Surgery in Gynecologic Cancers

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6 Week Course Agenda

I. Introduction to Women’s Cancers
II. Genetics of Gynecologic Cancers
III. Gynecologic Cancer Surgery
IV. Gynecologic Cancer Prevention
V. Gynecologic Cancer Treatment
VI. Sexual Health & Survivorship

Surgical Advances

Preoperative Risk Assessment
American Society of Anesthesiologists Classification

ASA Classification
1. Healthy
2. Mild systemic disease – no functional limitation
3. Severe systemic disease – definite functional limitation
4. Severe life threatening systemic disease that is constant threat to life
5. Moribund, unlikely to survive 24 hours

Increasing ASA associated with longer operative time and hospital stay, increased blood loss, higher likelihood of postoperative mechanical ventilation, higher rate of wound infection and bowel anastomotic leak.
Timed Up and Go Test (TUGT) Screening Tool for Predicting 30-Day Morbidity

- Begin timing
- Rise from standard arm chair
- Walk to line on floor (~10 feet away)
- Turn and return to chair
- Sit in chair
- End timing

10 seconds or less indicate normal mobility
>20 seconds means patient needs assistance and is fall risk

Preoperative Testing

- All patients
  - Complete blood count
  - Serum electrolytes
  - Chest radiograph
- Based on personal history and physical findings
  - Coagulation studies
  - EKG
  - Echocardiogram and/or stress test
  - Pulmonary function tests
  - Urinalysis

Preoperative Preparation

- Nutritional supplementation
  - Albumin < 3
  - Anergy to skin testing
  - Transferrin < 200
  - Total lymphocytes <1200
- Antibiotic prophylaxis
  - Cefazolin
- Thromboembolic prophylaxis
  - Low molecular weight heparin (Lovenox) 40 mg once a day
  - Pneumatic compression devices

Type of Incision in Open Surgery

- Midline
- Pfannenstiel
Surgical Staging in Early Disease

- Peritoneal cytology
- Peritoneal biopsies
- Pelvic and para-aortic node dissection
- Omentectomy
- Possible appendectomy

Lymphatic spread in 5-20% ~20% upstaged

Pelvic Node Dissection

Additional Biopsies

Appendectomy Peritoneal biopsies

Serous Borderline Tumors
Surgical Management of Borderline Tumors

- Histology and fertility should be considered with careful intraoperative exploration
  - Pelvic washings
  - Biopsies of omentum & peritoneum
  - Appendectomy if mucinous

- Recurrence rate higher after cystectomy (12-58%) than oophorectomy (0-20%)
  - Recurrence in the form of invasive disease <1% for early stage disease
  - Only 15% of unilateral tumors associated with extra-ovarian disease if no other suspicious peritoneal lesions or micropapillary pattern found

Fischerova D et al, Oncologist 2012

Mucinous Borderline Tumor

Frozen Section of Tumor

Frozen section of borderline tumors changes on final pathology 11-30%

Simple Hysterectomy

Frozen section of borderline tumors changes on final pathology 11-30%
Radical Hysterectomy

A hysterectomy removes the uterus and may also remove the cervix (total) and the vagina (radical).

Implications of Hysterectomy

- Generally, frequency of sexual activity increases and problems with sexual functioning decrease.
- Alters ovarian function over the long-term, even if the ovaries are conserved.
- Associated with a risk of subsequent surgery for pelvic organ prolapse and urinary stress incontinence.

Ovarian Cancer

Advances in imaging and treatment of ovarian cancer have improved outcomes. However, ovarian cancer is often diagnosed in advanced stages, making early detection and effective treatment crucial.

Advanced Ovarian Cancer

Early detection and effective treatment are crucial for improving outcomes in ovarian cancer.
First Line Therapy?

Surgery with maximum cytoreduction effort

Platinum + Taxane Chemotherapy


- Reduction in tumor mass
- Shorter chemotherapy exposure with less development of drug resistance
- Improved tumor perfusion
- Fewer non-active (G0) cells
- Enhanced immunological competence (smaller tumors may be more amenable to control by host defenses)

Each chemotherapy course produces 90% cell kill

Cytoreductive Surgery in Ovarian Cancer

Cytoreductive Surgery – Survival Benefit

- Significant survival advantage for women optimally cytoreduced
- 6885 patients with Stage III-IV ovarian carcinoma (6,885 patients) identified in MEDLINE (1989-98)
- Each 10% increase in maximal cytoreduction associated with a 5.5% increase in median survival time

Maximal Primary Cytoreduction

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Residual Disease</th>
<th>Patients</th>
<th>Median survival</th>
<th>5-Yr OS (%)</th>
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<tr>
<td>Hoskins</td>
<td>1994</td>
<td>No gross</td>
<td>41</td>
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<td>60</td>
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<td>&gt;1 cm ≤2 cm</td>
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<tr>
<td></td>
<td></td>
<td>&gt;2 cm</td>
<td>65</td>
<td></td>
<td>&lt;20</td>
</tr>
<tr>
<td>Chi</td>
<td>2006</td>
<td>No gross</td>
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<td></td>
<td>106</td>
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<td></td>
<td></td>
<td>≤0.5 cm</td>
<td>70</td>
<td></td>
<td>66</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;0.5 cm ≤1 cm</td>
<td>99</td>
<td></td>
<td>48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥1 cm ≤2 cm</td>
<td>53</td>
<td></td>
<td>33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2 cm</td>
<td>176</td>
<td></td>
<td>54</td>
</tr>
<tr>
<td>Du Bois</td>
<td>2010</td>
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<td>1,046</td>
<td></td>
<td>99.1</td>
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<td></td>
<td></td>
<td></td>
<td>975</td>
<td></td>
<td>36.2</td>
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<td></td>
<td></td>
<td>1,105</td>
<td></td>
<td>29.6</td>
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</table>

Bristow et al, J Clin Oncol 2002

Shih et al, J Gynecol Oncol 2010
Intraperitoneal Chemotherapy

Evidence of Advanced Disease

Upper Abdominal Disease

Upper Abdominal Procedures in Advanced Ovarian Cancer

- 2655 patients enrolled in GOG 182 who has OCRS
  - 590 underwent upper abdominal procedures
    - 13.1% diaphragm
    - 4.2% liver
    - 4% splenectomies
    - 0.5% pancreatectomies
    - 0.2% porta hepatis

Rodriguez et al, Gynecol Oncol 2013
Bowel mesentery with several small implants

Intestinal Surgery in Tumor Debulking

- Diverting Ileostomy
- Rectosigmoid Resection

Surgical Complications in Ovarian Cytoreduction

- Bowel resection necessary in 19-54% of cases
- En bloc resection/modified posterior extenteration
  - Operative mortality of <8% (ASA & age associated with 3-month mortality)
  - Colorectal anastomotic leak in 4%
    - Highest risk if <7 cm from anal verge
    - 21% leak rate with albumin <3
    - Protective intestinal diversion may be advisable in very low or technically low anastomoses
  - Wound complications 6-34%, particularly with albumin<3
    - 87% require blood transfusion
- Prolonged ileus in up to 40%
  - 25% in those with tumor debulking without bowel resection
- Pelvic drains may be helpful in prevention of fluid collections, reaccumulation of large volume ascites, infected hematomas, urinomas

Postoperative Complications

- Wound Infection
- Deep Vein Thrombosis

*Barakat et al, Principles and Practice of Gyn Onc 2013*
Postoperative Complications

- Ureteral Stent Placement
- Anastomotic Leak

Complications in Upper Abdominal Surgery

- Perioperative morbidity in 20% who require full thickness diaphragm resections
  - Pleural effusions develop in 9-64% following diaphragm peritonectomy or resection
  - Chest tube placement for large resection or effusions or worsening pneumothorax
- Acute complications with splenectomy
  - Hemorrhage, splenic vein thrombosis, arteriovenous fistula, infection
  - Vaccinations for Strep pneumo (most virulent post-splenectomy), H influenza B, meningococcus
- Pancreatic leak or pseudocyst
  - Intraoperative placement of drain
  - Mild enzyme leak has no impact
  - Enzyme leak <3 fold or presence of fevers, pain, leukocytosis requires delay of oral nutrition, antibiotics, possible TPN or octreotide

Emergence of Neoadjuvant Chemotherapy

- Resection of large volume disease leads to expanded drug delivery and decreased somatic mutations that often perpetuate drug resistance
- No available technology or clinical parameters exist that consistently allow physicians to anticipate which patients have unresectable disease
- Further complicated by variability in surgical expertise and perioperative care across institutions

Randomized EORTC-GCG/NCIC-CTG Trial on NACT + IDS Versus PDS

Primary Debulking Surgery

- Interval debulking (not obligatory)
- > 3 x Platinum based CT

Neoadjuvant chemotherapy

- 3 x Platinum based CT
- Interval debulking if no PD
- > 3 x Platinum based CT
**EORTC 2010**

Overall survival

HR for IDS: 0.98 (0.85, 1.14)

-**Properopredictors of Cytoreductive Outcome**

<table>
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<tr>
<th>Predictive Score</th>
<th>Suboptimal Rate</th>
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<tbody>
<tr>
<td>0</td>
<td>5%</td>
</tr>
<tr>
<td>1-2</td>
<td>10%</td>
</tr>
<tr>
<td>3-4</td>
<td>17%</td>
</tr>
<tr>
<td>5-6</td>
<td>34%</td>
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<tr>
<td>7-8</td>
<td>52%</td>
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<tr>
<td>&gt;9</td>
<td>74%</td>
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</tbody>
</table>

**Secondary Tumor Debulking (SCRS)**

- Cochrane review of 1194 women in 9 non-randomized studies
  - Cytoreduction to no visible disease in women with platinum sensitive recurrent ovarian cancer associated with significant improvement in OS

- CALYPSO Trial
  - 975 patient with platinum sensitive recurrent disease
  - Randomized
  - 19% SCRS, 80% chemotherapy alone
  - OS better in those with SCRS (49.9 vs 25.7 mos, p=0.004)
  - 3 year OS 72% in those with no measurable disease

**Identifying Ideal Candidates for SCRS**

- Pooled analysis of 1100 patients found that those with:
  - Longer progression free interval
  - No ascites
  - Localized disease

- Risk models have suggested prognosticators include:
  - Ascites
  - Number and size of implants
  - Performance status
  - Progression free interval
  - Preoperative CA-125 (<250)

1 Al Rawahi et al, Cochrane Database Syst Rev 2013
2 Lee et al, Gynecol Oncol 2015
3 Tian et al, Ann Surg Oncol 2012
Minimally Invasive Surgery

Surgery performed through small incisions
- Quicker recovery
- Less discomfort
- Less infection
- Less scarring
- Less blood loss

Vaginal Hysterectomy
- Removal of uterus & cervix through vagina
- May also remove ovaries & tubes
- May combine with laparoscopy

Laparoscopy
- Vaginal surgery
- Laparoscopy
- Robotic assisted laparoscopy
- Natural orifice transluminal endoscopic surgery (NOTES)
- Single incision laparoscopic surgery (SILS)
LAP2

1996-2005: Randomized study of Stage I-IIA endometrial cancer patients -- 1696 laparoscopy, 920 laparotomy
26% conversion to open (15% visualization)
Laparoscopy with shorter LOS, fewer post-op complications
Less LND performed but no difference in Stages
Median follow-up of 59 mo. HR for recurrence, 1.14 (90% CI 0.92-1.46),
3-year recurrence: 11.4% versus 10.2%
5-year survival: 89.8%

Walker et al, J Clin Oncol 2009
Walker et al, J Clin Oncol 2012

Sentinel Lymph Node Mapping

Robotics—The greatest thing since sliced bread?
Robotic vs laparoscopy

Meta-analysis of 22 studies—3403 robotic/laparoscopic, 1017 robotic/open surgery patients

Robotic vs laparoscopic—robotic with less EBL, fewer conversions to open, but more complications.

Similar operating time, length of stay, lymph node numbers

Robotic vs open—robotic with less EBL, complications, length of stay, but longer operating time

Similar lymph node numbers

Ran et al, PLoS One 2014