Minimally Invasive Gynecologic Surgery: Laparoscopic Treatment of the Pelvic Mass

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Conflicts of Interest

• I have no conflicts of interest relevant to this talk
• Other relationships
  - Alexion - consulting
  - Merck - consulting/research
  - Novocure - consulting
  - Biodesix - consulting
  - Genentech - consulting/speaker’s bureau
  - Clovis - consulting
  - Janssen - consulting
Objectives

• Ovarian cancer screening
• Risk reducing surgery
• What masses are appropriate for laparoscopy
• Risk of spillage
• Which masses can be safely removed with stroma sparing techniques versus oophorectomy
• Techniques for removal
  — Laparoscopic bags
  — Hand assisted ports

“Life is short, the art long, opportunity fleeting, experiment treacherous, judgment difficult.”

- Hippocrates
Ovarian Cancer and Age


United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS)

- Goal was to develop an acceptable Screening algorithm with minimal surgical complications
  - NORMAL risk women
- Trial run from April 2001 through September 2005
- Very large trial
  - 1,243,282 screened
  - 202,638 randomized
- Randomized to three arms
  - Control Group
  - Ultrasound only
  - Multimodal Screening

Jacobs IJ, Lancet 387:945, 2016
Patterns of Ca-125

Skates SJ, J Clin Oncol 21:206s, 2003

Stage Migration from Multimodal Screening

Stage I  Stage II  Stage IIIa

Jacobs IJ, Lancet 387:945, 2016
Multimodal Screening Mortality Compared to Control

Mortality reduction: 0 – 7 years 8% (-27, 43)
Mortality reduction: 7 – 14 years 28% (-3, 49)

Based on the FDA’s review of available clinical data from ovarian cancer screening trials and recommendations from healthcare professional societies and the U.S. Preventive Services Task Force, available data do not demonstrate that currently available ovarian cancer screening tests are accurate and reliable in screening asymptomatic women for early ovarian cancer.

http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm519413.htm
Model versus prediction
Start age = 61, 9 screens, 14 years follow-up

Actual Mortality Difference = 11%
Predicted Mortality Difference = 10%

Naumann RW, unpublished

Screening model

• Markov model based on stage shift seen in UKCTOCS trial
• Model accurately predicted mortality from ovarian cancer
• Adjusted for different stages seen in screening
• Looked at screening starting at age 50
  - Overall 5% reduction in ovarian cancer mortality
    • could prevent 51 deaths per 100,000 women screened for 20 yr
  - Not cost effective
    • Screening costs alone would be greater than $650,000/life yr

Naumann RW, unpublished
The Origin of Ovarian Cancer

Reactive Oxygen Species are Indispensable in Ovulation

- Ovulation involves ROS
  - LH stimulation is pro-inflammatory
- ROS may activate EGFR
  - inhibition of EGFR-specific phosphatases
- MAPK phosphorylation and activation of MEK signaling

Mechanism for Transformation

Precursor in fallopian tube

Genotoxic stress increases risk with DNA repair deficiency also explains tumor heterogeneity

Tubal (retrograde flow)

Ovulatory cycles increases genotoxic stress

Tubal intraluminal and invasive carcinomas
- Escape from cell cycle arrest
- BRCA mutations/CDH
- Dedifferentiation

\( \gamma S3 \) alpinum
- DNA damage
- TP53 mutations

Ruptured follicle
- Inflammatory mediators
- Hormone-rich milieu

Transformation of CSE-derived CECs
- Metaplasia to Müllerian epithelium
- Borderline tumors
- Low-grade carcinoma

Is the Fallopian Tube to Blame?

Progression to High Grade (Type II) Ovarian Cancer

Salpingectomy: Post Reproduction

- Most effective tubal sterilization\(^5\)
- No negative impact on ovarian function\(^2\)
- Can reduce incidence of:
  - Serous cancer\(^3\)
  - Surgery for tubal disease 8% after TL\(^4\)

   - Seidhoff et al, JMIG, 2013
   - Lessard-Anderson et al, SGO, 2013
   - Morse et al, AJOG, 2002
Swedish Cancer Registry Data

- Compared 251,000 women after Gyn procedures to 5.5 million women between 1973 and 2009
  - Included women after
    - Hysterectomy (n = 98,026)
    - Hysterectomy and BSO (n = 37,348)
    - Tubal ligation (n = 81,658)
    - Unilateral Salpingectomy (n = 472,263)
    - Bilateral Salpingectomy (n = 70,566)
  - Did not include women
    - Hysterectomy and salpingectomy (n = 2,646)

- Registry captures 99% of cancers and 95% cause of death


![RR of Ovarian Cancer](image-url)

SGO Clinical Practice Statement: Salpingectomy for Ovarian Cancer Prevention

November 2013
Salpingectomy may be appropriate and feasible as a strategy for ovarian cancer risk reduction.

In summary, women who have BRCA1 or BRCA2 germline mutations should be counseled regarding bilateral salpingo-ooophorectomy, after completion of childbearing, as the best strategy for reducing their risk of developing ovarian cancer. In the event that these women opt to delay or forego risk-reducing bilateral salpingo-ooophorectomy, they should be counseled regarding risk-reducing salpingectomy when childbearing is complete followed by oophorectomy in the future, although the safety of this approach has not been studied.

BRCA1 Carriers

<table>
<thead>
<tr>
<th>Age at Oophorectomy (years)</th>
<th>No. of Cancers</th>
<th>No. of Patients</th>
<th>Prevalence of Cancer (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-34</td>
<td>1</td>
<td>42</td>
<td>2.33</td>
</tr>
<tr>
<td>35-39</td>
<td>2</td>
<td>160</td>
<td>1.25</td>
</tr>
<tr>
<td>40-44</td>
<td>10</td>
<td>261</td>
<td>3.03</td>
</tr>
<tr>
<td>45-49</td>
<td>9</td>
<td>241</td>
<td>3.73</td>
</tr>
<tr>
<td>50-54</td>
<td>12</td>
<td>172</td>
<td>6.99</td>
</tr>
<tr>
<td>55-59</td>
<td>5</td>
<td>98</td>
<td>5.10</td>
</tr>
<tr>
<td>60-64</td>
<td>5</td>
<td>42</td>
<td>11.9</td>
</tr>
<tr>
<td>65-69</td>
<td>0</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>≥ 70</td>
<td>0</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>1,067</td>
<td>4.18</td>
</tr>
</tbody>
</table>

Fitch APM, J Clin Oncol, 32:1, 2014
BRCA2 Carriers

<table>
<thead>
<tr>
<th>Age at Oophorectomy (years)</th>
<th>No. of Cancers</th>
<th>No. of Patients</th>
<th>Prevalence of Cancer (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-34</td>
<td>0</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>35-39</td>
<td>0</td>
<td>31</td>
<td>0</td>
</tr>
<tr>
<td>40-44</td>
<td>0</td>
<td>55</td>
<td>0</td>
</tr>
<tr>
<td>45-49</td>
<td>0</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>50-54</td>
<td>0</td>
<td>57</td>
<td>0</td>
</tr>
<tr>
<td>55-59</td>
<td>0</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>60-64</td>
<td>1</td>
<td>99</td>
<td>1.23</td>
</tr>
<tr>
<td>65-69</td>
<td>1</td>
<td>11</td>
<td>9.09</td>
</tr>
<tr>
<td>≥ 70</td>
<td>0</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>333</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Finch APM, J Clin Oncol, 32:1, 2014

Surgery for Risk Reduction

- Skeletonize the ovarian vessels for complete removal
  - open the retroperitoneal space!!
- Inspect peritoneal surfaces and biopsy anything suspicious
- Peritoneal washings
- Identify patient as high risk to pathology
  - step section of entire fallopian tube
- Remove the adnexa in a bag to preserve epithelium
- There is a chance of finding cancer at the time of surgery - particularly in older women with BRCA1
- May still be at risk for peritoneal cancer (RR = 0.04-0.2)
Management of a Pelvic Mass

ACOG/SGO Referral Guidelines

ACOG PRACTICE BULLETIN
CLINICAL MANAGEMENT GUIDELINES FOR
OBSTETRICIANS-GYNECOLOGISTS
NUMBER 83, JULY 2007

Management of Adnexal Masses
When do you Refer a Patient to a Gynecologic Oncologist?

- When the risk of malignancy exceeds the 5-10% range
- When you do not feel confident that you can remove the mass without abdominal spillage if there is any risk of malignancy
- When you are likely to encounter difficult surgical conditions that might make you open
  - Multiple medical problems
  - Multiple previous surgeries
Work-up for a Pelvic Mass
ACOG/SGO Referral Guidelines

• Evaluation of Pelvic Mass
  - Obtain Ca-125 and CEA
  - Other tumor markers when appropriate
    › AFP, bHCG, inhibin
• Transvaginal ultrasound is the most cost effect test in evaluation of pelvic mass
• Routine CT scan or MRI NOT indicated except in the cases where malignancy is being evaluated

ACOG/SGO Referral Guidelines for a Pelvic Mass

• Premenopausal
  — Ca-125 >200 Markedly elevated
  — Ascites
  — Evidence of abdominal or distant metastasis
  — Family history of breast or ovarian cancer (1st degree relative)
• Postmenopausal
  — Same as Premenopausal with ANY elevation of Ca-125
  — Nodular or fixed mass
• Perimenarchal with elevated tumor markers
Validation of ACOG Guidelines at a Single Institution

- Reviewed 837 patients at Mayo Clinic
  - 20% (48/240) Premenopausal with Cancer
  - 44% (263/597) Postmenopausal with Cancer

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>Early - 56%</td>
<td>40%</td>
<td>92%</td>
</tr>
<tr>
<td></td>
<td>Late - 92%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>Early - 80%</td>
<td>60%</td>
<td>93%</td>
</tr>
<tr>
<td></td>
<td>Late - 98%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dearking AC, Obstet Gynecol 110:841, 2007

U/S Morphology Index

DePriest PD, Gynecol Oncol 55(2):174, 1994
Kentucky Morphology Index

Statistical Performance of the Morphology Index Score Using a Value of ≥5 as Indicative of Malignancy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.89</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.73</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.46</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>0.96</td>
</tr>
</tbody>
</table>

DePriest PD, Gynecol Oncol 55(2):174, 1994
Observation can be justified in an asymptomatic woman with a normal Ca-125 in the absence of transvaginal ultrasound findings suspicious for cancer.

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Proportion of Borderline and Ovarian Malignancy presenting as Simple (Unilocular) Cysts

<table>
<thead>
<tr>
<th></th>
<th>Borderline</th>
<th>Ovarian Ca</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacoustos</td>
<td>3/33</td>
<td>0/82</td>
<td>3/115</td>
</tr>
<tr>
<td>Fruscella</td>
<td>4/113</td>
<td>0/0</td>
<td>4/113</td>
</tr>
<tr>
<td>Valentin</td>
<td>0/1</td>
<td>0/27</td>
<td>0/28</td>
</tr>
<tr>
<td>Gramellini</td>
<td>0/5</td>
<td>0/15</td>
<td>0/20</td>
</tr>
<tr>
<td>Valentin</td>
<td>0/5</td>
<td>0/19</td>
<td>0/24</td>
</tr>
<tr>
<td>Hata</td>
<td>0/9</td>
<td>0/42</td>
<td>0/51</td>
</tr>
<tr>
<td>Jokubkiene</td>
<td>0/6</td>
<td>0/21</td>
<td>0/27</td>
</tr>
<tr>
<td>Granberg</td>
<td>-</td>
<td>-</td>
<td>0/39</td>
</tr>
<tr>
<td>Valentin</td>
<td>5/186</td>
<td>6/764</td>
<td>7/417</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>12/358 (3.4%)</td>
<td>6/970 (0.6%)</td>
<td>18/1367 (1.3%)</td>
</tr>
</tbody>
</table>
Unilateral Cysts in Post-Menopausal Women

- UK screened 15,106 women > 50 yo
  - 18% developed unilateral cysts
- Ovarian Cancer
  - 0.8% developed cancer
  - All had changes in cyst at the time of diagnosis
- F/U not standard
  - Some recommend stopping f/u after 1 year if no solid components and 2 years with solid components (no data - long term f/u unknown)

Management of Ovarian Torsion

- If fertility preservation is the goal reduction of torsion with cystectomy should be performed
- In most cases, the residual ovary will regain perfusion and remain viable
- Despite evidence of necrosis and ischemia at the time of surgical exploration, ovarian function will be preserved in 90% of cases
- Ovarian fixation is controversial, but may be considered, especially if torsion is recurrent
New Tumor Markers

Markers to Predict Ovarian Cancer

| Table 1. Serum Biomarker and Multimodal Test Results Considered Abnormal in Women With Adnexal Masses* |
|---|---|---|
| Test | Premenopausal | Postmenopausal |
| CA 125 | — | > 35 U/mL |
| MIA | ≥ 5.0 | ≥ 4.4 |
| ROMA | ≥ 1.31 | ≥ 2.77 |
| RMI | > 200 | > 200 |

FDA Approved for triage prior to surgery

Abbreviations: CA, cancer antigen; MIA, multivariate index assay; ROMA, Risk of Ovarian Malignancy Algorithm; RMI, risk of malignancy index.

ACOG Practice bulletin #174, November, 2016
Ca-125

- Antigen derived from coelomic and mullerian epithelium
- Normal < 35 U/ml
- Expressed in 80% of non-mucinous epithelial cancers
  - less often expressed in clear cell or mucinous cancer
  - Only 50% of patients with stage I ovarian cancer will have an elevated level
- FDA approved from treatment monitoring but not preoperative evaluation or screening
  - often false positive elevation

Tumor Markers for Pelvic Mass

<table>
<thead>
<tr>
<th>Tumor marker</th>
<th>Benign disease</th>
<th>Ovarian cancer</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HE4 (pM)</td>
<td>50 (40)</td>
<td>544 (231)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SMRP (nM)</td>
<td>0.3 (0.6)</td>
<td>4.6 (1.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CA125 (U/ml)</td>
<td>67 (1.4)</td>
<td>645 (264)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CA125-4 (U/ml)</td>
<td>3.5 (1.5)</td>
<td>33.0 (1.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Uterine SMRP (nM)</td>
<td>0.6 (0.1)</td>
<td>2.3 (0.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Uterine CA125 (U/ml)</td>
<td>5.8 (2.4)</td>
<td>8.7 (4.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Activin (ng/ml)</td>
<td>0.7 (0.5)</td>
<td>1.1 (1.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inhibin (ng/ml)</td>
<td>45 (26)</td>
<td>25 (8)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Osteopontin (ng/ml)</td>
<td>96 (37)</td>
<td>97 (24)</td>
<td>0.0004</td>
</tr>
<tr>
<td>EGFR²</td>
<td>5 (33)</td>
<td>40 (36)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Her2²</td>
<td>7.7 (7.3)</td>
<td>7.3 (7.3)</td>
<td>0.1913</td>
</tr>
</tbody>
</table>

Moore RG, Gynecol Oncol 108:402, 2007
HE4

- Antigen derived from Human Epididymis Protein
- Product of the WFDC2 (HE4) gene which is over expressed in ovarian cancer
  - 93% serous
  - 100% endometrioid
  - 50% clear cell
- Normal ≤ 150 pM
- FDA approval for monitoring cancer treatment
  - FDA approved algorithm for pre-operative evaluation or screening in 2011

Dapkin R, Cancer Res 65:2162, 2005

Logistic Regression Algorithm

- Pooled data from two Pilot Studies
- CA 125I derived using Abbott ARCHITECT
- CA 125I measured directly on WIHRI samples, but imputed for Boston samples
- Final algorithm

$P = \phi (Z_1 I + \gamma_3 \log(HE4) + 0.98725 \log(CA125))$

$P = \phi (Z_1 I + 1.08 \log(HE4) + 0.732 \log(CA125))$

$PP = \exp(P) / (1 + \exp(P))$
Stratification of Patients with Pelvic Mass using a Logistic Regression Algorithm

Post-menopausal women only

<table>
<thead>
<tr>
<th>Disease</th>
<th>Low Risk (N)</th>
<th>High Risk (N)</th>
<th>All (N)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>138</td>
<td>46</td>
<td>184</td>
<td>94.2%</td>
<td>75.0%</td>
<td>95.2%</td>
</tr>
<tr>
<td>EOC+LMP</td>
<td>7</td>
<td>113</td>
<td>120</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>159</td>
<td>304</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Stratification of Patients with Pelvic Mass using a Logistic Regression Algorithm

Pre-Menopausal Women

<table>
<thead>
<tr>
<th>Disease</th>
<th>Low Risk (N)</th>
<th>High Risk (N)</th>
<th>All (N)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>122</td>
<td>41</td>
<td>163</td>
<td>75.9%</td>
<td>74.8%</td>
<td>94.6%</td>
</tr>
<tr>
<td>EOC + LMP</td>
<td>7</td>
<td>22</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>129</td>
<td>63</td>
<td>192</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
OVA-1

• OVA-1
  - Qualitative assay of 5 tumor markers
• Approved for pre-operative diagnosis
  - over 18 years
  - pelvic mass prior to surgery when malignancy is not suspected
  - cost ~$650
• NOT to be used as a screening test

Components of OVA-1

- CEA
- CA125
- Apolipoprotein A1
- Transferrin
- Transglycosylase
Scoring

- Algorithm value from 0 - 10
- Cutoff value
  - Premenopausal
    ▪ less than 5 = low risk
    ▪ 5 or greater = high risk
  - Postmenopausal
    ▪ less than 4.4 = low risk
    ▪ 4.4 or greater = high risk

Ova1 Score and Risk of Malignancy

### OVA-1 Sensitivity

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>OVA-1</th>
<th>Ca-125 (II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cancers</td>
<td>161</td>
<td>92%</td>
<td>69%</td>
</tr>
<tr>
<td>All Ov Ca</td>
<td>96</td>
<td>99%</td>
<td>82%</td>
</tr>
<tr>
<td>Early EOC</td>
<td>41</td>
<td>98%</td>
<td>66%</td>
</tr>
<tr>
<td>Premenopausal EOC</td>
<td>14</td>
<td>93%</td>
<td>36%</td>
</tr>
</tbody>
</table>

NPV = negative predictive value, PPV = positive predictive value

### Ova-1 Assessment by Menopausal Status

<table>
<thead>
<tr>
<th></th>
<th>Premenopausal</th>
<th>Postmenopausal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preop</td>
<td>Preop + Ova-1</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>60%</td>
<td>89%</td>
</tr>
<tr>
<td>Specificity</td>
<td>83%</td>
<td>40%</td>
</tr>
<tr>
<td>NPV</td>
<td>90%</td>
<td>94%</td>
</tr>
<tr>
<td>PPV</td>
<td>46%</td>
<td>26%</td>
</tr>
</tbody>
</table>
Ova500 Trial

- 494 pts from 27 centers
- 92% sensitivity
  - 94% in premenopausal women
  - 91% in stage I/II
    ‣ Identified 78/84 women with early ovarian cancer
- NPV = 98%
- 51% specificity


Overa®

- Second generation test
  - Replaced 2 markers with HE4 and FSH
- Performance (testing OV500 sample)
  - NPP = 97.7%
  - Sensitivity = 93.5%
  - Specificity
    ‣ Alone = 69.1% (277/401)
    ‣ With clinical impression = 64.8% (260/401)
- PPV
  ‣ Alone = 40.4% (84/208)
  ‣ With clinical impression = 37.9% (86/277)
  ‣ Reduces False (+) by ~ 1/3
Laparoscopic Management

When Should you approach a mass laparoscopically?

- Anytime you can remove the mass without excessive risk of spillage or laparotomy
  - MUST carefully document the lack or presence of spillage
  - Should be confident that you will not need a laparotomy
  - If the risk of malignancy is low (pre referral guidelines)
  - You can get the patient in to see a gyn oncologist quickly if the mass is malignant
Laparoscopy with Ovarian Mass DON’Ts

• Don’t rupture mass
• Don’t remove mass without a bag
• Don’t leave a piece of the ovary
• Don’t open if Gynecologic Oncology not available

Predictors of Clinical Outcome in the Management of Laparoscopic Masses

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent (vs no) hysterectomy</td>
<td>13.4</td>
<td>7.5, 23.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prior (vs no) hysterectomy</td>
<td>4.2</td>
<td>2.3, 7.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mass size (1-cm increase)</td>
<td>1.1</td>
<td>1.0, 1.2</td>
<td>.01</td>
</tr>
<tr>
<td>Prior (vs no) abdominal surgery</td>
<td>1.3</td>
<td>1.1, 1.7</td>
<td>.006</td>
</tr>
<tr>
<td>Presence/absence of comorbidity</td>
<td>2.0</td>
<td>1.2, 3.4</td>
<td>.007</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent (vs no) hysterectomy</td>
<td>2.9</td>
<td>1.2, 7.1</td>
<td>.01</td>
</tr>
<tr>
<td>Mass size (1-cm increase)</td>
<td>0.80</td>
<td>0.67, 1.05</td>
<td>.01</td>
</tr>
</tbody>
</table>

Overall Rate of Rupture = 25%
Conversion Rate = 25%

Randomized Trials of Laparotomy vs. Laparoscopy for Pelvic Masses

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>OR Time (min)</th>
<th>Rupture*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scope</td>
<td>Open</td>
</tr>
<tr>
<td>Fanfani</td>
<td>2004</td>
<td>100</td>
<td>72</td>
</tr>
<tr>
<td>Yuen</td>
<td>1997</td>
<td>102</td>
<td>59</td>
</tr>
<tr>
<td>Deckardt</td>
<td>1994</td>
<td>192</td>
<td>97</td>
</tr>
</tbody>
</table>

*Rupture rate for Fanfani excluded endometrosis

Germ Cell Tumors

- All germ cell tumors will require treatment except
  - Stage IA Dysgerminoma
    - 30% recurrence rate but salvage rate very high
  - Stage IA grade 1 Immature Teratoma
- Rupture does not change number of cycles of chemotherapy given
- The tumors CAN be confused with epithelial tumors!!! (especially in the middle of the night)
  - BE CONSERVATIVE IN YOUNG WOMEN!
### Effect of Surgical Rupture on Prognosis in Stage I Ovarian Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>% Ruptured</th>
<th>Comments</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sevelda, P 1989</td>
<td>60</td>
<td>N.S.</td>
<td>All staged</td>
<td>Treated with WART</td>
</tr>
<tr>
<td>Dembo, A 1990</td>
<td>100</td>
<td>24%</td>
<td>Not staged</td>
<td>Rupture rate higher for Gr2/3</td>
</tr>
<tr>
<td>de la Cuesta, RS 1994</td>
<td>56</td>
<td>35%</td>
<td>Not staged</td>
<td>Only 35% ruptured got chemo</td>
</tr>
<tr>
<td>Kodama, S 1997</td>
<td>181</td>
<td>25%</td>
<td>Incompletely staged in 75%</td>
<td>Rupture significant in univariate but not multivariate analysis</td>
</tr>
<tr>
<td>Mizuno, M 2003</td>
<td>214</td>
<td>35%</td>
<td>Most not staged</td>
<td>Difference in ICs only in mucinous and endometrioid</td>
</tr>
<tr>
<td>Bakkum-Gamez, JN 2009</td>
<td>161</td>
<td>24%</td>
<td>All staged</td>
<td>Univariate higher RR with rupture</td>
</tr>
</tbody>
</table>

### 2014 FIGO Staging System for Ovarian Cancer

#### STAGE I: Tumor confined to ovaries

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>IA</td>
</tr>
<tr>
<td>IB</td>
<td>IB</td>
</tr>
<tr>
<td>IC</td>
<td>IC1</td>
</tr>
<tr>
<td></td>
<td>IC2</td>
</tr>
<tr>
<td></td>
<td>IC3</td>
</tr>
</tbody>
</table>

- **IA**: Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings/ascites.
- **IB**: Tumor involves both ovaries otherwise like IA.
- **IC**: Tumor involves 1 or both ovaries with any of the following: capsule rupture, tumor on surface, positive washings/ascites.

- **IA**: Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings.
- **IB**: Tumor involves both ovaries otherwise like IA.
- **IC1**: Surgical spill
- **IC2**: Capsule rupture before surgery or tumor on ovarian surface.
- **IC3**: Malignant cells in the ascites or peritoneal washings.
Summary of Risk: Meta-Analysis

• IC3 is worse than IC1
• HR 1.47 (1.01 - 2.14)

• IC1 is worse than IA
• HR 2.41 (1.74 - 3.33)
• IC1 is no different than IA if patients are completely staged and receive chemotherapy
• HR 1.49 (0.45-4.95)

Survival in Stage I Granulosa Cell Tumor with and without Rupture

Non-ruptured (n = 127)

Ruptured (n = 42)

P = 0.0001 in Multivariate analysis

Bjorkholm E, Gynecol Oncol 11:261, 1981

Tumor Rupture

• No convincing evidence that tumor rupture changes prognosis in epithelial and germ cell tumors
  — May change stage
  — May change treatment recommendation for chemotherapy in low grade malignancies
    — New bulletin states emphatically that risk is higher
• May change outcome in granulosa cell tumors
• No conclusive evidence that the risk of rupture is significantly higher with laparoscopy
  — Surgical morbidity is definitely lower
Atypically Proliferating Tumor of Uncertain Malignant Potential
(Borderline Tumors)

Overview of Conservative Surgery
Ovarian Borderline Tumors

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>2496</td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>140</td>
<td>5.6%</td>
</tr>
<tr>
<td>Death</td>
<td>5</td>
<td>0.2%</td>
</tr>
<tr>
<td>Fertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desire</td>
<td>222</td>
<td></td>
</tr>
<tr>
<td>Conceive</td>
<td>132</td>
<td>59%</td>
</tr>
</tbody>
</table>
Risk of Recurrence of Borderline Tumors by Approach and Surgery

Take Home Message for Borderline Ovarian Tumors

- Recurrence rate is higher after cystectomy compared to oophorectomy
  - risk of rupture higher with cystectomy
    - risk of recurrence higher after rupture
  - Most recurrences are borderline
  - Surgery should be guided by
    - size of tumor
    - appearance of contralateral ovary
    - patient wishes
- Staging surgery may be prognostic but does not appear to be therapeutic
  - Omentectomy optimal
  - Nodal Dissection not necessary
Conservative Management of Ovarian Cancer

Data on Conservative Therapy for Early Ovarian Cancer (<40 yo)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Total n</th>
<th>Conservative Surgery n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>39</td>
<td>24</td>
<td>62%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>13</td>
<td>8</td>
<td>61%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>7</td>
<td>4</td>
<td>57%</td>
</tr>
<tr>
<td>IB</td>
<td>5</td>
<td>1</td>
<td>20%</td>
</tr>
<tr>
<td>IC</td>
<td>35</td>
<td>19</td>
<td>54%</td>
</tr>
<tr>
<td></td>
<td>99</td>
<td>56</td>
<td>56%</td>
</tr>
</tbody>
</table>

Recurrence after Conservative Therapy for Early Ovarian Cancer

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Conservative</th>
<th>Radical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
</tr>
<tr>
<td>Sage IA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>1/24</td>
<td>8%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>1/8</td>
<td>1/5</td>
</tr>
<tr>
<td>Grade 3</td>
<td>1/4</td>
<td></td>
</tr>
<tr>
<td>Stage IB</td>
<td>0/1</td>
<td>1/4</td>
</tr>
<tr>
<td>Stage IC</td>
<td>0/19</td>
<td>2/16</td>
</tr>
<tr>
<td>Total</td>
<td>3/56</td>
<td>5%</td>
</tr>
</tbody>
</table>


Data on Conservative Therapy for Early Ovarian Cancer

<table>
<thead>
<tr>
<th>Reproductive Status</th>
<th>No. Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>No attempt at conception</td>
<td>39</td>
</tr>
<tr>
<td>Attempt at conception</td>
<td>17</td>
</tr>
<tr>
<td>Problem-free</td>
<td>17</td>
</tr>
<tr>
<td>Failure</td>
<td>0</td>
</tr>
</tbody>
</table>

NCCN Guidelines for Ovarian Cancer

- In stage I disease minimally invasive surgery can be considered
  - should be performed by experienced gyn oncologists
  - Adequate para-aortic nodal sampling required

- For patients with apparent early stage disease (germ cell, LMP, sex cord stromal tumors, and early ovarian cancer) can be treated by USO and comprehensive surgical staging

- Primary invasive mucinous tumors of the ovary are uncommon, thus the upper and lower GI tract should be examined to r/o an occult GI primary with ovarian metastases
  - Appendectomy should be performed in all mucinous tumors and considered in all patients with epithelial malignancies due to the frequent occult involvement of the appendix

Removal of the Mass

By three methods we may learn wisdom: First, by reflection, which is noblest; Second, by imitation, which is easiest; and third by experience, which is the bitterest.

-Confucius
Spleen Bags

Spleen Bag Introducer
12 cm Complex Mass in a Postmenopausal Woman

Anchor Bag
18 cm Complex Pelvic Mass

Large Containment Bag
Large Pelvic Mass in a 28 YO Woman
Large Pelvic Mass in a 28 YO Woman

Hand Assisted Access
Port Placement for Very Large Mass

8 cm Hand Assist Port
After Right Salpingo-oophorectomy

Post-op
“There is nothing like a challenge to bring out the best in man.”
- Sir Sean Connery
Can you just aspirate a simple cyst?

- Can be done if very low risk
  - Especially if high risk surgery
- Recurrence rate
  - Nikolaou 2014
    - 44% premenopausal
    - 25% postmenopausal
  - Garcia-Tejedor 2015
    - 39%
- Minimally invasive excision preferable