%
- **Bölgesel**: 37,3%
- **Uzak yayılım**: 10,6%
Cervical Cancer

Primary Prevention
- Stop smoking
- Barrier Contraceptives
- Monogamy
- Diatery (Folic, VitB, Caroten etc)
- Vaccination

Secondary Prevention
Screening
Conclusion-I

- Conservative surgery in selected patients

- Fertility sparing surgery

- Nerve sparing surgery decreases the complications while increasing the quality of life
Conclusion-II

- Sentinel lymph node dissection is getting popular but is not standardized yet
- Parametrial resection should be limited in low risk early stage CC patients
TEŞEKKÜRLER